Nigerian Medical Journal
NIGERIA MEDICAL ASSOCIATION
Print ISSN 0300-1652, E-ISSN 2229-774X

Original Article

# Incidental Prostatic Adenocarcinoma in Open Prostatectomy Specimens: An Institutional Experience

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## Abstract

**Background**: Prostatic diseases cause significant morbidity and mortality in African men. Most Nigerian patients presenting with huge prostate enlargement are availed open prostatectomy to relieve symptoms of prostatism. Some prostates removed for benign enlargement have indolent cancers that are only discovered after histopathological examination. The incidence of these incidental adenocarcinomas of the prostate varies widely.

**Methodology**: We carried out a 10-year retrospective review of open prostatectomy specimens received in the Department of Pathology, from January 2009 to December 2018. At grossing, a minimum of 6 cassettes were used depending on size, and tissue was taken from representative areas for microscopic examination. The data was analysed for the presence of, and the relationship between, incidental adenocarcinoma of the prostate and clinicopathological parameters in each case using relevant statistical tools in the SPSS version 23.

**Results**: Incidental adenocarcinoma of the prostate was found in 5.7% of 158 open prostatectomy specimens seen during the study period. High-grade prostatic intraepithelial neoplasm (HGPIN) was present in 1.9% of cases. Patients in the 7th and 8th decade accounted for 88.8% of all incidental adenocarcinomas. The mean weight of the excised glands was 89.8g (range10-500g). The weight of the prostate did not predict diagnosis of incidental adenocarcinoma. In-hospital consultation accounted for 66.9% of open prostatectomy samples received in the department but the majority (72.7%) of incidental adenocarcinomas were seen in specimens form external consultations. The tumours were mostly ISUP grade group one tumours.

**Conclusion**: The rate of diagnosis of occult prostate cancer is low with majority of the tumours being well differentiated. Organ weight had no relationship with histological diagnosis. Cases managed outside the teaching hospital were more likely to have incidental prostate cancer.

**Keywords**: Incidental adenocarcinoma; Prostatectomy; prostate cancer; HGPIN.

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**How to cite this article:** Omenai SA, Fashola OA, Takure AO, Ogunbiyi JO. Incidental prostatic adenocarcinoma in open prostatectomy specimens: an institutional experience. Niger Med J 2021;62;(6):298-304

**Quick Response Code:**

## Introduction

Diseases of the prostate result in significant morbidity and mortality in African men[1]. The common diseases of the prostate are benign nodular hyperplasia and adenocarcinomas. Simple prostatectomy is usually performed in selected patients with benign enlarged prostate to relieve obstructive symptoms[2]. Transurethral resection of the prostate (TURP), which is the gold standard is a minimally invasive procedure[2]. Large prostates are however better managed with open prostatectomy. Open prostatectomy appears to be a more routine procedure in Nigeria due to multiple factors including inadequate facilities, affordability, the available skills and the very large prostate seen in our patients who often present late[3,4]. Open prostatectomy however has an added advantage in that recurrence of urinary tract obstruction is infrequent, it is affordable and readily available in our locality[3-7].

At histopathological examination, incidental prostatic adenocarcinoma is defined as prostate carcinoma diagnosed in a prostate removed as treatment for other diseases except prostate cancer[8]. This incidental diagnosis of prostate cancer can be either from specimens examined from simple prostatectomy done for benign prostate enlargement, cystoprostatectomy done for bladder cancers, or/and at autopsies[8,9].

The reported prevalence of incidental prostatic carcinoma in simple prostatectomy specimens ranges from 2 to 16%.–It was up to 46% before the advent of the use of prostate specific antigen (PSA) in clinical evaluation of patients with lower urinary tract symptoms[9,10]. PSA screening alongside the use of digital rectal examination reduced the incidence of incidental prostate adenocarcinoma by 50%. Incidental prostatic adenocarcinomas are usually stage 1 and could either be T1a or T1b[11,12]. Tumours involving 5% or less of the resected tissue are staged as T1a while tumour size greater than 5% of the resected tissue is staged as T1b. They range from low grade tumours to high grade tumours[11,12].

Patients with a diagnosis of low grade (Gleason score  6) incidental adenocarcinoma of the prostate and stage T1a are offered active surveillance with regular PSA monitoring. Patients with stage T1a who are younger than 65 years and fit for surgery can have a radical prostatectomy offered. Stage T1b and all stage 1 tumours with high Gleason scores are managed actively with surgery or radiotherapy.  Stage T1a adenocarcinomas are the most common incidental adenocarcinoma of the prostate. Stillwell et al., demonstrated that 31% of patients with stage T1b were much more likely to progress to clinical disease with bone metastases. Lee et al., in a study in South Korea demonstrated that radical prostatectomy is an over treatment for incidental adenocarcinoma of the prostate as there was no significant difference in clinical outcome between stage T1a and T1b. High Gleason score at diagnosis, pre and post-surgery PSA values are factors that should be considered in making a decision to offer treatment to patients with incidental adenocarcinoma of the prostate.

The risk factors for finding incidental prostatic adenocarcinoma generally include age greater than 75 years, prostate volume less than 50cm3, and PSA greater than 4ng/ml.

During surgical cut up of simple prostatectomy specimens, it has been demonstrated that random selection using an average of eight blocks is effective in the diagnosis of occult adenocarcinoma of the prostate. Even morcellated tissue does not affect the detection of incidental adenocarcinoma, although the number of cassettes are usually more for morcellated tissue as up to 15 cassettes can be used.

In addition to incidental prostatic carcinoma, High grade prostatic intraepithelial neoplasia (HGPIN)may also be seen in prostates removed for non-cancer diagnosis. These have nuclear atypia that are similar to that of prostate cancer.This study reviews our experience in our institution and provides an update on the clinicopathological characteristics of incidental adenocarcinoma of the prostate, while comparing in-hospital to external consultations.

## Methods

This is a retrospective descriptive study done at the Department of Pathology, in our institution. All open prostatectomy specimens received in the department from January 1st 2009 to December 31st 2018 were reviewed and those that had clinical diagnosis of benign prostate enlargement were recruited. Open prostatectomy specimens done after clinical diagnosis of benign prostate enlargement received in the department are grossed with a minimum of 6 cassettes depending on size taken from representative areas. The weight of the prostate, Gleason

grade and score were extracted from the records. Patient's age, histological diagnosis, and source of consult (in-hospital or external consultations) were also extracted.

The study was conducted according to the Helsinki declaration guidelines. Confidentiality of patients' data was maintained with the data anonymized. Cases reviewed were part of a multi-centre study of prostate cancer genetics with ethical clearance from the institutional review board (UI/EC/15/0200).

The data was entered into SPSS version 23 and descriptive analysis was done. Chi-square test of significance was used for categorical variables. The Kruskal-Wallis nonparametric test was used to test the distribution of organ weight across histological diagnosis. Level of significance was set as $p < 0.05$.

## Results

There were 158 cases of open prostatectomy specimens over the review period. The mean age of patients having open prostatectomy was 68.5yrs (51-86yrs).Most patients (43%) having prostatectomy were in the 7th decade (Table 1). The minimum prostate weight was 10g while the maximum was 500g and the mean prostate weight was 89.8g. Incidental adenocarcinoma was seen in 9 cases(an incidence of 5.7%) while HGPIN was seen in 3(1.9%) cases.

Eight of nine cases(88.8%) with occult adenocarcinoma were in the 7th and 8th decade with only one case below 60 years. In addition, 66.7% of HGPIN were seen in the 8th decade (Table 2).Using the Mann-Whitney U test, there were no statistical differences in the distribution of age at diagnosis of neoplastic or non-neoplastic prostate disease following simple prostatectomies. [z = -0.714, p = 0.475]. Kruskal-Wallis test showed that here was no correlation between organ weight and the incidence of incidental prostate adenocarcinoma [H (2) = 0.54, p = 0.973]. (Table 3).

Whilst in-hospital consultation accounted for 67.1% of open prostatectomy specimens received in the department, the majority (77.8%) of incidental prostatic adenocarcinomas were seen in specimens from external consultations (Table 2). Simple prostatectomy specimens referred from external facilities were thus more likely to have incidental adenocarcinoma [x2 (2) = 8.714, p = 0.013].

The minimum Gleason score in this study was 6 while the highest Gleason score was 8 (Figure 1). Figure 2 shows a micrograph of an incidental prostate adenocarcinoma with a focus of infiltrating angulated glands on a background of benign prostate.

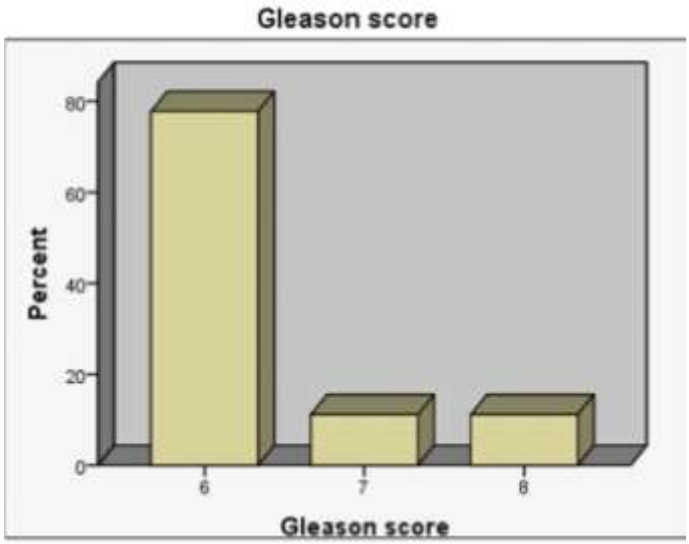


Figure 1: Bar chart showing frequency distribution of Gleason score.

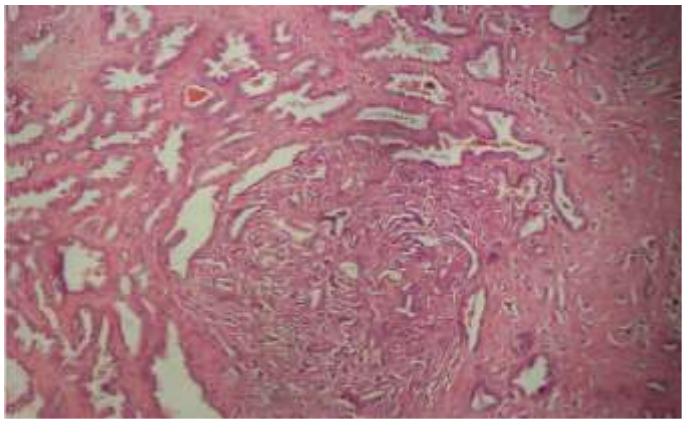

Figure 2: Section showing Gleason pattern 3 adenocarcinoma malignant nodule on background of benign prostate tissue. (H&E x100)

Table 1: Shows age distribution of prostate diseases

| Diagnosis | Age of patients | | | |
|---|---|---|---|---|
| | **50-59yrs** | **60-69yrs** | **70-79yrs** | **80-89yrs** |
| Nodular hyperplasia | 15 | 62 | 56 | 10 |
| Adenocarcinoma/HGPIN | 1 | 5 | 6 | 0 |
| Total | 16 | 67 | 62 | 10 |

Table 2: Showing frequency distribution of diagnosis of open prostatectomies

| S/No | Variable | Adenocarcinoma (%) | HGPIN (%) | Nodular Hyperplasia (%) |
|---|---|---|---|---|
| 1 | **Age group** | | | |
| | 50-59yrs | 1 (11.1) | 0 (0) | 15 (10.5) |
| | 60-69yrs | 4 (44.4) | 1 (33.3) | 62 (43.4) |
| | 70-79yrs | 4 (44.4) | 2 (66.7) | 56 (39.2) |
| | 80-89yrs | 0 (0) | 0 (0) | 10 (7.0) |
| 2 | **Source of consult** | | | |
| | In-hospital | 2 (22.2) | 2 (66.7) | 102 (69.9) |
| | External consultation | 7 (77.8) | 1 (33.3) | 44 (30.1) |

Table 3: Showing prostate diagnosis and organ weight.

| Prostate size (gm) | Adenocarcinoma | Nodular hyperplasia | HGPIN |
|---|---|---|---|
| | 2 | 13 | 0 |
| 21-40 | 1 | 21 | 0 |
| 41-60 | 1 | 23 | 0 |
| 61-80 | 1 | 24 | 2 |
| 81-100 | 3 | 29 | 1 |
| >100 | 1 | 29 | 0 |

HGPIN = High grade intraepithelial neoplasm.

## Discussion

Nodular hyperplasia of the prostate is not a premalignant lesion but it increases in incidence with advancing age just like prostate cancer. Bearing this in mind one would suggest that any prostate removed on account of benign prostate enlargement should rightly be examined for an indolent cancer as prostate cancer and nodular hyperplasia both require androgen for growth as androgen is responsible for the development and maintenance of prostatic epithelium. A precursor lesion of prostatic carcinoma on the other hand is HGPIN. HGPIN can be found alone in a prostate specimen or could be a component of an invasive disease. HGPIN also probably depends on androgen for its development and it has different morphological patterns including the cribriform, flat, micropapillary and

tufting forms. In all situations, androgen deprivation therapy has been shown to decrease the prevalence and extent of prostatic intraepithelial neoplasms

There are many reports showing the range of incidental prostate adenocarcinoma to be between 15% and 46%.In this study, incidental prostatic adenocarcinoma was diagnosed in 5.7% of patients who had open prostatectomy for clinically benign prostatic enlargement. This finding is very similar to a 6.3% incidence of incidental prostatic adenocarcinoma reported in an autopsy review from the same institution by Okani et al but it is relatively higher than what was documented by Aligbe et al., and Anunobi et al., in various studies from other institutions in Nigeria (1.3%, 4.2% respectively). These differences in prevalence might be due in part to sample sizes (Aligbe et al. and Anunobi et al reviewed a total 680 and 222 cases respectively) and may also be due to the sample types studied, which included both open prostatectomies and TURP in these other studies and not limited to open prostatectomies as was the same here. Obiorah et al. in Port Harcourt, Nigeria reported a 17.2% incidence for incidental prostate adenocarcinoma, which is significantly higher than our finding and those of most other Nigerian series.

It is noteworthy that the majority of the studies with high rates of incidental prostatic adenocarcinoma utilised data on cases diagnosed before the era of PSA estimation and screening. This is buttressed by the fact that the majority of incidental adenocarcinoma in this study were specimens sent from external facilities, which are mostly private and, sometimes, public secondary healthcare centres. A probable explanation for this could be related to the extent of pre-surgical evaluation available in some of our secondary healthcare facilities but other possibilities need to be explored still. In this study one would suggest that this low incidence of incidental prostate adenocarcinoma is likely attributable to adequate clinical work up in our hospital patients that includes the use of digital rectal examination, transrectal ultrasound scan and serum PSA. This is because a combination of these examination methods has higher positive predictive value for cancer detection and patients may not be subjected to prostatectomy if these parameters don't match up. On the contrary, the outside cases with inadequate workup could actually have been easily classified as 'cancer-bearing' rather than BPH at the time of their surgery thus providing for the higher prevalence of incidental cancers amongst the group. We note that there is no established national prostate cancer screening programme in Nigeria and the extent of work-up is institutionally determined. Thus more studies are required to establish the frequency or prevalence of incidental prostate cancer amongst Nigerans overall.

Beyond the incidental cancer, HGPIN was incidentally found in 3.8% in prostates removed for benign enlargement in one study in India but, again, it constitutes 1.9% of diagnosis in this study. It would thus seem to be rare in our environment just as the previous autopsy study on incidental prostate adenocarcinoma from this department did not report any HGPIN.

How does this study add to the discussion on the biology of prostatic carcinoma in Africans? A few observations should be considered. The first is that the majority of patients having open prostatectomies were in the 7th decade of life in keeping with well-established knowledge. Second, the occurrence of incidental adenocarcinoma in the 6th decade of life (55 years) is in keeping with the findings by Yin et al., who noted that adenocarcinoma increases from the 5th decade and it seems to support in some ways, the need to screen for prostate cancer from the 5th decade in our environment. This is because obstructive prostatic enlargement may not occur until a bit later. The third is that cases of incidental adenocarcinoma and HGPIN peaked in the 8th decade. It is difficult to suggest that HGPIN starts to occur a bit later than carcinoma itself if it is and accepted precursor lesion to prostatic carcinoma. Sakr et al had shown HGPIN in patients in their fourth decade. It is possible that the technique of studying these cases here impact on the appreciation of the occurrence of HGPIN in our environment.

On the other hand, the relationship between the weights of prostate glands and the incidence of incidental carcinoma seems to be in favour of large glands. Whereas glands seen in this study were large with an average weight of 89.8g, which is very much higher than a mean of 27g reported by Zigeuner et al.,Sakamoto et al. had reported that prostate volume less than 50cc were likely to have incidental adenocarcinomas. Varghese et al., in an Indian study also showed that organ weight less than 20g was predictive of incidental prostate adenocarcinoma. Organ weight, however, did not predict the diagnosis of incidental adenocarcinoma in our study.

The most common grade seen is the well differentiated cancers, with about 75% of the cases having Gleason score 6.Otto et al. in the United States found that cases were mainly Gleason score 6 and 7 and that the majority of the cases were stage T1a.This could be the reason why majority of the cases are actually incidental as these grades of tumour can be indolent with only a minority requiring treatment.

**Limitations**

Even though progression to clinical symptomatology of cancer has been documented, clinical progression of incidental adenocarcinoma (iPCa) in our environment is difficult to predict because of a high rate of loss to follow up for our patients. Also, virtually all external consults did not have PSA values, thus we were unable to show the relationship of PSA values at workup and the likelihood of diagnosis of incidental adenocarcinoma of the prostate. We cannot determine the level of pre-surgical investigation of external consults.

## Conclusion

This study affirmed the low rate of diagnosis of incidental prostatic adenocarcinomas in our environment. The majority of incidental adenocarcinomas are low grade and well differentiated. The rate of diagnosis of incidental prostate adenocarcinoma was higher in cases referred from external facilities. Although most prostatectomy specimens were large, organ weight was not predictive of diagnosis of carcinoma. Because it is mainly a disease of the 7th and 8th decades of life. Early screening for prostate cancer in our environment might be indicated from the 5thdecade since obstructive prostatic enlargement may not occur until a bit later.

**List of abbreviations**

HGPIN = High-grade prostatic intraepithelial neoplasm
SPSS = Statistical Product and Service Solutions
ISUP = International Society of Urological Pathology
TURP = Transurethral resection of prostate
PSA = Prostate specific antigen
iPCa = Incidental prostate carcinoma

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