ORIGINAL RESEARCH

Spectrum of prostatic lesions in a tertiary care hospital, north-east of India

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ABSTRACT

Introduction: Establishing or ruling out the diagnosis of carcinoma of prostate has been a challenging task for pathologists for many years .it was an observational study where patients who underwent TURP procedure were studied. The present study is an attempt to understand the histopathological spectrum of prostatic lesions and study the demographic distribution of various prostatic lesions.

Methods: The present study includes 125 cases of prostate specimen from January 2018 to September 2021 received in the post graduate department of Pathology, Tripura Medical College. H and E stained sections were examined. The relevant clinical details pertaining to age, clinical complaints and microscopic details are analyzed and compared with other similar studies.

Result: Total 125 case were studied among which 69 (55.2%) cases were found to be consistent with BPH and 24 cases were found to be malignant lesion (19.2%). 24 cases were found to be BPH with associated prostatitis like features, consistent with benign prostatic lesion. High grade Prostatic Intraepithelial lesions were seen in 8 cases (6.4%). Out of the 24 malignant cases, majority had Gleason score between 8-10. Perineural invasion was seen in 10 out of 24 malignant cases (41.6%). All malignant lesions were adenocarcinoma and 20 were incidental carcinoma which accounted for 16% of all prostatic lesions. Serum prostate specific antigen levels were available in 24 cases of prostatic adenocarcinoma cases. 21 out of 24 cases had serum prostate specific antigen levels greater than 10 ng/ml. (87.5%). Grade Group 4 had the maximum number of cases i.e 45.8%. Out of 125 cases, 89 (71.2%) cases were from urban areas and 36 (28.8%) cases were from rural areas. All the 24 cases with prostatic adenocarcinoma were from urban areas.

Conclusion: Our study concluded that Benign Prostatic Hyperplasia (BPH) is the commonest lesion among males with features of prostatism and most common type of inflammation associated with BPH is chronic inflammation. The commonest age group affected by both carcinoma and BPH is the seventh decade. Perineural invasion is a significant finding and guide and is usually seen with high Gleason score prostatic

cancer. Serum PSA is a useful test in cases where the values are higher. Awareness and accessibility to early diagnosis could be the result of majority of cases from urban areas.
Keywords: Prostatic Hyperplasia, Transurethral Resection of Prostate, Prostate Specific Antigen, Adenocarcinoma

INTRODUCTION

Worldwide, diseases of prostate gland are responsible for significant morbidity and mortality among adult males[1]. They can be broadly divided into inflammatory lesions (prostatitis), nodular hyperplasia (benign prostate hyperplasia) and prostatic carcinoma. Prostate cancer is the most common malignant tumor in men all over the world and is also the second important cause of cancer related deaths in men after lung cancer[2]. The incidence of prostate cancer increases with increasing age. Prostate gland of male reproductive system is about the size of walnut and surrounds the urethra. It produces and store a milky white fluid which becomes the part of semen and consists of sugars, proteins and other chemicals which help the sperm to survive in female genital tract[3]. Most hyperplasia occurs in transitional zone while most carcinoma originates in the peripheral zone. Most frequently encountered diseases affecting prostate are prostatitis, benign prostatic hyperplasia and prostate cancer[4].

Benign Prostatic Hyperplasia or Nodular Hyperplasia is the non-malignant adenomatous overgrowth of prostate gland. It is characterized by hyperplasia of prostatic stromal and epithelial cells, resulting in the formation of large discrete nodules in peri-urethral region of prostate.

It often presents with lower urinary tract symptoms. Symptoms include weak stream, hesitancy, frequency, urgency, nocturia, incomplete emptying, terminal dribbling, and overflow or urge incontinence and complete urinary retention. Incidence of prostatic cancer is increases proportionally after age of 50 years. In approximately, 70% of cases it arises in the peripheral zone of gland particularly in the posterior location. Adenocarcinoma is its most common histological variant. Most important risk factors for developing prostate carcinoma are positive family history, increasing age, lack of exercise and high calcium intake. In most cases, it is asymptomatic and develops slowly. However, it may present with pain, difficulty in urinating and problems during sexual intercourse[5].Androgens have an important role to play in the pathogenesis of benign prostatic nodules as well as in prostate carcinoma. Thus anti-androgen treatment is very effective in both scenarios, benign or malignant[6].

AIMS AND OBJECTIVES

1. To find out the prevalence of malignant and non- malignant prostatic lesions.
2. To study the demographic distribution of various prostatic lesions.

METHODOLOGY

STUDY SETTING

Pathology department of Tripura Medical College, Hapania

STUDY DESIGN

Observational study

STUDY DURATION

January 2018-September 2021

STUDY SUBJECTS

INCLUSION CRITERIA

All male patients who underwent TURP procedure

EXCLUSION CRITERIA
Patient not willing to participate, undiagnosed cases due to improper fixation, cases advised for repeat sample due to inadequacy.

SAMPLE SIZE
125 samples were taken for this study.

SAMPLING TECHNIQUE
Purposive sampling

DATA COLLECTION PROCEDURE
1. Histopathology registers of pathology department, TMC
2. **Staining of sections**: Prostatic Trucut biopsies were sent to pathology department for evaluation. Biopsies were fixed in 10% formalin. Routine paraffin processing of tissue and hematoxylin and eosin staining were done. New stained sections were made wherever required such as in case of old faded slides which were retrieved and reviewed. Hematoxylin stains the acidic part of the cell, i.e nucleus blue/black and eosin stains the basic part of the cell, i.e cytoplasm varying shades of pink[7].
3. Written consent was taken from the patient for participation in the study. As per the ethical guidelines, it is mandatory to provide consent to participate in this study.

DIAGNOSTIC CRITERIA
The major fundamental criteria for histologic diagnosis of adenocarcinoma of prostate were three things, assessment of glandular architecture, loss of basal polarity and altered nuclear features of the glandular lining cells[8].
Prostatic adenocarcinoma,exhibit an abnormal architectural glandular pattern with disarray of benign epithelial–stromal relationships.These changes were best appreciated at low-power scanning microscopy. A host tissue response is sometimes noted in stromal infiltration by adenocarcinoma, including a fibrogenic response and inflammatory response. The inflammatory response was seen, 10% lymphocytic and unusually intraluminal neutrophilic infiltration was also evident.Occasionally intraluminal neutrophic infiltrations are also appreciated.
Loss of basal cells is the second major defining attribute of invasive adenocarcinoma. In normal conditions, basal cells separate secretory luminal cells from the basement membrane.They are usually rounded or oblong cells with small hyperchromatic nuclei and scant cytoplasm. Sometimes it becomes a matter of challenge to distinguish basal cells of prostate glands from periglandular fibroblasts and myofibroblasts, based on examination of H&E-stained sections.Furthermore, prostatic adenocarcinoma cells that have thick sections, are mostly poorly fixed and preserved, and are distorted or crushed, they may mimic basal cells.Another diagnostically challenging work is to diagnose small foci of adenocarcinoma in otherwise benign prostate or benign looking deceptive adenocarcinomas.In such conditions, immunohistochemistry to detect basal cell specific are extremely beneficial[9].
Nuclear atypia in the form of nuclear enlargement and nucleolar enlargement is the third of the major criteria. Nuclear atypia in malignant glands is most often appreciated as nuclear enlargement and prominent nucleoli. A classical appearance of a prostatic carcinoma nucleus is a single large nucleus with chromatin clearing and a deeply staining macronucleolus. Presence of prominent nucleoli was advocated as diagnostic criterion of prostate cancer. Most of these prominent nucleoli were in areas of inflammation, basal cell hyperplasia, atrophy, or

Paneth cell-like change. In addition to nucleolar prominence, multiple nucleoli and nucleolar margination have also been suggested as diagnostic criteria for prostate cancer. Multiple nucleoli are never found in benign gland.Perineural invasion, presence of glands in a perineural location used to be considered as a diagnostic hallmark of malignancy. Circumferential growth or intraneural invasion should be regarded as pathognomonic of cancer.The presence of prostatic glands just adjacent to nerve is not, however, definitively diagnostic of malignancy. Benign prostatic glands can also wrap around nerves[10]. One should analyse the cytologic features of the epithelial cells around a nerve meticulously to distinguish benign from malignant perineural epithelium.

All the adenocarcinomas were graded on the basis of Modified Gleason score.

Pattern 1: Circumscribed nodule of closely packed uniform glands.

Pattern 2: Circumscribed nodule of loosely packed slightly variable glands.

Pattern 3: Single glands of variable size and density with an infiltrative pattern, each separated by at least a strand of stroma.

Pattern 4:

- Ragged infiltration with poorly formed glands or sheets and cords of fused glands.
- Poorly formed glands include small nests of cells with only a rudimentary formed luminal space (almost rosette like).
- Cribriform pattern.
- Glomeruloid bodies are pattern 4 by definition.
- Clear cell hypernephroid is pattern 4 by definition.
- **Pattern 5:** Ragged infiltrative single cells, cords or sheets without gland formation, small solid cylinders or any pattern with comedo-necrosis.

GRADING OF ADENOCARCINOMA OF PROSTATE

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 lesser component of poorly formed/fused/cribriform glands

Grade Group 3

- Gleason score 4+3=7
- Predominantly poorly formed/fused/cribriform glands with lesser component of well formed glands*

Grade Group 4

- Gleason score 4+4=8, 3+5=8, 5+3=8
- Only poorly formed/fused/cribriform glands or
- Predominantly well formed glands and lesser component lacking glands** or
- Predominantly lacking glands and lesser component of well formed glands**

Grade Group 5

- Gleason score 9-10
- Lacks gland formation (or with necrosis) with or without poorly formed/fused/cribriform glands*

*For cases with > 95% poorly formed/fused/cribriform glands or lack of glands on a core or at radical prostatectomy, the component of <5% well formed glands in not factored into the grade.

**Poorly-formed/fused/cribriform glands can be a more minor component [11].

RESULT

During the period of 3 years and 8 months from 1st January 2018 to 31st September 2021, 125 prostatic specimens were received. Age range of patients was 40-90 years. Majority of cases were in the age group 61 -70 years (48.8%).Most common presenting feature was increased frequency of micturition and secondmost was difficulty in starting and stopping of urine. Out of the 125 cases, most of the prostatic lesions were benign (80.8%) with 24 cases presenting with prostatitis. Malignant lesions comprised of 19.2% of all prostatic lesions. Majority of the cases were seen above 60 years of age with most cases falling in 61-70 year age group. Prostatic cancer was most commonly seen in 71-80 year age group. All the cases werehistopathologically adenocarcinoma. Out of the 24 cases of carcinoma prostate all cases had a Gleason Score of more than 6. Perineural invasion was seen in 10 cases out of 24 cases (41.6%).Out of the 24 malignant cases, all were adenocarcinoma and 20 were incidental carcinoma which accounted for 16% of all prostatic lesions.

Table 1

Age group	BPH	BPH with Prostatitis	Prostatic intraepithelial neoplasia(high grade)	Prostatic Carcinoma
41-50	08	3	0	0
51-60	19	3	1	4
61-70	32	15	3	7
71-80	8	5	3	12
81-90	02	1	1	1
Total	69	24	8	24

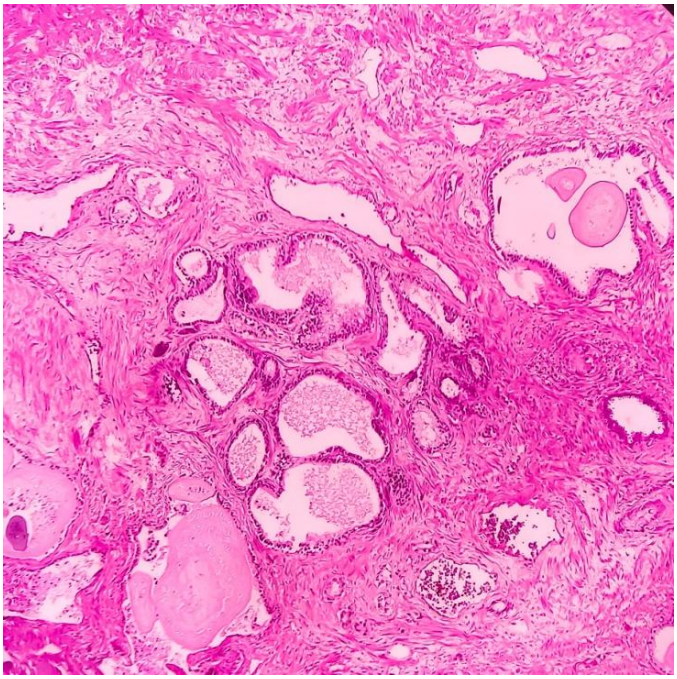

Figure 1- Corpora amylacea in Benign Prostatic Hyperplasia (10X)

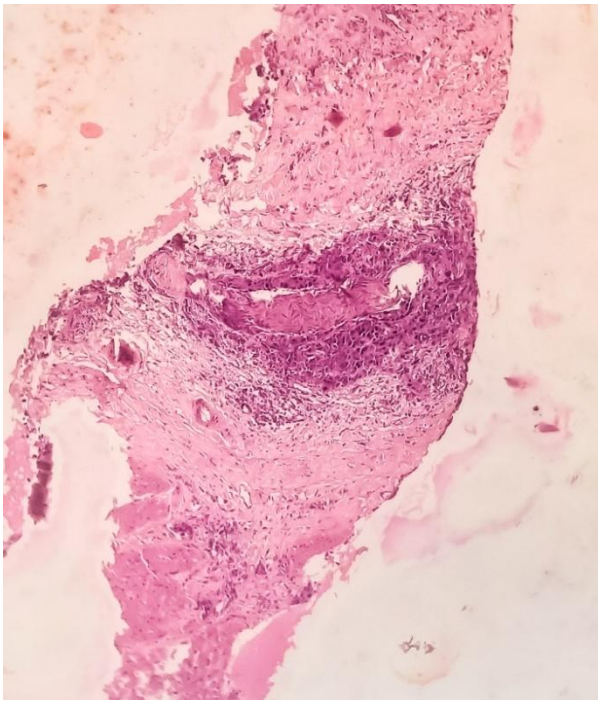

Figure 2- Perineural invasion in prostatic adenocarcinoma (10X)

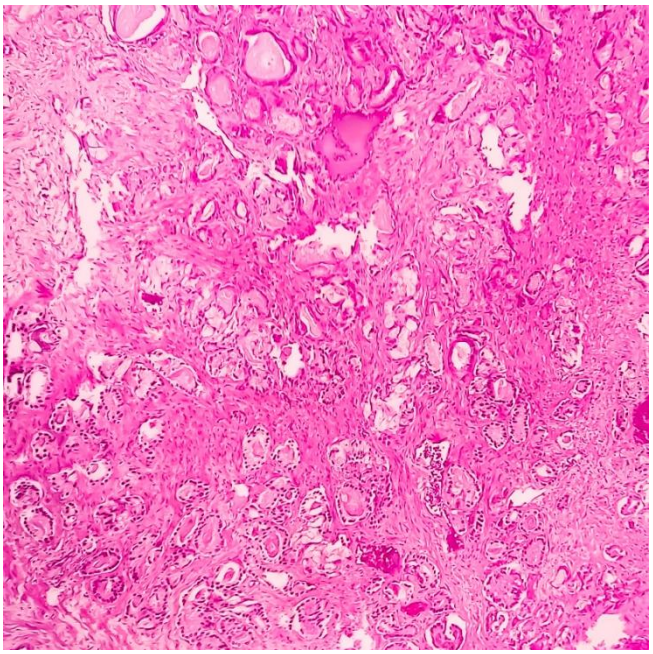

Figure 3-(Gleason Grade 3) Infiltrating malignant cells in prostatic adenocarcinoma (10X)

Table 2 – Gleason score in carcinoma prostate

Gleason Score	Number of cases	Percentage (%age)
5	0	0%
6	0	0%
7	5	20.8%
8	11	45.8%
9	5	20.8%
10	3	12.5%

Grade Group 4 had the maximum number of cases i.e 45.8% Serum prostate specific antigen levels were available in 24 cases of prostatic adenocarcinoma cases. 21 out of 24 cases had serum prostate specific antigen levels greater than 10 ng / ml. (87.5%).Out of 125 cases, 89 (71.2%) cases were from urban areas and 36 (28.8%) cases were from rural areas. All the 24 cases with prostatic adenocarcinoma were from urban areas.

DISCUSSION

Prostatic ailments are the most common cause of morbidity and mortality in elderly men worldwide. The present study comprises of a group of patients presenting with prostatic disease in a tertiary hospital of northeast India. Prostate is involved by various pathological conditions including nodular hyperplasia of prostate, inflammation, premalignant and malignant lesions. Although tools such as trans-rectal ultrasound, prostate specific antigen (PSA) are used for screening of prostate cancer, still biopsy remains the gold standard for final diagnosis[12].Most of studies describe increased frequency of micturition, nocturia, difficulty in starting and stopping the urine, dribbling and dysuria as most common presenting features of prostatic disease[13]. In our study, increased frequency of micturition is the most common complaint as in Farooq et al[14]. The most frequent benign histopathological entity observed in our study was benign nodular hyperplasia mostly observed in sixth to seventh decade of life. Studies show benign nodular hyperplasia as the frequent benign histopathological pattern with peak incidence of occurrence in seventh decade of life[15]. The occurrence of prostatic adenocarcinoma before 50 years of age was nil. These findings are consistent with findings of earlier studies[16]. Prostatitis was associated with 13.48% cases of BPH. Patel SK et al had reported chronic prostatitis associated with nodular hyperplasia of prostate in 26.78%[17]. Sharma A et al 12 found prostatitis in 33.06% cases[1]. Among prostatic carcinoma 21 out of 24 cases had serum prostate specific antigen levels greater than 10 ng / ml. (87.5%) which is comparable to Kavita kumari et al. and Lakhey M[18,19]. High Grade Prostatic Intraepithelial Neoplasia is a premalignant condition of prostatic carcinoma. The finding of High Grade Prostatic Intraepithelial Neoplasia along with elevated serum prostatic specific antigen levels is an indication of repeat biopsy and routine follow up. In our study, High Grade Prostatic Intraepithelial Neoplasia was seen in 8 out of 125 cases (6.4%) and in Bhatta S et al 2.08% cases presented with High Grade Prostatic Intraepithelial Neoplasia.

All the cases of carcinoma prostate were histologically adenocarcinoma, which were similar in other studies also. The cases were graded in accordance with Gleason's score. Gleason grading correlates with tumor aggressiveness and thus helps in prognosis. Tumors with Gleason score 8-10 have advanced cancers with poor prognosis. In our study, 19 cases had Gleason score between 8-10. Perineural invasion is a pathognomic feature of prostatic cancer if there is circumferential or intraneural invasion by the tumour cells. In our study, perineural invasion was seen in 10 cases out of 24 cases (41.6%). Similarly in Bhatta et al, perineural invasion was noted in 3 (37.5%) cases out of all prostatic cancer[20].Similarly in Wasim K et al, maximum number of adenocarcinoma cases had Gleason scorebetween 8-10[21].

CONCLUSION

A variety of benign and malignant lesions are seen in prostatic specimens. These need to be differentiated and classified. Benign nodular hyperplasia is the most common benign lesion.Chronic prostatitis may also be associated with BPHand prostatic adenocarcinoma is the most common malignant lesion of prostate. Perineural invasion is a significant finding and guide and is usually seen with high Gleason score prostatic cancer. Serum PSA is a useful test in cases where the values are higher. All cases of carcinoma prostate were adenocarcinoma and many were an incidental finding. Thorough sampling of all cases is

mandatory so as not to miss malignancy. Awareness and accessibility to early diagnosis could be the result of majority of cases from urban areas.

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