

ORIGINAL ARTICLE

The Histologic Pattern of Prostate Specimens in Lagos State University Teaching Hospital Lagos and their Correlation with Serum Total Prostate Specific Antigen

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INTRODUCTION

Prostate gland in adult men measures approximately 4.0 x 3.0 x 2.0 cm and is roughly the size and shape of a chestnut. It lies beneath the bladder and above the urogenital diaphragm.¹ Histologically, the prostate has a fibromuscular stroma within which is embedded prostate glands.² The three pathologic lesions that affect prostate

gland frequently are prostatitis, benign prostatic hyperplasia (BPH) and prostatic carcinoma.²

Prostatitis is an inflammation of the prostate gland. Just like other forms of inflammation in the body, it can be seen as an appropriate response of the body to infection, but it can also occur in absence of infection.³ Acute

ABSTRACT

Background: Prostate carcinoma (PCA) is one of the most common causes of cancer death in men. Prostate glands have three major pathologic diseases which includes prostatitis, benign prostatic hyperplasia and carcinoma. The aim of this study is to determine the hospital prevalence of the prostate gland diseases and to determine their relationship with the total prostate specific antigen (tPSA) in LASUTH, Nigeria.

Methodology: This is a four-year retrospective study of prostate samples submitted to our department in Lagos State University Teaching Hospital, Ikeja between 1st January, 2010 and 31st December 2013. All slides were retrieved and reviewed; broken and lost slides were re-cut from the tissue blocks, and tPSA value was determined using chemiluminescent immunometric method in an auto-analyser machine.

Results: A total of 394 surgical prostatic specimens were received which represents a percentage of 3.97% of total biopsy. Only 230 specimens had tPSA done and were included in the study. The age range was 48-91 years with a mean age of 67.0±7.3 years. Benign prostatic hyperplasia (BPH) had the highest prevalence (65.7%), followed by PCA (27.4%). Isolated BPH had a mean tPSA value of 16.0±12.0ng/ml and isolated PCA 66.4±54.0 ng/ml.

Conclusion: BPH was found to be the commonest prostate gland disease followed by the prostatic carcinoma. Prostatic adenocarcinoma was the most frequent carcinoma of the prostate. A tPSA value greater than 84.0 ng/ml are seen only in prostate carcinoma patients.

Keywords: Adenocarcinoma, Cancer death in men, Prostate biopsy, Prostatitis

prostatitis presents with fever, chills and dysuria, although the chronic type is commoner. BPH consists of variable sized nodules that are soft to firm, yellow-gray tissue that bulges from the cut surface on grossing.⁴ Microscopically, the hallmark of BPH is nodularity. In a surgical biopsy study by Iyare on the diseases of the prostate among the Igbos in South-East Nigeria, he found out that 69.5% were BPH.⁵

Prostate adenocarcinoma originates from the acini and ducts of the prostate glands.⁶ Most prostate carcinomas arise in the peripheral zone.⁷ The malignant cells seen in prostatic carcinoma have cytological features of nuclear and nucleolar enlargement as well as prominent nucleoli.⁸ Transitional cell carcinoma of the prostate can arise from the transitional epithelium of the distal prostatic ducts.⁹ This variant comprises less than 2% of all prostatic carcinomas.⁶

High-grade prostate intraepithelial neoplasia (HGPIN) is an abnormal growth within the prostatic ducts, ductules, and large acini without stromal invasion.¹⁰ Singh *et al.* showed 4.2% had isolated HGPIN in their study with a median age of 68 years amongst the patients.¹¹

Currently, conventional use of the term 'PIN' without qualification is referred to as only high-grade PIN.¹² It is characterized by proliferation of epithelial cells with significant cytological atypia within the prostate glands. These cells exhibit high nuclear: cytoplasmic ratio and prominent nucleoli. Unlike prostate carcinoma, basal cell layer is retained and is also often discontinuous in HGPIN.¹³

Prostate specific antigen (PSA) is produced by the epithelial cells of the ducts and acini of the normal, hyperplastic, inflammatory and neoplastic tissues of the prostate.¹⁴ It is a tumour marker of prostate adenocarcinoma and is used in the detection, and management of prostate cancer.¹⁵ Total PSA (tPSA) is elevated beyond the arbitrary cut-off point of 4.0ng/ml in the majority of patients being

screened for prostate cancer.¹⁶ Cavit *et al.* found that of the total of 214 patients they analyzed, the mean tPSA value was 15.82 ± 22.34 ng/ml. They also found out that the mean value of tPSA of patients with isolated BPH was 10.36 ± 8.98 ng/ml while BPH co-existing with prostatitis had 13.0 ± 11.87 ng/ml.¹⁷

The aim of this paper is to determine the hospital prevalence of different types of prostate diseases and to determine the level of tPSA seen in prostate diseases in LASUTH, Nigeria.

METHODOLOGY

This is a four year hospital-based retrospective study of all prostatectomies, trucut biopsies and transurethral resection of prostate (TURP) specimens that were submitted to the Mayo Heights Laboratories, in the Department of the Pathology and Forensic Medicine, Lagos State University Teaching Hospital (LASUTH), Nigeria between 1st January 2010 and 31st December 2013.

Total prostate specific antigen (tPSA) was determined by using chemiluminescent immunometric method in an automatic analyzer machine in Bola Tinubu Diagnostic Laboratory LASUTH, Nigeria. Pre-treatment serum tPSA values were used in this study.

All histologically diagnosed prostate specimens were retrieved and the slides were reevaluated. This is because some of the slides were not previously reported by the authors. All lost and broken slides were re-cut from formalin-fixed paraffin blocks and were prepared using routine histological techniques. There were no discrepancies seen in the microscopic diagnosis. Pre-treatment serum total PSA results of the patients, and patients' biodata were obtained from laboratory registers and patients folders. Analysis of data collected was carried out and the use of Statistical Package for Social Science (SPSS) software version 19. The

results were presented in tables and bar chart. The level of the significance was set at $p < 0.05$ in the test for significance.

RESULT

A total of 394 surgical prostatic specimens were received which represents 3.97% of all specimens submitted to the laboratory in the hospital. Only 230 surgical prostatic specimens had the PSA done and hence are suitable for this study.

The age range of the patients was 48-91 years with mean age of 67.0 ± 7.3 years. Table 1 shows the most common age group as 60-69 years and accounted for 63.0% of all the subjects. Patients aged ≥ 80 years accounted for 3.9% while those cases within the 40-49 years were the least (2.6%). There was significant difference among age groups seen in prostatic gland diseases $p < 0.001$ (Table 1). The age group 60-69 years accounted for 80% of BPH while age group 70-79 years constituted over half (54%) of those with prostatic adenocarcinoma (PCA).

Table 2 shows the average age of prostatic disease seen in LASUTH. There is increasing mean age from prostatitis to PCA.

BPH had the highest prevalence seen in prostate gland diseases which accounted for 65.7% (Figure 1), followed by PCA which was the second most common prostate disease with prevalence of 27.4%.

Table 3 shows that fifty three patients (84.1%) out of all the prostatic carcinoma ($n=63$) were isolated prostatic carcinoma (PCA*), while PCA with prostatitis represents 12.7% of all prostate cancer. PCA co-existing with HGPIN accounted for 3.2% of cases. Primary transitional cell carcinoma of the prostate was seen in only one patient and did not co-exist with any disease.

Isolated BPH had a mean tPSA value of 16.0 ± 12.0 ng/ml, while BPH co-existing with prostatitis were found to have higher mean tPSA values of 38.6 ± 28.8 ng/ml. PCA co-existing with prostatitis were found to have higher mean tPSA values of 116.0 ± 82.0 ng/ml than subjects with isolated PCA (66.4 ± 54.0 ng/ml). It was also found that all the benign as well as some malignant lesions were accountable for tPSA levels ranging from 1.0 ng/ml to 84.0 ng/ml, while tPSA values of 85.0 ng/ml and above were seen only in malignant (prostatic carcinoma) cases. There was statistical difference of the mean tPSA seen among the subjects with BPH and prostate carcinoma in this study ($p < 0.01$).

Fifty two (82.5%) out of 63 subjects with prostate carcinoma had tPSA value > 10.0 ng/ml while the remaining eleven (17.5%) had tPSA value ≤ 10.0 ng/ml. Ninety four (62.2%) out of 151 cases of BPH had tPSA > 10.0 ng/ml but the remaining cases 57 (37.8%) had tPSA of ≤ 10.0 ng/ml (Table 4).

Table 1. Age distribution of prostatic diseases seen in LASUTH

Age (years)	Prostate gland disease				Total
	BPH	PCA	BPH+Prostatitis	HGPIN	
40-49	4(2.7%)	0(0.0%)	2(16.7%)	0(0.0%)	6(2.6%)
50-59	10(6.6%)	5(7.9%)	2(16.7%)	1(25.0%)	18(7.9%)
60-69	120(79.5%)	17(27.0%)	7(58.3%)	1(25.0%)	145(63.0%)
70-79	15(9.9%)	34(54.0%)	1(8.3%)	2(50.0%)	52(22.6%)
≥ 80	2(1.3%)	7(11.1%)	0(0.0%)	0(0.0%)	9(3.9%)
Total	151(100%)	63(100%)	12(100%)	4(100%)	230(100%)

There was positive significant difference ($X^2=0.00$) among age groups seen in prostatic diseases.

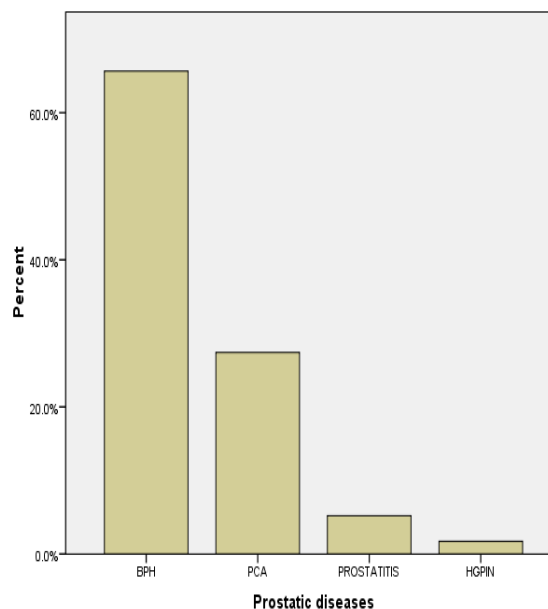
Table 2. Age distribution and mean age of prostatic diseases

Cases	Age Range	Mean Age	SD
BPH	48 - 82	65.0	±6.0
PCA	53 - 91	72.0	±8.0
Prostatitis with BPH	48 - 81	62.0	±8.0
HGPIN	58 - 78	68.0	±9.0

Table 3. Prostate carcinoma seen in LASUTH, Nigeria

Prostate carcinoma (PCA)	No. (%)
Isolated PCA*	53(84.1%)
i. Prostate adenocarcinoma*	52(82.5%)
ii. Primary transitional cell carcinoma of the prostate*	1(1.6%)
PCA + Prostatitis	8(12.7%)
PCA + HGPIN	2(3.2%)
Total	63(100%)

*Isolated lesion

Figure 1. Relative frequency of prostatic diseases**Table 4.** Levels of tPSA in prostatic diseases seen in LASUTH

tPSA Levels ng/ml	Prostate gland diseases						Total
	BPH	BPH + Prostatitis	PCA	PCA + Prostatitis	PCA+ HGPIN	HGPIN*	
<4	6(2.6%)	2(0.9%)	2(0.9%)	0(0.0%)	0(0.0%)	4(1.7%)	14(6.0%)
4 - 10	46(20.0%)	7(3.0%)	6(2.6%)	2(0.9%)	1(0.4%)	0(0.0%)	62(27%)
>10	79(34.3%)	23(10.0%)	45(19.6%)	6(2.6%)	1(0.4%)	0(0.0%)	154(67%)

p<0.01. *Isolated lesion

DISCUSSION

The age range of patients in this series is 48-91years with a mean age of 67 ± 7.3 years. This age range is similar to that of another study in Nigeria which showed age range between 40 - 94years and mean age of 67years.¹⁸ Benign prostate hyperplasia (65.7%) was the most common histologic specimens of prostate gland disease in LASUTH, Nigeria which is lower than 70.9% reported by Anunobi *et al.*, in Lagos.¹⁸ Anunobi *et al.* also found that the age range of those with BPH was 40-94years with a mean of 67years and a peak age-group at 60-69years which are similar to that seen in

our study with age range of 48-82year and a mean age of 65 years.¹⁸ Wadgaonkar *et al.* revealed that prostate lesions are common in the geriatric age group and that benign hyperplasia and carcinoma of the prostate are increasingly frequent with advancing age and are uncommon before the age of 40.¹⁹ In South Africa, Edlin *et al.* established that the prevalence of BPH is 55.3%; and also that prostatitis coexisting with BPH and PCA has prevalence rates of 61.0% and 29.7% respectively.²⁰ Gienn *et al.* showed that the prevalence of BPH in USA rises from 8% in men aged 31-40years to 40-50% in men aged

51-60 years and over 80% in men older than 80 years.²¹ A study done by Dawam showed that BPH was confirmed in 291 (55%) specimens, and BPH with inflammation (infarction, epithelial necrosis and prostatitis) in 182 specimens (35%).²² The prevalence of BPH seen in our study however is lower than the prevalence obtained by Wadgaonkar *et al.* (83.8%) from India.¹⁹ The reason for this variation is not known. However, future studies could attempt to provide the reason for this.

Prostatic carcinoma was the second most common prostate gland disease, constituting 27.4% of all the subjects in this study. This is closely related to the findings from Jos, Nigeria and Cavit *et al.* from Turkey which showed a prevalence of 24.6% and 29% respectively.^{17,23} Akang *et al.* in Nigeria found that incidental carcinoma of the prostate gland had a peak age incidence in the seventh and eight decades of life, accounting for 75.4% of the 61 cases.²⁴

This prevalence was higher compared with the prevalence of 20.5% from Asian Japanese population.²⁵ The difference in the prevalence of prostatic carcinoma seen in this study compared to that of Caucasians and Asians might suggest the possibility of some underlying factors such as genetic basis, difference in lifestyle and food habits; although these were not investigated in this study.²⁵

Prostatic adenocarcinoma was the most common subtype of prostatic carcinoma constituting 98.4% of all cases of PCA seen in this study. This was found to be in tandem with the reports documented by Corriere *et al.* and Wadgaonkar *et al.*, which showed prevalence of 95.0% and 91.6% respectively.^{19,26}

Prostatitis was the third most common prostate gland disease with a prevalence of 5.2% with a mean age of 62 years. Ejike *et al.* found that 12% of adult male Nigerians were reported to have prostatitis.²⁷ In Finland, Mehik *et al.* reported that prostatitis has been

the most common urologic diagnosis in men younger than 50 years.²⁸ Nickel and his group in USA found that the prevalence of all cases with prostatitis was 20% and that their mean age was 50 years.²⁹ The relative low percentage in this study is because other studies were symptom based as against histologic diagnosis in our study. Many cases of prostatitis may not need a biopsy as many of them can be relieved by drug therapy.

High-grade prostate intraepithelial neoplasia had a prevalence of 1.7%. Two (0.9%) cases of HGPIN co-existed only with PCA (prostatic adenocarcinoma) and constituted 3.2% of all cases of prostatic carcinoma. Ahmed in Zaria, showed that 4(3%) out of 131 patients with suspected cancer of the prostate had HGPIN in his prospective study in 2011, while Anunobi *et al.* in another Lagos study showed 19.1% (42) of cases of prostatic carcinoma had HGPIN.^{18,30}

The mean tPSA seen in subjects with isolated BPH (16.0±12.0ng/ml) was found to be lower than that in isolated prostatic carcinoma (66.4±54.2ng/ml). Patients with BPH co-existing with prostatitis had a higher serum mean tPSA (38.6 ±28.8 ng/ml) than those with isolated BPH (16.0±12.0ng/ml). These findings were in consonance with the study done by Edlin in South Africa which revealed that BPH with prostatitis had higher serum tPSA than cases with BPH alone.²⁰ This could be due to the fact that inflammation has the propensity to increase serum tPSA in patients with prostate gland disease.

Total prostate specific antigen was within normal range (0-4ng/ml) in cases with isolated high-grade prostate intraepithelial neoplasia but higher in subjects with HGPIN co-existing with prostatic carcinoma. Ronnett *et al.* also recorded that high-grade prostate intraepithelial neoplasia alone was not accountable for elevated serum tPSA levels seen in HGPIN, but were rather due to other prostatic lesions that co-existed with HGPIN.³¹

Aghaji in Enugu showed that high serum tPSA levels (>10.0ng/ml) have been associated with histological diagnosis of prostate carcinoma, and ranges of 4-10ng/ml (grey zone) are associated with lower rate of positive histology (25%).³² His results supported the findings in this work which revealed that 82.5% (n=52) of subjects with prostate carcinoma had mean tPSA value >10.0ng/ml while the remaining 17.5% (n=11) had mean tPSA value ≤10.0ng/ml.

In this study serum tPSA values above normal range were seen in both benign and malignant lesions, but values ≥ 85.0 ng/ml were seen only in malignant lesions. This is higher than that seen by Anunobi et al, which showed that serum tPSA values ≥50.0 ng/ml were seen exclusively in prostate cancers.¹⁸ There is, therefore, the need for additional studies that could distinguish between benign and malignant lesions.

We found a significant difference between tPSA of the patients with BPH and prostatic carcinoma seen in this study ($p=0.00$) which is in agreement with the study done by Horniger *et al.* but at variance with Christian *et al.*, which found no significant difference.^{33,34}

CONCLUSION

BPH was found to be the most common prostate gland disease followed by prostatic carcinoma. Prostate adenocarcinoma was the most frequent carcinoma of the prostate. There is a higher mean age of patients with prostatic cancer compared with people with BPH. Values of tPSA greater than 84ng/ml are seen only in prostatic carcinoma patients.

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