

Original Research Article

Histopathological features of prostatic carcinoma in a Southwest tertiary institution in Nigeria

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ABSTRACT

Background: The diagnosis of prostatic adenocarcinoma is often straightforward, in some cases there may be benign lesions that mimic prostatic cancer histologically. This study aimed to describe the morphological features of prostatic carcinoma from laboratory specimens.

Methods: This was a retrospective study using histologically diagnosed cases of prostatic carcinoma from prostatectomy and trucut biopsy specimens. The histological sub-typing of the tumors according to WHO classification scheme of 2003 was done. The tumors were graded and scored using Gleason's scoring scheme revised and modified at the consensus conference of the international society of urological pathology (ISUP), in 2005.

Results: Prostate cancer constituted 18.7% of all malignant tumors and 4.4% of all neoplastic diseases. The majority of cases were small acinar adenocarcinoma 275 (73.7%). Others include pseudo-hyperplastic variant 47 (12.6%), atrophic variant 35 (9.3%), foamy gland carcinoma 16 (4.2%) and signet ring/colloid carcinoma 1(0.2%). More than half were classified as well-differentiated Gleason prognostic group A tumors. There was a statistically significant association between the age of the patient and the Gleason histologic grade and the histologic grade and histologic variant $p < 0.05$.

Conclusions: Prostatic carcinoma was thought to be a malignancy associated with elderly men but people of younger age less than fifty years are now diagnosed with the malignancy. Accurate diagnosis with the right grade and scores will go a long way in the management of the malignancy.

Keywords: Histopathology, Features, Prostatic carcinoma, Nigeria

INTRODUCTION

The most prevalent cancer in males, prostatic adenocarcinoma, is an invasive epithelial tumor made up of prostate gland secretory cells.¹ It was first described by an anatomist, Niccolo Massa in 1536, but was not officially identified as a malignancy until 1853. At that time, prostate cancer was considered a rare disease, due to the shorter life expectancy of the population and poor detection methods.² Since then research interest in prostatic adenocarcinoma has been on the rise.

Male morbidity and mortality are significantly attributed to prostatic diseases. Prostatic adenocarcinoma surpassed lung cancer to become the most common cancer diagnosed in American males in 1990.³ An estimated 220,000 new cases are diagnosed yearly in the United States with about 30,000 dying annually of this malignancy, a figure that is still far lower than the mortality from lung cancer.³ Prostate cancer is largely a disease of elderly men with 75% of cases between 60 to 80 years of age.³ Patients under 50 years of age constitute less than 10%.³ However, research conducted over the

years has shown that the incidence is increasing in patients younger than 50 years old.³

Not only have the screening techniques become more accessible, but they have also enhanced the likelihood of successful patient management. Nonetheless, the condition is becoming more commonplace and causing more cases globally. The advent of screening procedures has been primarily related to an increased prevalence of prostate cancer among African-American males in the United States, which is currently the second most common cause of cancer death. This has allowed for earlier patient discovery.⁴ A study done in Ibadan, Nigeria reviewed male cancer patients recorded in the Ibadan cancer registry to assess the current prevalence of prostate cancer in Nigeria. For comparison, data were broken into two groups: 1980-1988 and 1989-1996. Only the top 10 cancers occurring in both periods were considered initially in this report. However, for emphasis, an analysis of adult male cancers has been done per decade since 1960. The results showed that prostate cancer has become the most common cancer in the Nigerian men constituting 11 percentages of all cancers in males.⁴

Nevertheless, not enough research has been done on the molecular changes of prostatic cancer in our environment, despite the advancements in screening techniques and early identification. This would significantly advance not just the knowledge of the biology behind prostate cancer but also its management, lowering associated morbidity and mortality rates, particularly in our setting. The WHO has estimated that the prevalence of prostate cancer in developing countries is 4% of all male cancers.⁶ There are, however, differing opinions that suggest that the prevalence has been underestimated particularly in Africa.⁵ Interestingly, only a few reports have dealt with the incidence of prostate cancer in Africa.⁵ For example in South Africa, the age-adjusted incidence is 90 cases per 100,000 males while in Zimbabwe, the figure is 35 cases per 100,000 males' cases.⁵

There is a paucity of clinical and epidemiologic data from African populations, and this will need to be remedied in the immediate future as attention is focused on cancer care in Africa.⁸ Prostatic cancer has become the number one cancer in men with increasing incidence and morbidity in black Africans.⁶ Several studies have shown that its incidence and prevalence in black men are in multiples of those from other races.⁷

In our local environment, the diagnosis of prostatic adenocarcinoma relies on a constellation of architectural and cytological features. Although the diagnosis of prostatic adenocarcinoma is straightforward, in some cases there may be benign lesions that mimic prostatic cancer histologically.⁸ In addition, the widespread use of various screening methods has made the diagnosis of early disease possible with pathologists being

increasingly challenged in the diagnosis of small foci of cancer when only a few atypical glands are present, especially in needle biopsies.⁹

The study aimed to describe the morphological features of prostatic carcinoma as seen in the department of morbid anatomy and histopathology, Ladoke Akintola university of technology teaching hospital (LTH), Osogbo, Nigeria.

METHODS

Study design

This was a retrospective study, where all histologically diagnosed cases of prostatic carcinoma from prostatectomy and trucut biopsy specimens received at the histopathological laboratory of the department of morbid anatomy and histopathology of the LTH, Osogbo between January 2005 and December 2014 were selected for the study.

Procedure

The original request forms were retrieved and studied, and essential clinical details including age, and the nature of the specimen submitted were documented. Also, the gross morphological appearance of the lesions in prostatectomy samples was noted for the following variables: the site of the tumor in the prostate gland, the size of the tumor and the number of the accompanying lymph nodes.

The paraffin blocks of all cases were retrieved and fresh sections were cut and stained with hematoxylin and eosin and were examined histologically. The histological subtyping of the tumors according to WHO classification scheme of 2003 was done.¹ The tumors were graded and scored using Gleason's scoring scheme revised and modified at the consensus conference of the ISUP, in 2005. Thus, the tumors were sub-classified into three prognostic groups including group A well-differentiated carcinoma with a Gleason's score of 6 and below as well as a score of 7 (3+4)]; 'pp' B [moderately differentiated with a Gleason score of 7(4+3) and 8] and the group C [with a Gleason score of 9 and 10]. All cases with incomplete data and those with missing blocks (where the archived slides could not be retrieved) were excluded from the study. Cases for which both prostatic biopsies and the prostatectomy specimens were assessed were sought out to avoid the duplication of data. In such cases, only information from the prostatectomy specimen was used.

Data analysis

The data obtained were analyzed for differences in proportion using the statistical package for social sciences (SPSS) version sixteen. Chi-square was used to compare discontinuous variables. The level of statistical

significance was set at $p=0.05$. Ethical approval was obtained from the local ethics committee of the LTH, Osogbo, Osun State, Nigeria.

Ethical approval

Approval was obtained from the ethical and review committee of the LAUTECH teaching hospital Osogbo Osun State Nigeria.

RESULTS

A total of 8,517 neoplastic lesions were received between 2005-2014 out of which 1,987 cases were diagnosed as malignant diseases and 374 cases of prostatic carcinoma were diagnosed. Thus prostatic carcinoma constituted 18.7% of all malignant diseases and 4.4% of all neoplastic disorders during the study period. However, other male malignancies were 300 (15.1%).

There were 159 (40.1%) prostatectomy samples, 221 (59.1%) prostatic biopsies and 3(0.8%) transurethral resection of the prostate (TURP) samples. Surgical intervention was performed on account of benign prostatic hyperplasia (BPH) in 127 cases (35.8%) and carcinoma of the prostate (CAP) in 247 (64.2%).

The patients' ages ranged from 44 to 102 years. The mean age was 71.3 years \pm 2.0 SD. There was a steady rise in the frequency of prostatic carcinoma with each decade from the 5th decade of life up until the 8th decade from where the frequency begins a steady decline. The lowest frequency of cases was seen in patients older than 100 years old with 3 cases (0.8%) while the peak age frequency was in the 71-80-year age group with 142 cases (38.1%). There were 129 and 52 cases in the 61 to 70-year and 51 to 60-year age groups respectively. A total of 271 cases (72.8%) were between the ages of 61 and 80 years. There were only five cases (1.3%) seen in patients younger than 50 years. No cases were recorded below the age of 40 years (Figure 1).

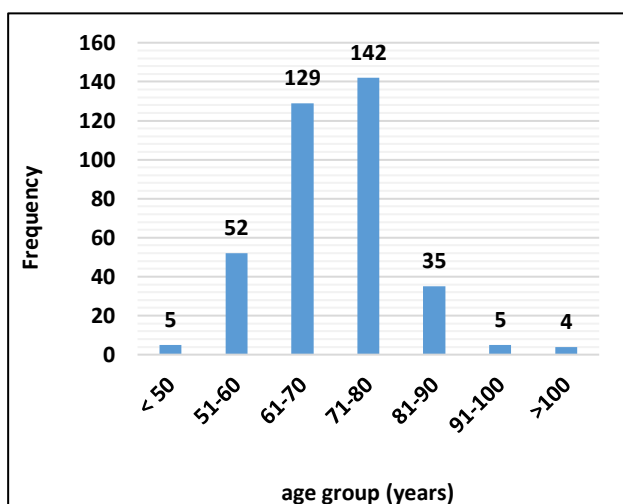


Figure 1: Frequency of patients age with prostatic

carcinoma.

The vast majority of cases were small acinar adenocarcinoma accounting for a total of 275 cases (73.7%). Out of the other less common variants, the pseudo-hyperplastic variant accounted for 47 cases (12.6%) while the atrophic variant accounted for 35 cases (9.3%). There were only 16 cases (4.2%) of foamy gland carcinoma. The least common variant was the signet ring/colloid carcinoma which accounted for only 1 case (0.2%). There were no cases of sarcomatoid or large duct carcinoma (Figure 2).

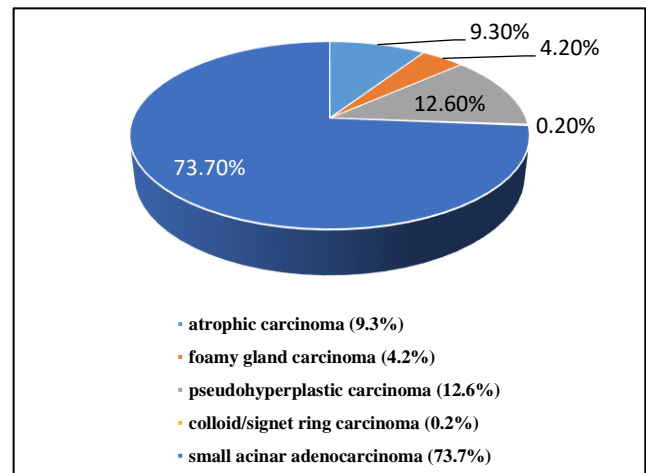


Figure 2: Frequency of histological variants of prostatic carcinoma.

More than half of all cases of prostatic carcinoma were classified as well-differentiated Gleason prognostic group A tumors [with either a Gleason score of less than 6 or 7 (3+4)], accounting for a total of 204 cases (54.8%). Moderately differentiated carcinomas accounted for 104 cases (28.0%) while poorly differentiated tumors accounted for only 64 cases (17.2%).

A comparison of the histologic grade with the patient's age showed that all cases of prostatic carcinoma seen in patients younger than 50 years were poorly differentiated accounting for 7.8% of all such poorly differentiated tumors. Similarly, all cases of prostatic carcinoma seen in patients older than 100 years were poorly differentiated carcinomas and these accounted for 6.3% of all such tumours. The highest frequency of poorly differentiated tumours was seen in the 51-60-year age group with 20 cases (31.3%) while the least frequently affected age group was the 91-100-year age group which accounted for only 2 cases (3.1%).

In contrast to this, the 71-80-year age group accounted for the highest frequency of well-differentiated tumors with a total of 97 cases (47.5%). The 61-70-year age group also had a high frequency of well-differentiated tumors accounting for 67 cases (32.8%). The highest frequency of moderately differentiated tumours was in the 61-70-year age group which accounted for 51 cases

(49.0%). There were no cases of either well-differentiated or moderately differentiated tumors in individuals younger than 50 years or older than 100 years.

There was a statistically significant association between the age of the patient and the Gleason histologic grade with a p value less than 0.05.

The vast majority of each variant of prostatic carcinoma were of the well-differentiated type. And the atrophic and pseudo-hypertrophic variants, 80.0% and 89.4%

respectively were well-differentiated carcinomas. In contrast, well-differentiated carcinomas constituted only 62.5% and 45.1% of foamy gland and acinar adenocarcinomas respectively. The only case of colloid/signet ring carcinoma was a moderately differentiated carcinoma. Similarly, all cases of poorly differentiated carcinoma were of the acinar adenocarcinoma variant. The association between the histologic grade and histologic variant was found to be statistically significant with a p value less than 0.05 (Chi-square=470.634) (Table 2).

Table 1: Gleason histological grading of prostatic carcinoma.

Gleason prognostic group	Age group (in years)							Total (%)
	<50 (%)	51-60 (%)	61-70 (%)	71-80 (%)	81-90 (%)	91-100 (%)	>100 (%)	
A	-	23 (11.3)	67 (32.8)	97 (47.5)	15 (7.4)	2 (0.9)	-	204 (100)
B	-	9 (8.7)	51 (49.0)	33 (31.7)	10 (9.6)	1 (0.9)	-	104 (100)
C	5 (7.8)	20 (31.3)	11 (17.2)	12 (18.8)	10 (15.6)	2 (3.1)	4 (6.3)	64 (100)
Total	5 (1.3)	52 (14.0)	129 (34.7)	142 (38.2)	35 (9.4)	5 (1.3)	4 (1.1)	372 (100)

(p<0.05; chi square=404.699).

Table 2: Gleason histologic grade and histologic variants of prostatic carcinoma.

Gleason prognostic group	Histologic variants					Total (%)
	Acinar (%)	Atrophic (%)	Pseudo-hyperplastic (%)	Foamy gland (%)	Colloid/ signet ring (%)	
A	124 (45.1)	28 (80.0)	42 (89.4)	10 (62.5)	-	204 (100)
B	87 (31.6)	7 (20.0)	5 (10.6)	6 (37.5)	1 (100)	104 (100)
C	64 (23.3)	-	-	-	-	64 (100)
Total	275 (100)	35 (100)	47 (100)	16 (100)	1 (100)	372 (100)

(p<0.05; Chi square=470.634).

High-grade prostatic intraepithelial neoplasia (HGPIN) was associated histologically with prostatic carcinoma in only 111 (29.9%). The highest frequency of cases was seen in the 71-80-year age group with 61 cases (55%) followed by the 81-90-year age group with 25 cases (22.5%).

There was a steady rise in the frequency of cases up to the 61-70-year age group from where there is a very sharp rise in the frequency of HGPIN to the mode. From here the frequency gradually falls reaching the lowest frequency in patients older than 100 years old with only 2 cases (1.8%). The mean age of cases was 65 years \pm 3.5SD (Figure 3).

Overall, a total of 111 cases (29.9%) of prostatic carcinoma were associated with the presence, histologically, of high-grade prostatic intraepithelial neoplasia (HGPIN). Out of these 111 cases, 60 (29.4%) were well differentiated prostatic carcinomas while only 20 cases (19.2%) of moderately differentiated prostatic carcinoma were associated with HGPIN. For poorly differentiated carcinomas, however, 31 cases (48.4%) were associated with HGPIN. The association between the presence of high-grade prostatic intraepithelial neoplasia and the histologic grade of the tumor was found

to be statistically significant with a p=0.04 (Chi-square=8.096) (Figure 4).

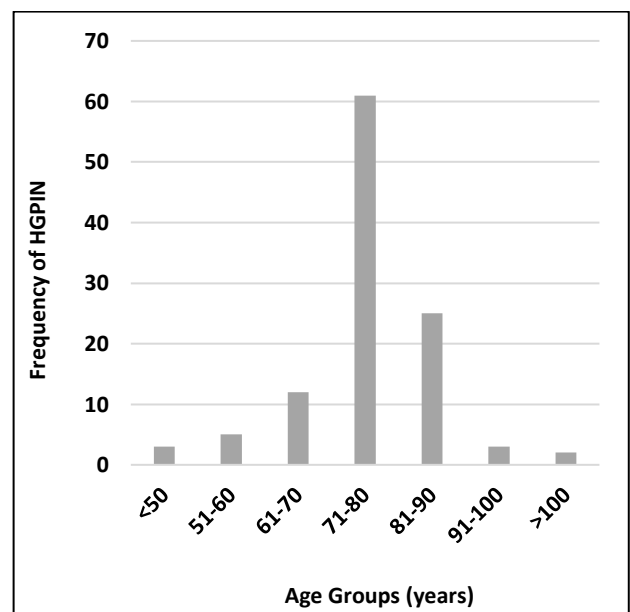


Figure 3: Patients' age and frequency of high-grade prostatic intraepithelial neoplasia.

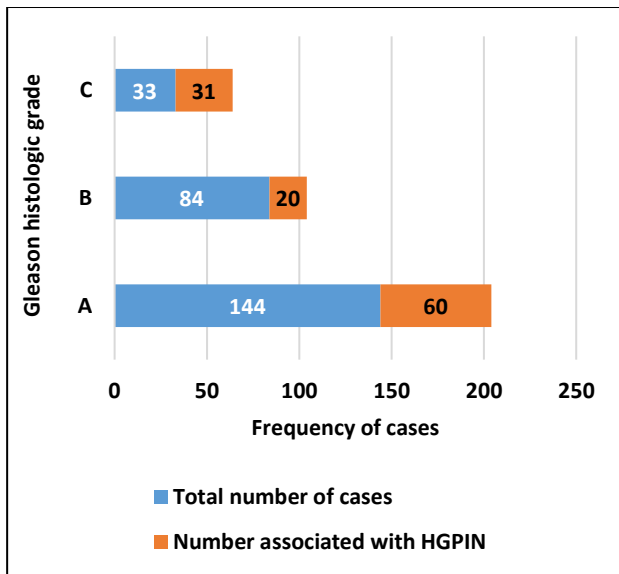


Figure 4: Gleason histologic grade and high-grade prostatic intraepithelial neoplasia, ($p=0.04$).

DISCUSSION

Globally, prostate cancer has become the most common cancer in men with an ever-increasing incidence and mortality in black African ancestry.⁶ In fact, a 2012 report by GLOBOCAN showed prostate cancer incidence and mortality rates in Africans to be 23.2 and 17.0 per 100,000 respectively.¹⁰ This fact is supported by our study which showed that prostate cancer constituted 18.7% of all malignant tumors and 4.4% of all neoplastic diseases diagnosed in our hospital. Thus, prostatic carcinoma contributes significantly to the health burden, not only in our local environment but the entire nation at large.

It is well-recognized that age is a very important independent risk factor in the development of prostatic carcinoma. The disease is extremely rare before the age of 40 years but the risk increases greatly with age with more than 60% of cases diagnosed over the age of 65 years.¹¹ According to this study, the patients' ages ranged from 44 to 100 years while the mean age was 71.3 years ± 2.0 SD. The peak age incidence was found to be in the 71-80-year age group. The mean age according to this study, however, contrasts sharply with that from studies done by Oluwale et al in Lokoja, Eke et al in Port Harcourt, Osegbe in Lagos and Mohammed et al in Jos and Kano, where the mean age for patients with prostatic carcinoma was found to be 60 years.¹²⁻¹⁵ The reason for this disparity is unknown although it could possibly be due to the fact that the patients in this study presented late to the hospital. Nevertheless, this disparity may actually suggest local geographic differences in the age of occurrence of prostatic carcinoma which may be due to differences in the biological behavior of prostatic carcinoma in our local environment.

The earliest age at presentation in this study was in the

fifth decade, precisely in a patient aged 44 years. This also sharply contrasts with various studies from different parts of Nigeria and Africa where the earliest presenting age was in the seventh decade.¹³⁻¹⁵ The mean age in our study, however, is similar to that in a study carried out in the United Kingdom which put the mean age at 69 years ± 2.0 SD with a steady rise in the incidence of prostatic carcinoma from 50-54 years to a peak at 75-79 years followed by a steep decline by 80-84 years.¹¹

Similarly, our study revealed a steady rise in the incidence of prostatic carcinoma to a peak at 71-80 years followed by a sharp decline in individuals older than 80 years. This sharp decline could be due to the short life expectancy in our country which has resulted in a marked reduction in the number of individuals over the age of 80 years as suggested by the Nigerian population structure.

According to this study, acinar adenocarcinoma was the most common variant of prostatic carcinoma as previously reported from other parts of Nigeria.¹²⁻¹⁵ Our study also showed that among the other variants of prostatic carcinoma, the pseudo-hypertrophic and atrophic variants were the most common while the colloid/signet ring and the sarcomatoid variants were extremely rare. These findings are similar to a study done by Levi et al in the USA.¹⁶ Similar findings have also been reported in a study done at Washington university school of medicine, USA by Peter A Humphrey which showed that colloid/signet ring carcinomas constituted 0.3% of all prostatic carcinoma as compared to 0.2% in our study.¹⁷ It is important however to recognize these variants because of the diagnostic errors that may be associated with them since many of them are associated with deceptively bland microscopic features.

This study showed that, overall, a little over half of all cases of prostatic carcinoma were well-differentiated tumors with only 28.0% and 17.2% being moderately differentiated and poorly differentiated tumors respectively. This is similar to other studies.^{14,15} But in contrast to those from Lokoja and Port Harcourt where poorly differentiated carcinomas were most common.^{12,13} This probably suggests that there are geographical variations in the biological behavior of prostatic carcinoma in our country. The fact that a large proportion of these tumors are well differentiated suggests that screening techniques and emphasis on early diagnosis may play significant roles in improving the poor prognosis typically associated with prostatic carcinoma.

Our study also showed that moderately and poor differentiated tumors were more commonly encountered in younger patients with 57.7% and 56.3% of each tumor grade respectively occurring in patients younger than 70 years old. Only poorly differentiated tumors were encountered in patients younger than 50 years as well as in those older than 100 years old. This is similar to findings from various reports in and outside Nigeria some of which have linked androgen receptor repeat

polymorphism of CAG and CGN microsatellites to a relatively high risk of advanced prostatic cancer and diagnosis at younger age.¹⁸ It is widely known that one of the important characteristics of prostatic carcinoma is its ability to de-differentiate to higher grades within the same tumor, a feature more commonly associated with younger age at presentation.¹⁹ This also is in tandem with a study done by Claudia et al which showed that prostatic carcinoma occurring in young men of less than or equal to 55 years differs from that occurring in older men in several ways, including the unexpected poor prognosis of advanced early onset and rapidly growing and more aggressive tumor.²⁰

High-grade prostatic intraepithelial neoplasia (HGPIN) was seen in 111 (29.9%) of all the prostatic carcinoma cases in this study. HGPIN was, however, associated with all the histologic grades. Its frequency was also observed to correspond fairly well with the age distribution of prostatic carcinoma. These probably suggest that HGPIN is a true precursor of prostatic carcinoma irrespective of the histologic variant.²¹ The fact that HGPIN was also associated with all Gleason prognostic groups of prostatic carcinoma seems to buttress this point further. This suggests that prostatic carcinoma is a progressive disease that in many instances will contain tumour cell populations at different stages of differentiation.

The ability of tumor cells to undergo dedifferentiation may also partly explain this observation. The presence of HGPIN in prostatic biopsies negative for prostatic carcinoma has been significantly associated with a high probability of the presence of prostatic carcinoma in other parts of the prostate gland. Thus, such patients are typically either re-biopsied or placed on long-term follow-up. It, therefore, becomes imperative to look out for and report this lesion in prostatic biopsies. Its presence in a prostatectomy or TURP specimen should also warrant the submission of more samples or indeed the entire specimen especially since prostatic carcinoma may be detected incidentally in 8-10% of such samples.²²

Limitations

Although the study was a nine-year review with a significant sample size, it was however carried out in a single southwest center. A multicentre study in the future may be required for collaboration of findings to improve the generalisability potential.

CONCLUSION

Prostatic carcinoma is on the increase and it is now seen amongst younger men. It was thought that it is a malignancy associated with elderly men but people of younger age of less than fifty years are now diagnosed with the malignancy. Accurate diagnosis with the right grade and scores will go a long way in the management of the malignancy.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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