Original Research Article

# Histopathological Study of Lesions of Prostate - A Five Year Study

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#### ABSTRACT

#### Aims and objectives:

- 1. To study the incidence, age distribution and gross and histopathological features of lesions of prostate.
- 2. To classify tumours of prostate as per recommendations of WHO and to analyse cases of adenocarcinoma of prostate according to Gleason grading system.

**Material and methods:** This is a retrospective and prospective study of 226 cases of lesions of prostate during the period of August 2004 to July 2009. The gross specimens were in the form of prostatectomies, transurethral resections and tru cut biopsies. The tissue was fixed in 10% formalin. Sections were cut at 3-5 micron thickness and were subsequently stained by haematoxylin and eosin stain. All the cases were analysed according to age, description of gross specimen and microscopic examination. Morphological types of benign prostatic hyperplasia were described. The tumours of prostate were diagnosed and classified as per WHO classification (2002). The cases of adenocarcinoma were analysed according to Gleason grading system.

**Results and conclusion:** The commonest prostatic lesion was benign prostatic hyperplasia, seen most frequently in 7<sup>th</sup> decade with fibromyoadenomatous type being the most common morphological pattern. Eighteen cases of adenocarcinoma were observed, out of which one showed mucinous features. Maximum numbers of cases of adenocarcinoma were seen in 8<sup>th</sup> decade. The most common Gleason primary pattern was pattern 3 and the most frequent Gleason score was 9.

*Key words:* lesions, prostate, histopathology.

#### **INTRODUCTION**

The immense medical problems caused by prostate gland are increasing at an alarming rate. The number of cases has continuously increased over the past decades, partly due to the higher life expectancy. Prostate gland specimens account for the significant percentage of diagnostically challenging cases in surgical pathology practice. The goal of tissue sampling is to maximise the opportunity to recognize the presence of carcinoma of prostate and to provide information regarding its histological grade. A confirmed diagnosis with an indication of tumour grade helps in rational management approach. In short, lesions of prostate are an area of constant interest to clinicians as well as to Pathologists.

## MATERIALS AND METHODS

This retrospective is a and prospective study of five years duration consisting of 226 cases of lesions of prostate. The gross specimens received were prostatectomies, transurethral resections of prostate (TURP) and tru cut biopsies. The clinical data was collected from indoor case papers and biopsy requisition forms. The tissue was fixed in 10% formalin. The relevant data inclusive of gross appearance of the specimen and the histopathological findings was recorded. Routine paraffin processing of the tissue and haematoxylin and eosin staining was done. Special stains (20% ZN staining, PAS) were performed wherever required.

All the cases were analysed according to age, description of gross specimen and microscopic examination. The various lesions of prostate were listed. Morphological types of benign prostatic hyperplasia (BPH) were described as per classification given by Franks.<sup>(1)</sup> The tumours of prostate were diagnosed and classified as per WHO classification (2002). The cases of adenocarcinomas were analysed according to Gleason grading system.<sup>(2)</sup>

## RESULTS

Two hundred twenty six cases of lesions of prostate were studied from the hospital records of histopathology section of Government medical college and hospital, Miraj, Maharashtra, over a period of five years i.e. from August 2004 to July 2009.

Out of 226 cases, 214 (94.69%) were prostatectomy specimens. Grossly, the prostatectomy specimens were bosselated or nodular varied from 2-12 cm in size. The consistency varied from soft to firm to hard. The TURP specimens were in the form of multiple pieces, gray tan to gray pink in colour and soft to firm in consistency. The biopsy specimens were in the form of elongated pieces of gray tan tissues ranging from 0.4-1 cm in size.

The most common lesion was BPH seen in 207 (92.04%) cases with peak incidence in seventh decade. Acinar adenocarcinoma of prostate was seen in 18 (7.96%) cases with peak incidence in eighth decade. One case showed adenocarcinoma with mucinous features. In one (0.44%) case we found high grade prostatic intraepithelial neoplasia. (HGPIN) (Table 1 and 2).

Table 1: Dist	ribution of cases on histopath	ological basis and nature of specimen	:
URE OF SPECIMEN	BENIGN PROSTATIC	ACINAR ADENOCARCINOMA	HGPIN

NATURE OF SPECIMEN	BENIGN PROSTATIC HYPERPLASIA	ACINAR ADENOCARCINOMA OF PROSTATE	HGPIN	Total
Prostatectomy	198	15	1	214
Biopsy	7	2	-	009
Transurethral resection of prostate	2	1	-	003
Total	207	18	1	226
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HGPIN- High Grade Prostatic Intraepithelial Neoplasia.

### Benign Prostatic Hyperplasia

Microscopically, glandular and stromal hyperplasia was seen. The acini were lined by double layered cuboidal to columnar epithelium which at places showed papillary infoldings. Some of the acini contained corpora amylacea.

Maximum numbers of cases of BPH [106 (51.21%)] were seen in  $7^{\text{th}}$  decade followed by 72 (34.78%) cases in  $8^{\text{th}}$  decade. (Table 2).

AGE RANGE	BENIGN PROSTATIC	ACINAR ADENOCARCINOMA	HGPIN
(YEARS)	HYPERPLASIA	OF PROSTATE	
40-49	3 (1.45%)	-	-
50-59	16 (7.73%)	3 (16.66%)	-
60-69	106 (51.21%)	3 (16.66%)	-
70-79	72 (34.78%)	9 (50%)	1 (%)
80-89	9 (4.35%)	3 (16.66%)	-
90-99	1 (0.48%)	-	-
TOTAL	207 (100%)	18 (~100%)	1 (%)

Table 2: Age wise distribution of cases of benign prostatic hyperplasia and acinar adenocarcinoma of prostate:

Microscopically, the nodular hyperplasia is the result of proliferation of epithelial cells, smooth muscle cells and fibroblasts in variable proportions. On the basis of histological composition five types of nodules described: are Stromal. Fibromuscular, Muscular, Fibroadenomatous and Fibromyoadenomatous.<sup>(1)</sup>

In fibromyoadenomatous type, hyperplasia of both glandular and stromal element was seen. The hyperplastic stroma was fibromuscular. In fibroadenomatous hyperplasia, the predominant hyperplasia was of the glandular component. The glands were closely packed together with less stromal component. In fibromuscular hyperplasia, the hyperplastic nodules were predominantly stromal devoid of glandular element. In stromal hyperplasia, the nodules were made up of a loose fibrous tissue with groups of spindle or star-shaped cells often arranged around well formed blood vessels. Some of the cells resembled fibroblasts; others resembled smooth muscle cells.

Fibromyoadenomatous hyperplasia was found in majority of the cases [97 (46.86%)]. Seventy eight (37.69%) cases were of fibroadenomatous hyperplasia, 31 (14.97%) cases were of fibromuscular hyperplasia and 1(0.48%) case was of stromal hyperplasia. (Table 3)

able 5: Morphological types of hype	erplasia in cases of benign	prostatic nyperplasia.
PATTERN OF HYPERPLASIA	NUMBER OF CASES	PERCENTAGE
Fibromyoadenomatous	97	46.86%
Fibroadenomatous	78	37.69%
Fibromuscular	31	14.97%
Muscular	-	-
Stromal	1	0.48%
Total	207	100%

Table 3: Morphological types of hyperplasia in cases of benign prostatic hyperplasia.

Of these cases of BPH, 105 (50.73%) cases were associated with chronic nonspecific prostatitis, 63 (30.43%) case were associated with acute on chronic nonspecific prostatitis, 8 (3.86%) cases were associated with granulomatous prostatitis, 4 (1.93%) with acute prostatitis, 3 (1.45%) cases with chronic nonspecific prostatitis with infarction and remaining 24 (11.60%) cases were not associated with any inflammatory process.

Acinar Adenocarcinoma

The microscopic grading system developed by Gleason is currently the preferred grading system. It is based on the degree of glandular differentiation and the growth pattern of the tumour in relation to the stroma as evaluated on low power examination. <sup>(2)</sup> This system described 5 different patterns; recognised as primary pattern (predominant) and the secondary (second most prevalent) architectural patterns and assigned a grade from 1 to 5 with 1 being most differentiated and 5, the least differentiated. The two grades are added together to obtain the Gleason score.

Most frequently observed predominant patterns were pattern 3 and 4 seen in 8 (44.44%) and 7 (38.89%) cases respectively. No cases showed pattern 1 or 2 in present study (Table 4)

Gleason score 9 was the commonest score found [6 (33.34%)] followed by 5 (27.77%) cases each with Gleason score 7 and 8. (Table 5)

Table 4: Analysis of cases of acinar adenocarcinoma of prostate according	
to gleason predominant pattern.	

PREDOMINANT PATTERN	NUMBER OF CASES	PERCENTAGE
1	-	-
2	-	-
3	8	44.44%
4	7	38.89%
5	3	16.67%
TOTAL	18	100%

Table 5: Analysis of cases of acinar adenocarcinoma of prostate according of gleason score.

GLEASON SCORE	NUMBER OF CASES	PERCENTAGE
6	1	5.56%
7	5	27.77%
8	5	27.77%
9	6	33.34%
10	1	5.56%
TOTAL	18	100%

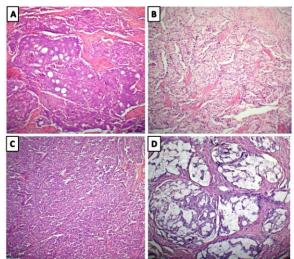


Fig 1: Adenocarcinoma of prostate.

- A- Tumour cells arranged in cribriform pattern without necrosis (Gleason grade 3c).
- B- Tumour cells having clear cytoplasm- Hypernephomatoid pattern (Gleason grade 4b).
- C- Infiltrative tumour cells arranged in sheets. (Gleaason grade 5b).
- D- Adenocarcinoma with mucinous features.

#### DISCUSSION

BPH and adenocarcinoma are the two pathological processes which frequently affect the prostate gland.

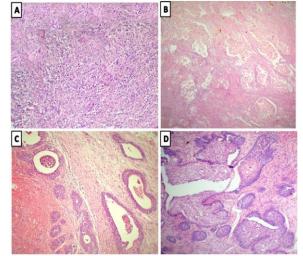


Fig 2: A- Granulomatous prostatitis B- Prostatic infarct C- Transitional metaplasia D- Squamous metaplasia.

In our study, we had more of [214 (94.69%)] prostatectomy specimens. Other studies conducted by Mittal et al<sup>(3)</sup> and Shakya et al<sup>(4)</sup> had higher percentage of TURP specimens. This may be due to the

different protocols used for the diagnosis and treatment of patients with lesions of prostate.

In the present study, we had 91.6% cases of BPH, 7.96% cases of acinar adenocarcinoma and 0.44% case of HGPIN. The findings in our study are comparable with those of Mittal et al,<sup>(3)</sup> Sharma et al<sup>(5)</sup> and Mohammed et al.<sup>(6)</sup>

BPH is a regional nodular growth of variegated histological composition that is almost ubiquitous development in men if they have testes and live sufficiently long. The clinical incidence is 8% during the 4<sup>th</sup> decade but it reaches 75% in the 8<sup>th</sup> decade.

Before the recognition of the hyperplastic nature of BPH, the prostatic enlargement in elderly men had been variously interpreted to reflect neoplastic process, compensatory hypertrophy, а response to inflammation or arteriosclerosis. (7) Pure stromal hyperplasia with nodule formation was first reported by Reischauer in 1925.<sup>(8)</sup> Deming et al<sup>(9)</sup> confirmed this observation and further regarded that the glandular element of prostatic nodule as an event to the stromal stimulus to epithelial proliferation within adjacent ducts.

With the development of the BPH, the weight of the gland significantly increases and averages 33±16 gm. Grossly, there are well defined soft to firm nodules with variable solid and cystic composition.<sup>(3)</sup> The cut surface is gray to yellow. If there is epithelial hyperplasia prominent the abundant luminal spaces create soft and grossly spongy nodules from which oozes watery fluid. If the BPH is predominantly fibromuscular, there are numerous trabeculations without prominent nodularity. haemorrhage, calcification Focal and macrocystic change may be present. TURP specimens yield multiple boat shaped, grevish pink chips which do not have distinct appearance.<sup>(8)</sup>

Microscopically the nodular hyperplasia is the result of proliferation of epithelial cells, smooth muscle cells and fibroblasts in variable proportions. On the basis of histological composition five types nodules are described: Stromal. of Fibromuscular. Muscular. Fibroadenomatous and Fibromyoadenomatous.<sup>(1)</sup>

The earliest change is the stromal proliferation which contains more smooth muscle and less elastic tissue than the normal stroma, followed by hyperplasia of the glandular component. The glands are dilated or even cystic and often contain corpora amylacea which is sometimes calcified. The epithelium ranges from flat to columnar. The cytoplasm is pale and nucleoli are inconspicuous. Papillary infoldings are common. A continuous basal cell layer is present.<sup>(8)</sup>

Comparing the incidence of BPH with nature of specimen, in the present study, maximum of our cases [198 (95.65%)] were obtained from prostatectomies. Anim et al<sup>(10)</sup> and Shaky et al<sup>(4)</sup> had more number of BPH in TURP specimens whereas Mwakyoma<sup>(11)</sup> had more of BPH in biopsies. This may be due to different protocols used for the diagnosis and treatment of prostatic lesions in different set ups.

Maximum cases of BPH were in the 7<sup>th</sup> decade which was similar to other studies like that of Sharma et al<sup>(5)</sup> but studies conducted by Kim KB et al<sup>(12)</sup> had more cases in  $8^{\text{th}}$  decade while Matapurkar et al<sup>(13)</sup> found highest incidence in 6<sup>th</sup> decade. Very studies have classified **BPH** few morphologically. We had maximum number cases [97] (46.86%)] of showing fibromyoadenomatous hyperplasia which was comparable with that of Kim KB et al.<sup>(12)</sup>

Chronic prostatitis is most commonly observed in nodular hyperplasia. Kohnen et  $al^{(14)}$  and Anim et  $al^{(10)}$  found

nonspecific prostatitis in 90-98% cases of BPH.

The spectrum of chronic prostatitis includes bacterial, abacterial and Bacterial granulomatous prostatitis. prostatitis caused strains is by of Enterococcus fecalis. The etiologic agent of chronic abacterial prostatitis is unknown but chlamydia, ureaplasma and trichomonas infection has been proposed. Grossly a chronically inflamed prostate is firm or hard in consistency. Microscopically, there is interstitial fibrosis and diffuse patchy or very discrete foci of intraglandular or periglandular infiltrate of lymphocytes, plasma cells and histiocytes. In long standing cases the lining epithelium of large ducts may show squamous metaplasia.

Granulomatous prostatitis can be clinically confused with prostatic carcinoma. The reported incidence of granulomatous prostatitis is 0.36-4%.<sup>(15,16)</sup> Epstein et al<sup>(17)</sup> classified it depending on the possible causative agent into idiopathic (nonspecific), iatrogenic infectious, and allergic (eosinophilic) granulomatous prostatitis and malakoplakia. Granulomatous prostatitis is probably caused by blockage of prostatic ducts and the stasis of secretions, regardless of its aetiology. It is thought to represent an immune mediated process accompanied by reaction to the prostatic secretions released from the obstructed ducts.

Grossly the gland is firm to stony hard. The cut surface shows obliteration of the architecture with the formation of yellow granular nodules. Microscopy is characterized by large nodular aggregates of pale staining histiocytes, epithelioid cells, plasma lymphocytes and cells. Characteristically these granulomas are centred in the lobules.<sup>(8)</sup>

Prostatic infarcts are common in markedly enlarged prostate gland. Circulatory disturbances, in which there is distortion of blood supply or venous drainage resulting from mechanical compression may be the contributing factor.<sup>(18)</sup> Serum Prostate specific antigen and prostatic acid phosphatase levels are elevated. We had 3 (1.45%) cases of BPH with infarction. Milord et al<sup>(18)</sup> and Moore<sup>(19)</sup> reported prostatic infarcts in 0.07% and 25% cases of BPH respectively.

Grossly prostatic infarcts vary in size. They are speckled, greyish yellow. The peripheral margins are usually sharp and haemorrhagic. Microscopy shows discrete foci of coagulative necrosis involving both epithelial and fibromuscular stromal element with haemorrhage. The surrounding noninfarcted prostatic gland may show immature squamous metaplasia.<sup>(18)</sup>

WHO classification of adenocarcinoma prostate (2002) is based primarily on the microscopic characteristics of tumours like morphologically identifiable cell types and histological patterns as seen with conventional light microscopy.

Prostate cancer is now the 6<sup>th</sup> most common cancer in the world (in terms of new cases) and 3<sup>rd</sup> important in men. It is predominantly a disease of elderly men. The risk rises steadily with age. Worldwide about three quarters of all cases occur in men aged 65 years or more.

Approximately 20% cases are hereditary. Patients with familial prostate cancer tend to present at an earlier age. The risk of prostate carcinoma increases with number of affected first degree relatives. The positive history of prostate carcinoma in one first degree relative increases the risk by approximately two folds. It may exceed five folds if two or more first degree relatives have history of prostate cancer and increases 11 times for those with three affected first degree relatives. Prostate cancer initiation and progression are influenced by androgens. A meta-analysis of previously published studies on hormonal predictors of prostate cancer concluded that men whose

total testosterone level is in highest quartile are 2.34 times more likely to develop prostate cancer.<sup>(20)</sup>

A higher incidence has been reported in men working in industries including machine and rubber manufacturers, plumbers and news paper workers. Reduced risk is associated with increased levels and index of beta carotene intake. Beta carotene may influence carcinogenesis by minimizing free radical damage or by enhancing immunologic function<sup>(21)</sup>

The search for the precursor of prostatic adenocarcinoma has focussed in recent years on two distinct histopathological findings: Prostatic Intraepithelial Neoplasia (PIN) and Atypical Small Acinar Proliferation (ASAP).

Grossly, the gland is hard or firm yellow gray. The size varies ranging from minute focus to massive growths. On cut surface the carcinomatous foci appear as ill defined, greyish white areas merging into surrounding tissue.

Microscopically there is only a single cell type without the basal layer. The pathological diagnosis of carcinoma is indicated by<sup>(2)</sup> crowded glands growing in haphazard fashion, large acini without convolutions, fused glands, glands in glands, columns, cords and solid sheets. The glands oriented perpendicular to each other and glands irregularly separated by bundles of smooth muscle are indicative of an infiltrative process. Nuclear enlargement with prominent nucleoli is the frequent finding. Prostatic crystalloids are the dense eosinophilic rectangular. hexagonal, triangular and rod like crystal like structures seen in low grade prostatic carcinoma. Although not diagnostic of carcinoma, crystalloids are seen more frequently in association of malignancy than benign glands. Intraluminal pink acellular dense secretions or blue tinged mucinous secretions are additional findings seen in

low grade prostatic carcinoma. In contrast, corpora amylacea is common in benign glands. Malignancy specific features are perineural invasion, mucinous fibroplasias (collagenous micronodules), and glomerulations.

Adenocarcinoma accounted for 7.96% cases in our study. The reported incidence is 10.9- 21%.<sup>(22,23)</sup> Maximum numbers of our cases (50%) were in the 8<sup>th</sup> decade whereas Sharma et al<sup>(5)</sup> had more cases in 7<sup>th</sup> decade while Gilliland et al<sup>(24)</sup> in 7<sup>th</sup> & 8<sup>th</sup> decade. Matapurkar et al<sup>(13)</sup> found maximum number of cases in the 7<sup>th</sup> decade.

Adenocarcinomas are classified by taking into account morphological appearance of glandular cells and the glandular pattern.

We found maximum number of cases (50%) showing predominant pattern 3 which was comparable with those of Vollmer.<sup>(25)</sup> Maximum number of cases (33.33%) had Gleason score 9. Brawn et al<sup>(26)</sup> had score 6 & 7 whereas Vollmer<sup>(25)</sup> had score 6 most common. This discrepancy may be due to the less number of cases of acinar adenocarcinoma observed in our study or delayed presentation of patients.

PIN is characterized by spectrum of atypical cytological features ranging from minimal changes to those that are indistinguishable from carcinoma. A basal layer is consistently present. Antibodies directed against the high molecular weight keratins (34  $\beta$ E12) have been employed immunohistochemically to selectively label the prostatic basal cell layer. Initially PIN was categorised as PIN 1, PIN 2 and PIN 3 which is now replaced by low grade PIN and high grade PIN which is based mainly on the cytological characteristics of the cells.

Currently conventional use of the term 'PIN' without qualification refers to only high grade PIN. The clinical importance of recognising PIN is based on its strong association with prostatic carcinoma. PIN has a high predictive value as a marker for adenocarcinoma and its identification in biopsy specimens of the prostate warrants for further search for concurrent invasive carcinoma.

In the present study, we found 1(0.44%) case of HGPIN in the prostatectomy specimen. We did not observe HGPIN in the biopsy and the TURP specimens.

The reported incidence of HGPIN is 2.3-5.5% in TURP and needle biopsies.<sup>(27-29)</sup> This discrepancy in the observation of HGPIN in present study as compared to other studies is due to the small number of biopsy and TURP specimens received for histopathological examination at our institute.

# CONCLUSION

Histopathological diagnosis and grading plays an important role in the management of prostatic cancer. For satisfactory management of patient, a high degree of the awareness of the advances along with team approach has become imperative.

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