Original Article

Histopathological Study of Prostatic Lesions in a Tertiary Care Hospital, Lahore

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ABSTRACT

Objective: To determine the spectrum of pathological lesions seen in prostatic biopsies & to grade prostatic cancers according to the modified Gleason score & grade.

Methodology: It was a retrospective study conducted at the Department of Pathology, Mayo Hospital/King Edward Medical University, Lahore commencing from January 2018 to December 2020. Previous histopathology reports, blocks, & recut slides were studied for the type of biopsy specimen, age of the patient, histopathological diagnosis, and morphological patterns (Gleason score and grade) in cases of prostatic carcinoma.

Results: A total of 629 prostate specimens were received during the study period. These constituted 500(79.49%) transurethral resection of prostate (TURP) specimens, 87(13.84%) core needle biopsies, and 42(6.67%) radical prostatectomy specimens. The specimens constituted 549(87.28%) benign lesions and 80(12.71%) malignant cases. Benign lesions included benign prostate hyperplasia constituting 461(73.3%) cases & hyperplasia associated with prostatitis constituting 88(14%) cases. Malignant cases included 76(12.1%) cases of prostatic adenocarcinoma and 4 cases of metastatic deposits. Two hundred and twenty eight (41.53%) cases of benign prostatic hyperplasia and 37(46.25%) cases of prostatic carcinoma were observed in 61-70 years age group. Collectively, a total of 543(86.73%) cases were seen in the age range of 51-80 years. The maximum number of prostatic cancers (45 cases/59.20%) had the highest Gleason scores of 9 & 10(grade group 5) & only 2 cases had the lowest score of 6(grade group 1).

Conclusion: Benign prostatic hyperplasia & prostatic carcinoma are the two most common pathological lesions affecting the prostate.

Keywords: *Benign prostatic hyperplasia. Prostatitis. Prostate adenocarcinoma.*

INTRODUCTION

The prostate gland, a fibromuscular organ that encircles the neck of the urinary bladder normally weighs up to 20 gms.[1] On histological examination, the normal prostate gland comprises of variable sized glands lined by bilayered epithelium surrounded by spindle-shaped stromal cells.[2] Pathological lesions of the prostate occur more frequently after the age of 50 years and constitute a significant cause of morbidity and mortality in males of advancing age.[3] The incidence of prostatic lesions increases with advancing age with 8% occurring during the 4th decade, followed by 50% in the 5th decade and rising dramatically to 75% in the 8th decade.[4] Patients usually present with symptoms of urinary dribbling/incontinence, hesitancy, urinary retention, and rarely hematuria.[5] Benign prostatic hyperplasia (BPH), prostatic carcinoma, and prostatitis are the main pathological lesions affecting the prostate gland.[6] Amongst these, benign prostatic hyperplasia is the most common urological condition in men. At 40 years of age, the incidence of benign prostatic hyperplasia is reported to be 20% whereas, it rises to 90% by the 8th decade of life.[7] Worldwide, prostatic carcinoma is the second most commonly reported malignancy after lung cancer and the 6th most common cause of cancer death amongst males.[8] Prostatitis, an inflammation of the prostate gland can be classified as acute, chronic, and granulomatous. It is usually seen in association with nodular hyperplasia of the prostate & accounts for approximately 10-15% of cases.[9]

Serum prostate-specific antigen (PSA), digital rectal examination (DRE), and transrectal ultrasound are the main first-line screening methods for prostate carcinoma but biopsy remains the ultimate gold standard diagnostic tool.[10] The normal range for PSA levels is 0-4 ng/dl, with a borderline value ranging between 4-10 ng/dl, and more than 10 ng/dl is considered high and worrisome. Prostatitis, prostatic trauma, benign prostatic hyperplasia, and prostatic carcinoma lead to raised serum PSA levels.[11] High-grade prostatic intraepithelial neoplasia (HG-PIN) is a well-established precursor lesion of invasive prostatic cancer and its identification in biopsies along with elevated serum PSA levels is an indication for repeat biopsy and close follow-up.[12]

The modified Gleason grading system is the gold standard for the management and grading of prostate cancers. It was introduced by Dr. Donald Gleason in 1966, modified by the International Society of Urology Pathology (ISUP) in 2005, subsequently revised in 2014, and accepted by the World Health Organization

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in 2016.[13] It depends on observing the degree of glandular architectural differentiation & growth pattern of the tumor relative to the stroma at low to medium power of the microscope rather than concentrating on the cytological details, therefore it is reliable, simple, and not time-consuming.[14]

The Gleason grading system comprises of 5 histological patterns of prostate adenocarcinoma. Gleason grade group 1 and 2 are the most differentiated types with discrete well-formed glands arranged back to back with little intervening stroma and may mimic benign lesions.[15] Grade group 3 cases have infiltrating glands, lined by single-cell layer, grade group 4 shows ragged infiltrating glands with cribriform & fusion of glands and lastly grade group 5 demonstrates sheets, cords, comedocarcinoma pattern with central necrosis as well as singly infiltrating cells but no glandular formations.[16]

The purpose of this study was to determine the age distribution and the histological spectrum of various prostatic lesions in our population and to grade prostate adenocarcinoma according to the modified Gleason grading system.

METHODOLOGY

The study was conducted in the Department of Pathology, Mayo Hospital/King Edward Medical University, Lahore, Pakistan. It was a 3-year retrospective study commencing from January 2018 to December 2020. The study was approved by the ethical review committee of the University (Letter No: 498/RC/KEMU, 09-07-2021). The data for prostate lesions was collected from the histopathology database of the Department of Pathology. During this period, a total of 629 prostate specimens comprising of transurethral resection of the prostate (TURP), radical prostatectomy (RP), and core needle biopsy (CNB) specimens were evaluated. The histopathology reports and blocks were retrieved from previous records. Fresh slides were prepared and reviewed to reconfirm the previous diagnosis and to analyze the following parameters: type of specimens, age of the patients, benign & malignant categories, & histopathological diagnosis.

In cases diagnosed as prostate cancer, modified Gleason scoring & grading were applied according to the new morphological guidelines as shown in Table 1.

STATISTICAL ANALYSIS

The data was analyzed using Statistical Package for the Social Sciences (SPSS) version 21. Frequency & percentages were calculated for the type of prostate specimens received, age, benign & malignant categories, and Gleason score & grade.

RESULTS

The present study included a total of 629 prostate surgical specimens with 500(79.49%) cases of TURP specimens, 42(6.67%) cases of radical prostatectomy, and 87(13.84%) cases of CNB specimens. The specimen constituted 549(87.28%) benign lesions and 80(12.71%) malignant cases.

Out of a total of 629 prostate specimens, 461(73.3%) cases were reported as benign prostatic hyperplasia

Table 1: The New Contemporary Prostate Cancer "ISUP Modified Gleason Grading System"[13]

New Grading System Morphologic Patterns and Grade Group Pattern Composition	
Grade Group	**Pattern Definition**
Grade Group 1(Gleason score ≤6)	Only individual, discrete, well-formed glands
Grade Group 2(Gleason score 3 + 4 = 7)	Predominantly well-formed glands with a lesser component of poorly formed/fused/cribriform glands
Grade Group 3(Gleason score 4 + 3 = 7)	Predominantly poorly formed/fused/cribriform glands with a lesser component of well-formed glands[a]
Grade Group 4(Gleason score 8)	Only poorly formed/fused/cribriform glands or predominantly well-formed glands with a lesser component lacking glands[b] or predominantly lacking glands with a lesser component of well-formed glands[b]
Grade Group 5(Gleason scores 9-10)	Lacks gland formation/necrosis with or without poorly formed/fused/cribriform glands[a]

[a] For cases with more than 95% poorly formed/fused/cribriform glands or lack of glands on a needle core or at radical prostatectomy, the component of less than 5% well-formed glands is not factored into the grade.
[b] Poorly formed/fused/cribriform glands can also be a more minor component.

(Figure 1), 88(14%) cases as prostatic hyperplasia with associated prostatitis (Figure 2), including one case of granulomatous prostatitis (Figure 3), 76(12.1%) cases of prostatic carcinoma and 4(0.6%) cases of metastatic carcinoma deposits from the urinary bladder were observed. No case of prostatic-intraepithelial neoplasia (PIN) was reported.

The present study was distributed in the age range of 42-94 years. The age range was stratified as ≤50 years, 51-60 years, 61-70 years, 71-80 years, 81-90 years, and above 90 years of age. The maximum number of prostatic lesions were observed in the age range of 61-70 years accounting for 265(42.13%) cases, followed by the 71-80 years age range with 140(22.25%) cases. Two hundred and twenty eight (41.53%) cases of benign prostate hyperplasia and 37(46.25%) cases of prostatic carcinoma were observed in the 61-70 years age group (Table 2).

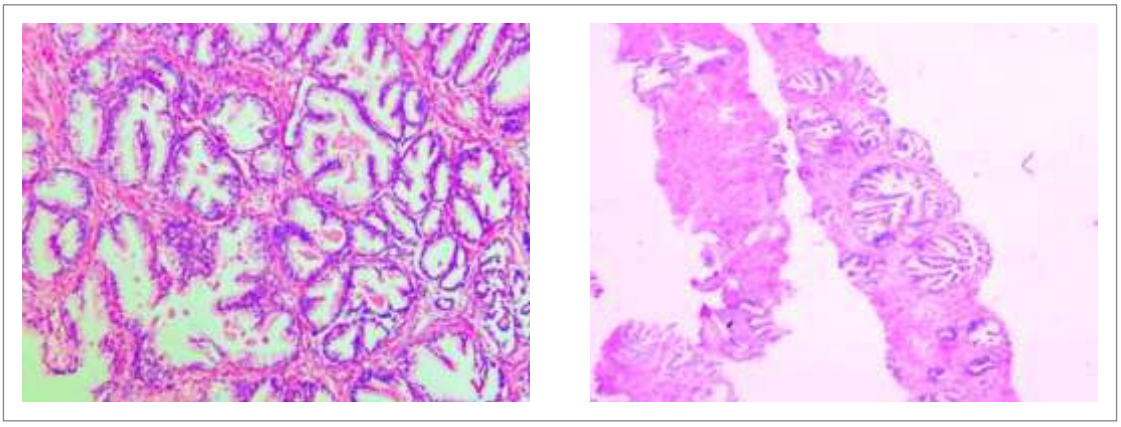

Figure 1: Benign Prostatic Hyperplasia (Left: Section from Radical Prostatectomy Specimen. Right: Core Needle Biopsy). Benign Hyperplastic Glands Lined by Bilayered Epithelium with Surrounding Fibromuscular Stroma. The Lumina Show Corpora Amylacea (Left: H & E stain, 100x magnification, Right: H & E stain, 40x magnification)

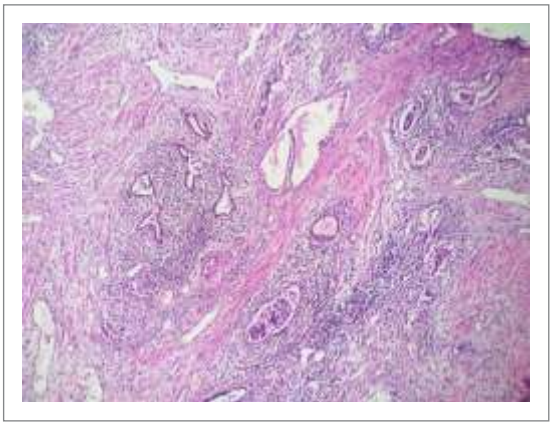

Figure 2: Chronic Prostatitis: Lymphoplasmacytic Infiltrate Surrounding Prostatic Acini & Ducts (H & E stain, 40x magnification)

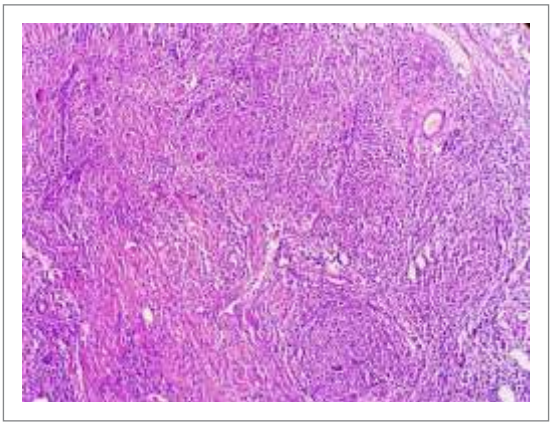

Figure 3: Chronic Granulomatous Prostatitis: Well-Formed Granulomas with Langhan's Type of Giant Cells (H & E stain, 40x magnification)

Table 3 depicts the number of prostate cancer cases with their assigned Gleason scores & grade groups. There were only 2(2.63%) cases having the lowest score of 6 with a grade group 1. A score of 7(grade group 2 & 3) was assigned to 8(10.52%) cases (Figure 4 & 5), 21(27.63%) cases were given a score of 8(grade group 4, Figure 6), 37(48.68%) cases were assigned a Gleason score of 9(grade group 5), & 8(10.52%) cases

were assigned a score of 10(grade group 5, Figure 7 & 8). Collectively, grade group 5 was observed in 45(59.20%) cases which accounted for the maximum number of cases in the study. In the present study, the perineural invasion was seen in 52 out of 76 prostatic cancers of which 32(43.2%) cases had high Gleason scores of 9 & 10 (Figure 9).

Table 2: Age Distribution of Cases (n=629)

Age in Years	Benign Cases 549(87.28%)	Malignant Cases 80(12.71%)	Total No. of Cases 629(100%)
≤50	73(13.3%)	4(5%)	77(12.24%)
51-60	109(19.85%)	29(36.25%)	138(21.93%)
61-70	228(41.53%)	37(46.25%)	265(42.13%)
71-80	132(24.04%)	8(10%)	140(22.25%)
81-90	4(0.73%)	1(1.25%)	5(0.79%)
>90	3(0.55%)	1(1.25%)	4(0.63%)

Table 3: Categorization of Prostatic Cancer Cases according to Modified Gleason Grade Group & Score (n=76)

Gleason Grade Group (Score)		Frequency (Percentage)
Grade Group 1(3+3=6)		2(2.63%)
Grade Group 2(3+4=7), Grade Group 3(4+3 =7)		8(10.52%)
Grade Group 4(4+4=8), (3+5=8), (5+3= 8)		21(27.63%)
Grade Group 5	(4+5=9), (5+4=9)	37(48.68%)
	(5+5=10)	8(10.52%)

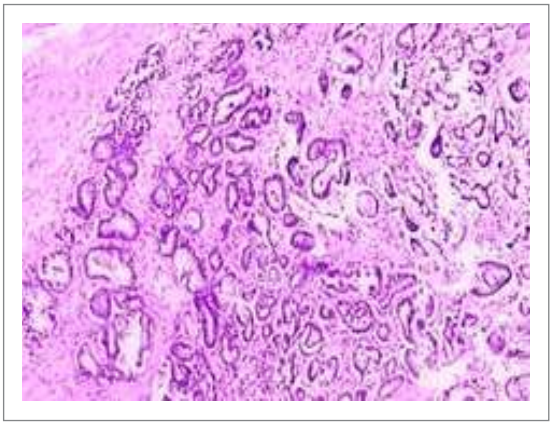

Figure 4: Gleason Grade Group 2(3+4=Score 7): Crowded, Predominantly Well-Formed Neoplastic Glands, Arranged in a Back to Back Pattern (H & E stain, 100x magnification)

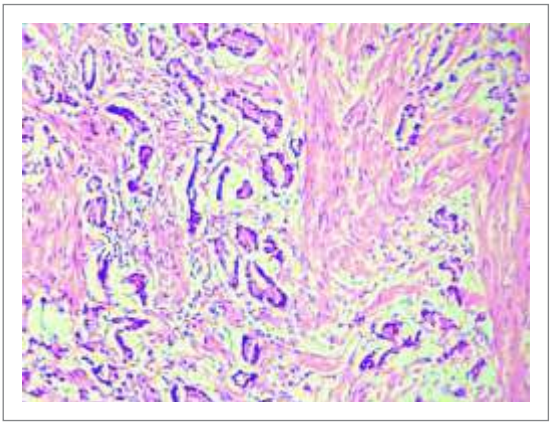

Figure 5: Gleason Grade Group 3(4+3 = Score 7): Neoplastic Glands Showing Infiltration into the Surrounding Stroma (H & E stain, 100x magnification)

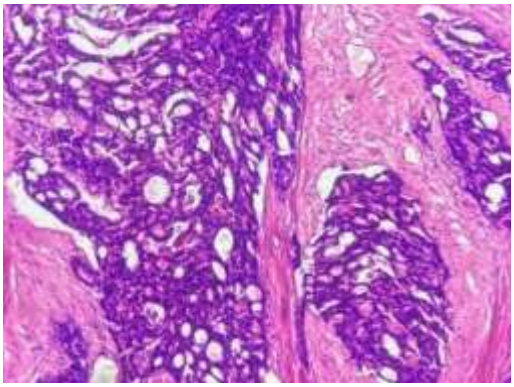

Figure 6: Gleason Grade Group 4(4+4 = Score 8): Fused Glands with a Cribriform Pattern (H & E stain, 100x magnification)

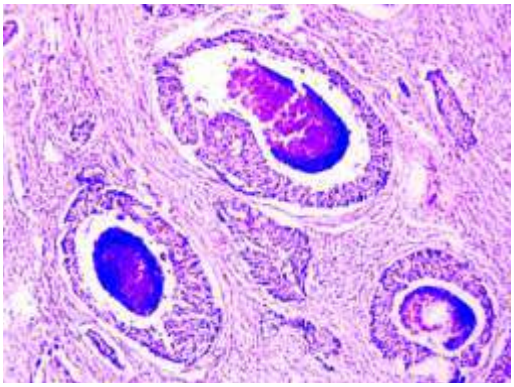

Figure 7: Gleason Grade Group 5(5+5 = Score 10) Showing Comedonecrosis: Central Necrosis with Intraluminal Necrotic Cells (H & E stain, 100x magnification)

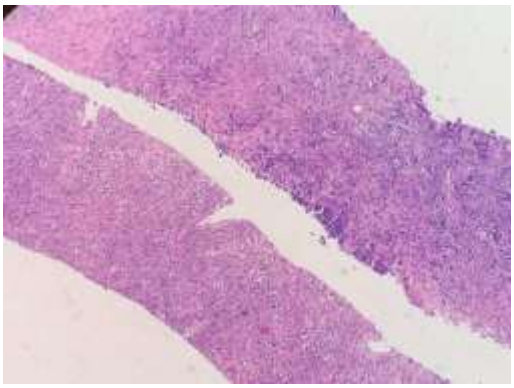

Figure 8: Gleason Grade Group 5(5+ 5 = Score 10): Core Needle Biopsy Showing Complete Lack of Gland Formations & Tumor Cells Disposed of as Sheets (H & E stain, 100x magnification)

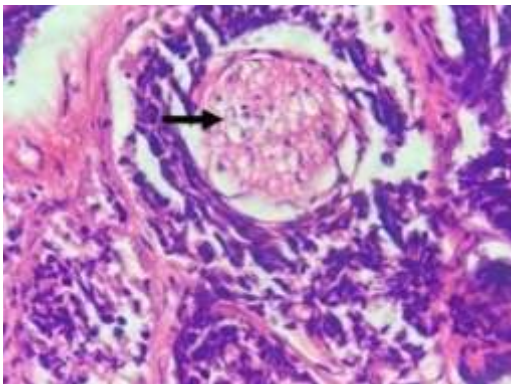

Figure 9: Perineural Invasion: Malignant Glands Circumferentially Enclosing & Surrounding a Nerve (Arrow) (H & E stain, 400x magnification)

DISCUSSION

Prostatic biopsy specimens constitute a substantial percentage of the histopathology workload in tertiary care hospitals.[7] Various benign and malignant entities present with similar clinical features, however, their further management and prognosis differ widely. So, exact histological diagnosis plays a crucial role.[10]

In the present study, TURP chips constituted 500(79.49%) cases, core needle biopsies 87(13.83%) cases, and radical prostatectomy specimens constituted 42(6.67%) cases. Other studies also reported a high percentage of TURP specimens in different settings.[3,4,17] Transurethral resection of the prostate is comparatively simple with fewer complications. It aids in the early diagnosis and identification of premalignant, malignant lesions, and incidental prostatic cancer lesions.[3]

According to our results, out of a total of 629 prostatic biopsies, 549(87.28%) cases were benign and 80(12.71%) cases were malignant. The commonest benign lesion reported was benign prostatic hyperplasia accounting for 461(73.3%) cases followed by 88(14%) cases of prostatitis associated with nodular hyperplasia. In the malignant category which constituted 80(12.71%) cases, 69(86.25%) cases were reported as acinar adenocarcinoma, 7(8.75%) cases as ductal adenocarcinoma, and 4(5%) cases as metastatic deposits to the prostate of urothelial origin.

A study published in 2018 on 321 prostatic specimens reported 279(86.91%) cases as non-neoplastic &

42(13.09%) cases as neoplastic which included 27 malignant cases & 15 cases of premalignant lesions like PIN. The most common non-neoplastic entity reported was nodular hyperplasia which constituted 279(86.91%) cases in which 117(42.09%) cases had an associated component of prostatitis.[17] A study by Sabalpara et al., in 2019 on 156 prostatic biopsies categorized 112(71.79%) cases as benign and 44(28.21%) cases as malignant. All benign cases constituted of nodular hyperplasia and no case of prostatitis was reported. Out of the 44 malignant cases, 43 were acinar adenocarcinoma and 1 case was ductal adenocarcinoma.[18]

In a 14-year retrospective review study conducted in Nigeria, 4292 prostate biopsies were reported in which benign nodular hyperplasia constituted 3257(76%) cases and prostate cancer 1035(24%) cases. In 81(2.5%) cases, nodular hyperplasia was associated with prostatitis.[19] A study conducted in Jaipur, Rajasthan, India reported that out of a total of 150 cases, 131(87.33%) cases were of nodular hyperplasia, 16(10.66%) cases were carcinoma prostate, and 3(2%) cases were PIN.[12]

Regarding the age distribution of prostatic lesions, 265(42.13%) cases were reported in the age group of 61-70 years and 140(22.25%) cases in the age group 71-80 years. Out of 629 cases, 543(86.73%) were seen in the age range of 51-80 years. Similarly, a study published in 2020 on 160 cases also reported a maximum of 63(39.38%) cases in the age range of 61-70 years.[2] Similarly, another study by Yadav et al., on 100 prostatic biopsies also reported 42(42%) cases in the 61-70 year age range with 38 benign and 4 malignant cases.[1]

Sumaya et al. reported a maximum of 37(41.1%) cases of prostatic lesions in the age group of 61-70 years followed by 71-80 years age group with 23(25.6%) cases.[3] In another study it was found that maximum cases (51.9%) of nodular hyperplasia and prostatic adenocarcinoma (43.8%) were in the age category of 61-70 years.[19] A similar result was noted by Bhatta et al., who reported that the benign lesions are common in the age group of 61-70 years but malignant cases predominate in the age group of 71-80 years.[9]

In the present study, prostatitis associated with hyperplasia was observed in 88(14%) cases. In the study by Yadav et al., prostatitis associated with nodular hyperplasia was observed in 10% of cases.[1] Rajani et al. reported 6.9% cases of chronic prostatitis with BPH.[2] In a study of 321 cases, 117 cases were reported as chronic prostatitis, of which 05 cases were granulomatous prostatitis and 112 non-granulomatous prostatitis.[17]

In the present study, out of 76 cases of carcinoma prostate, a maximum of 37(48.68%) cases were assigned a high Gleason score of 9(grade group 5) & 8(10.52%) cases the highest score of 10(grade group 5). A score of 8(grade group 4) was observed in 21(27.63%) cases, score 7(grade group 2 & 3) in 8(10.52%) cases, & only 2(2.63%) cases had the lowest score of 6(grade group 1). A study by Shah et al., reported a Gleason score of 9(grade group 5) in 40% cases, a score of 8(grade group 4) in 30% cases & a score of 7(grade 2) & 6(grade 1) in 20% & 5% cases, respectively.[6] Similarly, another study reported that 37.3% cases had Gleason score 9(grade group 5).[9] Sujatha et al. reported a Gleason score of 7 in 47.36% cases.[10] Another study showed that in 23 cases of prostate cancer, Gleason score 7 was assigned to 11(47.8%) cases, 7 cases had Gleason score 8 & 2(8.7%) cases had score 6 & Gleason score 9 also included 2(8.7%). Only one (4.35) case had the highest Gleason score of 10.[2]

An increasing Gleason score & grade is associated with a poor prognosis with 5-year recurrence-free survival rates. The study estimated that a Gleason score of ≤6(grade 1) was associated with an 88.8% 5-year survival rate, a score of ≤7(grade 2 & 3) with 55.8%, a score of ≤8(grade 4) with 50.4%, and a score of ≥9(grade 5) with 23.5 % 5-year survival rates.[20]

In the present study, the perineural invasion was seen in 52 out of 76 prostatic cancers, of which 32(43.2%) cases were associated with high Gleason scores of 9 & 10. Perineural invasion is associated with a poor disease outcome.[21] It is commonly seen in prostatic cancers with higher Gleason scores & is a predictor of extraprostatic extension of tumor & ultimately recurrence.[14] A study by Bhatta et al., reported perineural invasion in 37.5% cases & Sujatha et al., reported perineural invasion in 5(26.31%) cases out of 19 prostate cancers, which are in accordance with the present study statistics.[9,10]

CONCLUSION

Benign lesions of the prostate are more common than malignant cases. The most common benign lesion is nodular hyperplasia. Prostate adenocarcinoma is a commonly occurring malignant lesion.

RECOMMENDATIONS

- Modified Gleason grading and scoring system should be applied in cases of prostate adenocarcinoma to improve management and disease surveillance.
- All TURP chips should be thoroughly examined to rule out premalignant lesions like PIN and for the detection of incidental cancers.

- Mass awareness programs should be created and projected in the male population.

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