HISTOMORPHOLOGICAL STUDY OF TRANSURETHRAL RESECTION OF PROSTATE SPECIMENS

SUPARNA V SUVERNAKAR, DEEPAK SADHU, NITISH P INGOLE*

Department of Pathology, Dr. Shankarrao Chavan Government Medical College, Nanded, Maharashtra, India.
*Corresponding author: Nitish P Ingole; Email: nitish.ingole144@gmail.com

ABSTRACT

Objectives: (The objectives of the study are as follows: 1) To study various histomorphological patterns of transurethral resection of prostate specimens. (2) To classify malignant lesions with Gleason's grading and to do Prostate-specific antigen (PSA) level and immunohistochemistry as required.

Methods: It was a cross-sectional study conducted from January 2022 to June 2023 in a tertiary care hospital. Fifty-seven patients study who underwent transurethral resection of the prostate (TURP) surgery with hypertrophied prostate during the study period were included in the study on the basis of a predefined inclusion and exclusion criteria. Demographic characteristics of all the cases were analyzed. Clinical features, presenting complaints, histopathological findings, and the final diagnosis were studied. For statistical purposes, p value < 0.05 was taken as statistically significant.

Results: The majority of the participants were in the age group of 60–69 years (42.11%) followed by people in the age group of 70–79 years (35.09%). Benign disease of prostrate was common than the malignant disease. BHP was the most common disease encountered and was seen in 37 (64.91%) cases. Among 37 patients with BHP, 70.27% (26) patients had increased PSA levels. Among 10 patients of BHP with CP 8 (80%) patients had increased levels of PSA. Serum PSA levels were increased in all the cases of malignancy, Adenocarcinoma prostate and PIN.

Conclusion: In patients undergoing TURP modified Gleason scoring patterns and prognostic grade grouping should be done in conjunction for assessing prognosis and management. Immunohistochemistry and molecular genetic analysis are valuable adjuncts to the diagnosis in these cases.

Keywords: Benign prostatic hyperplasia, TURP, Prostatic carcinoma, Molecular genetics.

INTRODUCTION

With advancing age, there is a significant increase in the prevalence of prostatic pathologies such as benign prostatic hyperplasia (BPH) and prostatic carcinoma. BPH is a prevalent condition is a common condition seen in elderly male individuals and is characterized by the non-cancerous enlargement of the prostate gland. This enlargement often leads to lower urinary tract symptoms (LUTS), which can significantly impair the quality of life. Transurethral resection of the prostate (TURP) remains a gold-standard surgical intervention for BPH, particularly in cases where medical management is ineffective. TURP not only alleviates symptoms but also provides valuable histopathological specimens for examination. The histomorphological study of these specimens offers insights into the pathophysiology of BPH and associated conditions, contributing to both diagnostic and prognostic advancements in urology. It is also important to differentiate between benign and malignant conditions of prostate [1].

TURP is the most frequently performed surgical procedure in the clinical practice, and it aids in the early identification of premalignant lesions and incidental prostate cancer which can improve the treatment outcome of patients. Gleason's microscopic grading with prostate-specific antigen (PSA) is important for the diagnosis, management, and prognosis of carcinoma [2].

The histopathological confirmation of diagnosis is also critical since malignant and benign lesions of prostate may have a very similar presentation but their management and prognosis are quite different. Histomorphological analysis in TURP specimens has the capacity to reveal subtle pathological changes that often go undetected in clinical assessments and imaging studies. This analysis encompasses the examination of tissue architecture, cellular morphology, stromal-epithelial interactions, and the presence of any atypical features. Recent advancements in histopathological techniques, including immunohistochemistry and molecular pathology, have further refined our understanding of prostatic diseases [3].

The histomorphological study of TURP specimens is also pivotal in understanding the etiology and progression of BPH. The enlargement of the prostate in BPH is primarily due to the proliferation of both stromal and epithelial elements. Histologically, this is seen as nodular hyperplasia, with varying degrees of stromal and glandular components. The role of hormones, particularly androgens, and estrogens, in modulating this proliferation, is a subject of ongoing research. In addition, the inflammatory component, as evidenced by the presence of chronic inflammatory cells in the stroma, has been increasingly recognized in the pathogenesis of BPH. This inflammatory infiltrate has been linked to prostatic enlargement and the worsening of LUTS, providing a potential therapeutic target [4].

Another critical aspect of histomorphological studies is the identification of incidental prostate cancer. The widespread use of TURP has inadvertently led to the detection of unsuspected prostate cancers, which might be clinically significant. The distinction between benign hyperplastic tissues and carcinoma, particularly in cases of small, well-differentiated tumors, can be challenging. Histopathological examination, therefore, plays a crucial role in the accurate diagnosis and staging of these cancers. The detection of incidental carcinoma in TURP specimens has substantial implications for patient management, influencing decisions regarding further treatment and surveillance [5].

The present study was taken to evaluate various histopathological lesions and correlate the histopathological findings with PSA level and immunohistochemistry as required.

METHODS

This was a prospective cohort study in which 57 patients who had undergone TURP were included on the basis of a predefined inclusion and exclusion criteria. The study was conducted in the Department of Pathology of Dr. Shankarrao Chavan Government Medical College, Vishnupuri Nanded, India. The sample size was calculated on the basis of pilot studies done on the subject of histopathological features of prostatic pathologies. Assuming 90% power and 95% confidence interval, the sample size required was 55 patients. Based on the central limit theorem, the sample size was calculated to be sufficient; if it was more than 55, thus 57 patients were included in the study. Demographic details such as age, gender, occupation, and socioeconomic status were noted.

The specimens were analyzed for histopathological patterns. The histopathological features were classified as either "glandostromal," (equal proportion of glandular proliferation and fibromuscular stroma), or stromal (stromal elements predominated). Prostatitis was differentiated into acute, marked by neutrophils within glands, and chronic, which was either nonspecific with mononuclear infiltrate or granulomatous. We also noted the presence of necrotic glands, typically surrounded or replaced by localized inflammatory infiltrate. Various types of epithelial hyperplasia, including papillary, basal, and cribriform, were observed mainly in glandular and stromal patterns. Atypical adenomatous hyperplasia was identified. Proliferative inflammatory atrophy was also noted. Assessment of the extent and severity of inflammation was noted. Incidental carcinoma prostate was identified by histopathological features. Prostatic-specific antigen level estimation was done in all cases.

The statistical analysis was done using Epi Info 7, presenting quantitative data as mean and standard deviation, while qualitative data were analyzed using frequency and percentage tables. Unpaired t-tests were employed for quantitative data, and Chi-square tests were used for qualitative data. $p < 0.05$ was taken as statistically significant.

Inclusion criteria
Patients with hypertrophied prostate with urinary complaints who had undergone transurethral resection of prostate were included in the study.

Exclusion criteria
Prostate samples of patients received by other surgeries (suprapubic prostatectomy, laparoscopic prostatectomy, laser prostatectomy, etc.) were excluded from the study.

RESULTS

The analysis of the age groups of the patients showed that the majority of the participants were in the age group of 61–70 years (42.11%) followed by people in the age group of 71–80 years (35.09%). The mean age of the cases was found to be 73.24±16.98 years (Table 1).

The majority of the cases 37 were of BPH. It was followed by BHP with CP seen more commonly in the age group of 60–69 years. PIN high grade was seen in two subjects. Prostatitis was seen in two subjects out of which one had squamous metaplasia. Poorly differentiated adenocarcinoma of prostate Gleason grade 4–5 was seen in 70–79 years age group. Two cases of adenocarcinoma prostate Gleason Grade 3 were noted in the age group of 60–69 and 70–79 years (Fig. 1).

The analysis of age-wise distribution of pathologies showed that BHP, accounting for 37 cases, was predominantly observed in the 61–70 and 70–79 age groups. BHP was often associated with chronic prostatitis (CP), evident in 10 cases. Adenocarcinoma of the prostate, particularly of Gleason grade 3, was identified in two patients, while high-grade prostatic intraepithelial neoplasia (PIN) was found in three cases across different age groups. Notably, acute on CP and its variant with squamous metaplasia were each reported in only one case. The data indicates

a higher prevalence of prostate-related conditions in the older age groups, particularly between 61 and 79 years (Figs. 2-5 and Table 2).

The most common symptom of presentation in our study was frequency of micturition which was seen 100% of the study subjects. Followed by incomplete voiding (96.49%), urgency (94.74%), straining (94.74%) intermittency (84.21%), and nocturia (80.70%). Hematuria was relatively less common and was seen in 3 (5.26%) cases (Table 3).

The analysis of prostate-specific antigen levels showed that significant prevalence of increased PSA levels, accounting for 77.19% (44 cases). In contrast, only 22.81% (13 cases) of the patients had normal PSA levels (Table 4).

Among 37 patients with BHP, 26 (70.27%) patients had increased PSA levels. Among 10 patients of BHP with CP 8 (80%) had increased

Table 1: Mean age of patients undergoing TUPR

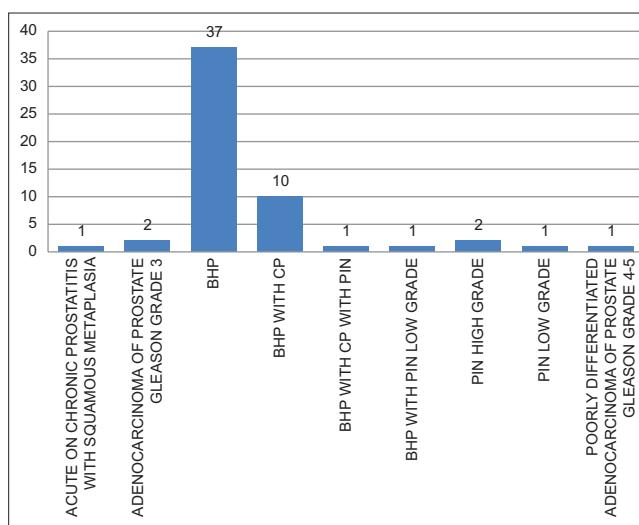| Age (in years)	Number of cases	Percentage
<60 years	5	8.77
61–70 years	24	42.11
71–80 years	20	35.09
Above 80 years	8	14.04
Total	57	100.00

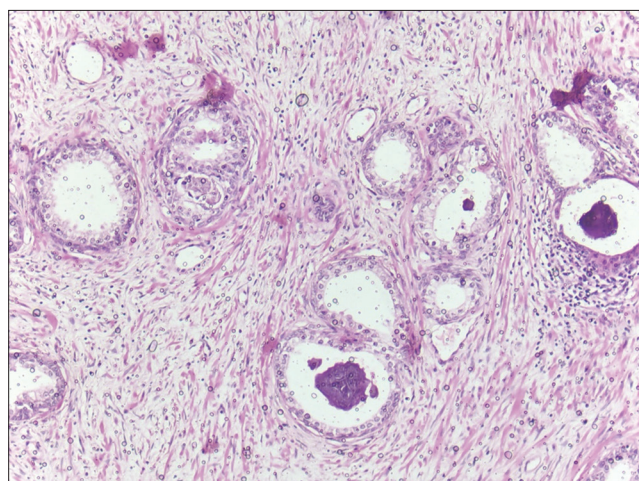**Fig. 1: Histopathological diagnosis of the studied cases**

Fig. 2: Benign hypertrophy of prostate (10×) glandular and stromal hyperplasia

Table 2: Age-wise distribution in individual cases

Histopathology report and age of patients	<60 years	61–70 years	70–79 years	80–89 years	Total
Acute on chronic prostatitis	0	1	0	0	1
Acute on chronic prostatitis with squamous metaplasia	0	1	0	0	1
Adenocarcinoma of prostate gleason Grade 3	0	1	1	0	2
BHP	4	14	14	5	37
BHP with CP	1	5	2	2	10
BHP with CP WITH PIN	0	1	0	0	1
BHP with PIN low grade	0	0	0	1	1
PIN high grade	0	1	1	0	2
PIN low grade	0	0	1	0	1
Poorly differentiated adenocarcinoma of prostate gleason Grade 4–5	0	0	1	0	1
Total	5	24	20	8	57

Table 3: Symptomatology of the studied cases

Symptoms	Frequency	Percentage
Frequency of micturition	57	100.00
Incomplete Voiding	55	96.49
Urgency	54	94.74
Straining	54	94.74
Intermittency	48	84.21
Nocturia	46	80.70
Haematuria	3	5.26

Table 4: Prostate specific antigen levels

PSA	Frequency	Percentage
Increased (Above 4.0 ng/mL)	44	77.19
Normal (<4.0 ng/mL)	13	22.81
TOTAL	57	100.00

Fig. 4: Prostatic intraepithelial neoplasia high grade (40×) overcrowding, clumping with variation in size of cells with prominent nucleoli
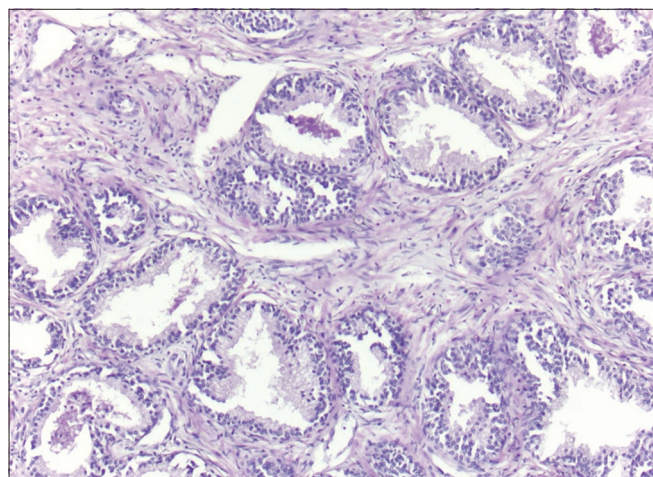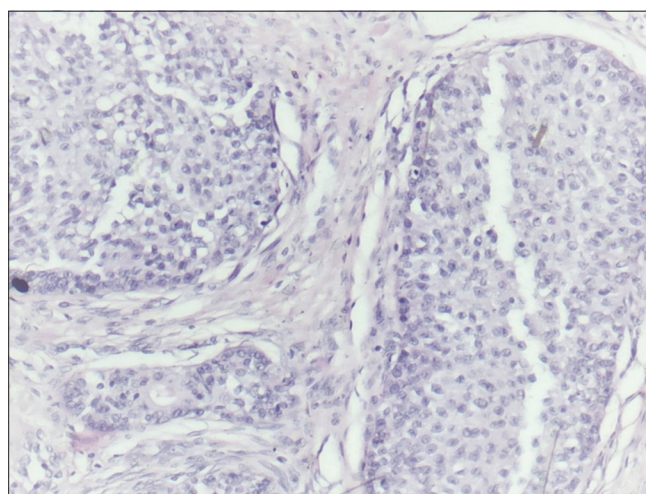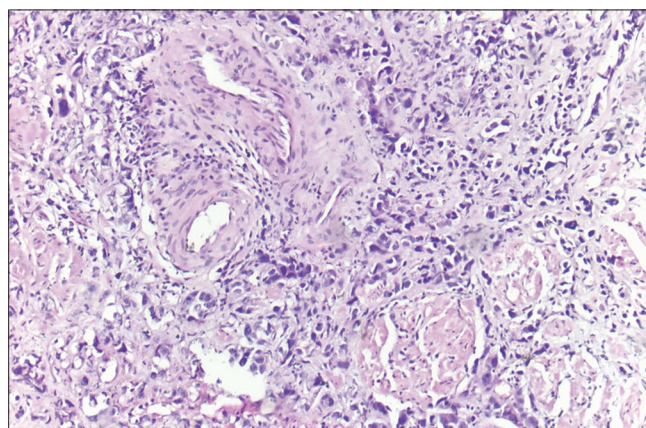

Fig. 3: Prostatic intraepithelial neoplasia high grade (10×)-overcrowding, clumping, and irregular stratification of epithelial cells with discontinuous basal layer

Fig. 5: Adenocarcinoma of prostate (40×) tumour cells arranged in ill formed glands and cords within stromal tissue

levels of PSA. Serum PSA levels were increased in all the cases of malignancy, adenocarcinoma prostate, and PIN. Poorly differentiated adenocarcinoma of prostate Gleason grade 4–5 was seen in 70–79 years age group. 2 cases of adenocarcinoma prostate Gleason grade 3 was noted in the age group of 60–69 and 70–79 years (Table 5).

DISCUSSION

In our study, out of the 57 TURP specimens received, 82.45% were non-neoplastic and 15.78% were reported as neoplastic and 11.11%

were inflammatory lesions. Diseases of the prostate, that is, both benign and malignant tumors are hormone (androgen) dependent and are associated with significant morbidity and mortality in man. Comparable results were recorded by Puttaswamy *et al.* [6].

Digital rectal examination (DRE) and transrectal ultrasonography are a preliminary practical diagnostic method but has low specificity and sensitivity. Abnormal DRE suspected of malignant prostatomegaly though appeared to be more sensitive in diagnosing the malignant cases, but it is confounding as many of the abnormal DRE turns out

Table 5: correlation of S. PSA LEVELS with HPE diagnosis

Histopathology report	Increased	Normal	Total
Acute on chronic prostatitis	1	0	1
Acute on chronic prostatitis with squamous metaplasia	1	0	1
Adenocarcinoma of prostate Gleason grade 3	2	0	2
BHP	26	11	37
BHP with CP	8	2	10
BHP with CP with PIN	1	0	1
Bhp with pin low grade	1	0	1
PIN high grade	2	0	2
PIN low grade	1	0	1
Poorly differentiated adenocarcinoma of prostate Gleason Grade 4–5	1	0	1
Total	44	13	57

to be benign by PSA estimation and tissue diagnosis thus suggesting discordance of abnormal DRE and the PSA level.

In our study, the most common prostatic lesion was BPH accounting for 85.96% of the cases studied, which is similar to other studies done in India. Similar findings that BPH is the most common lesion were noted in the studies conducted by Sumaya *et al.* [7], and Joshee and Sharma [8].

Prostatic lesions are extremely common over the age of 50 years. The clinical incidence of this disease is only 8% during the 4th decade but it reaches 50% in 5th decade and 75% in 8th decade of life [9]. Both BPH and carcinoma of prostate show parallel rise in incidence with advancing age [10]. In our study, the most common age group affected was between 60 and 69 years (7th Decade). These findings are similar to Yadav *et al.* [11] and Sharma *et al.* [12].

In our study, increased frequency of micturition was the most common presenting symptom followed by storage, incomplete voiding and urgency. In a study conducted by Gajjar *et al.* [13] difficulty in micturition was the most common presenting symptom followed by increased frequency of micturition.

Of the 48 non-neoplastic lesions, the PSA levels were within normal range of <4 ng/dL in 27.08% of cases, modestly elevated (4.1–10 ng/dL) in 41.66% and markedly elevated (>10 ng/dL) in 31.24% of cases. In our study, the lowest PSA level was 0.5 ng/dL, and highest was 27.66 ng/dL. In the study by Maru *et al.* [14], they found normal levels of PSA in 67.5%, modest elevation in 29.3% and marked elevation in 3.18%. The study done by Sinha *et al.* [15] showed 48% of non-neoplastic lesions with significantly elevated PSA of more than 20 ng/dl. The higher levels noted by us could possibly be related to the increased incidence of prostate hyperplasia in our study.

The Gleason grading system is based on histologic pattern of prostate tumor cells and is the most widely used grading method for prostatic adenocarcinoma. It determines microscopic heterogeneity of tumor cell present in prostate biopsy specimen through primary and secondary pattern of tumors cell. These patterns are added to obtain Gleason score ranging from ≤6 to 10, and group grade is assigned. Grade group I represents the most well differentiated tumors, in which neoplastic glands are uniform and round in appearance. By contrast, grade 5 tumors show no glandular differentiation and tumor cell infiltrates stroma into sheets, nest and cord [16].

In our study, the common primary Gleason scores is 4 (100%) which is similar to other study by Kumar *et al.* [17] with scores 4(43.6%). Another study by Krishnappa *et al.* [18] reported primary score 4 (54.5%) as the most common score; they also reported Score 2 (12.7%) commonly, which is not the case in our study. In our study, the most common secondary score is 3 (66.67%) which is contrast to studies by Kumar *et al.* [17], who scored 4 (43.6%and 50% respectively) commonly.

Secondary scores of 1 and 2 were not reported in our study as well as in the comparative studies.

Combined Gleason Scores of 2 and 3 are not assigned as Gleason pattern one is unusual. Gleason Score 4 is also unusual because pattern 2 is usually mixed with pattern 3 resulting in a combined score of 5. Tumors with Gleason scores 2–4 may be seen in TURP material sampled from the transitional zone but not in needle biopsy which samples the peripheral zone [19].

Low-grade lesions were not encountered in our study probably because these lesions are usually asymptomatic. All the cases in this study had a Gleason score of seven or more. This could be due to a delay in accessing the healthcare due to various factors. These findings were similar to the findings reported by Atchyuta *et al.* [20].

CONCLUSION

Modified Gleason scoring patterns and prognostic grade grouping should be done in conjunction for assessing prognosis and management until it is widely accepted and practiced for early diagnosis, treatment, and for reducing mortality and morbidity. Immunohistochemistry and molecular genetic analysis should be done along with screening protocols and awareness programs should also be carried out.

SOURCE OF FUNDING

None.

CONFLICTS OF INTEREST

None.

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