

Histopathological Study of Prostatic Lesions: Our Experience at a Rural Medical College, Uttar Pradesh

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Abstract

Introduction: Prostatism is a common disease in the geriatric age group. Benign prostatic hyperplasia and Carcinoma of the prostate are increasingly frequent with advancing age. Aim of the present cross-sectional study is to evaluate the complete spectrum of histopathological types of various prostatic lesions. **Materials and Methods:** A total of 75 prostate biopsies were received from January 2016 to December 2016 in the Department of Pathology, in a tertiary care hospital, Uttar Pradesh. Routine Hematoxylin and Eosin staining was performed. Reporting of malignant cases included Gleason's grade and score. Relevant clinical data including the age, presenting complaints, and radiological findings were documented for all the cases. **Results:** A total of 75 prostate biopsies were received, the mean age was 63.04 years. Most common presenting complaint was difficulty in micturition. Study included, 56 (74.66%) cases of Benign prostatic hyperplasia alone and 5 (6.66%) were of Adenocarcinoma. Chronic Prostatitis 6 (8%) was the most common non-neoplastic lesion associated in cases of benign prostatic hyperplasia. Two (2.66%) cases were of benign prostatic hyperplasia along with Basal cell hyperplasia. One (1.33%) case each of granulomatous prostatitis, cystitis glandularis (urothelium), and squamous metaplasia were associated with benign prostatic hyperplasia. One (1.33%) case each of Prostatic intraepithelial neoplasia, Undifferentiated carcinoma, and post operative spindle cell nodule were also noted. **Conclusion:** Benign prostatic hyperplasia is the most commonly encountered prostatic lesion. In spite of availability of various investigations, a definitive diagnosis of prostatic lesions can be made by histopathological study only.

Keywords: Benign Prostatic Hyperplasia; Chronic Prostatitis; Basal Cell Hyperplasia; Prostatic Intraepithelial Neoplasia; Carcinoma Prostate; Post Operative Spindle Cell Nodule.

Introduction

Diseases of the prostate constitute a significant portion of cases and are substantial sources of morbidity and mortality among adult male population worldwide [1,2,3,4]. Three pathologic processes mainly affect the prostate gland: Inflammatory (prostatitis), Benign prostatic hyperplasia (BPH), and tumors (pre-malignant and malignant lesions) [2,4]. BPH is the most common urological problem of ageing

men interpreted as a "normal" ageing process and has a complex disease from etiological and pathogenesis point of view [1,5,6,7]. Both BPH and carcinoma prostate are increasingly frequent with advancing age. Prevalence of BPH increases from 20% at 40 years of age, 70% by age 60 years and 90% by age 80 years [6,7,8]. Globally, BPH affects about 210 million males [1]. Various studies reported the rate of BPH to be in the range of 67.5-87.5% of prostatic lesions and gave a peak age of 6th and 7th decades for those affected [1,3,4,5,9]. Studies from Saudi Arabia and India reported the 7th decade while study in Pakistan and all Nigerian studies except that from Benin reported the 6th decade as the peak age group affected [1,3,4,5,9].

Development of the histologic features of BPH is dependent on the bioavailability of testosterone and its metabolite, dihydrotestosterone [1]. Additional risk

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factors include several modifiable factors involved in metabolic syndromes such as obesity, diabetes, high levels of alcohol consumption, and physical inactivity [1]. The mechanisms underlying these associations remain poorly understood [1].

It is estimated that number of males in the U.S who will experience prostatitis during their lifetime range up to 50% [2]. Prostatitis may be acute or chronic bacterial prostatitis, chronic abacterial prostatitis, or granulomatous prostatitis [1,8]. Prostatitis, is characterized by urinary frequency, dysuria, body aches and sometimes fever [2].

Carcinoma Prostate is globally the second most frequently diagnosed cancer and the sixth leading cause of cancer death in males [10]. In India, it constitutes about 5% of all male cancers [11]. The worldwide incidence of Carcinoma prostate has been rising rapidly, likely due to intensified effort in early detection and screening [1]. The American Cancer Society's estimates for prostate cancer in the United States for 2013 are such that about 238,590 new cases of prostate cancer will be diagnosed and about 29,720 men will die of prostate cancer [2,12]. It is of such a great magnitude that in the United States, it is postulated that 1 in 6 American men will develop carcinoma prostate over his lifespan [13]. Carcinoma prostate rates in various studies were in the range of 12.5-30.9% of prostatic lesions [1,2,4,5,9]. Carcinoma Prostate can be a serious disease, but most men diagnosed do not die from it. In fact, more than 2.5 million men in the United States who have been diagnosed with Carcinoma Prostate at some point are still alive today [12].

About 6 cases in 10 are diagnosed in men aged 65 or older. Average age at the time of diagnosis is about 67 [2,12]. Incidence of prostatic cancer increases proportionally after age of 50 years [4]. The major risk factors for Carcinoma Prostate are race, increasing age, and family history of prostate cancer, lack of exercise and high calcium intake [2]. Other suggested but inconclusively agreed risk factors include association with bladder cancer, cigarette smoking, vasectomy, and sexual behavior [1,2]. In most cases, it is asymptomatic and develops slowly. However, it may present with pain, difficulty in urinating and problems during sexual intercourse [2]. In approximately, 70% of cases it arises in the peripheral zone of gland particularly in the posterior location [14]. Adenocarcinoma is its most common histological variant [4]. Histodiagnosis of carcinoma prostate is based on morphological features such as growth pattern, nuclear atypia, and absence of basal cells. However, this can be challenging, when the malignant tissue is limited and is mixed with benign prostatic

glands, or because of the presence of benign mimickers of carcinoma [15].

Diagnosis of prostatic lesions require careful history, physical examination including digital rectal examination (DRE), serum prostate specific antigen (PSA) estimation and transrectal ultrasound (TRUS) and TRUS-guided needle biopsies of the prostate. The present study was conducted to evaluate the complete spectrum of various prostatic lesions histopathologically.

Materials and Methods

A total of 75 prostate biopsies were received from January 2016 to December 2016 in the Department of Pathology, in a tertiary care hospital, Uttar Pradesh. Of these 75 biopsies, 70 were of transurethral resection of prostate (TURP) tissue bits and 5 biopsies were of open prostatectomy. All the prostate biopsies were fixed in 10% neutral buffered formalin and 5 micron sections were stained with routine Hematoxylin and Eosin (H&E) stain. Reporting of malignant cases included Gleason's grade and score. Relevant clinical data including the age, presenting complaints and radiological findings were documented for all the cases.

Results

A total of 75 prostate biopsies were received and processed during the period under review. The youngest patient was 30 years old while the oldest patient was 85 years old with a mean of 63.04 years. The peak incidence was age group of 60-69 years, closely followed by 50-59 years accounting for 26 (34.66%) and 18 (24%) respectively (Table 1). Common presenting complaints were increase in frequency and burning micturition 60 (80%) whereas urinary retention was present in 20 (26.66%) patients, followed by incontinence in 10 (13.33%) (Table 2). The present study, included, 56 (74.66%) cases of Benign prostatic hyperplasia alone and 5 (6.66%) were of Adenocarcinoma.

Chronic Prostatitis 6 (8%) was the most common non-neoplastic lesion associated in cases of benign prostatic hyperplasia. Two (2.66%) cases were of benign prostatic hyperplasia along with Basal cell hyperplasia. One (1.33%) case each of granulomatous prostatitis, cystitis glandularis (urothelium) and squamous metaplasia were associated with benign prostatic hyperplasia.

Table 1: Age distribution of the patients

Age in years	No. of cases (%)
30-39	1 (1.33)
40-49	5 (6.66)
50-59	18 (24)
60-69	26 (34.66)
70-79	16 (21.33)
80-89	9 (12)
Total no. of cases	75 (100)

Table 2: Various prostatic lesions and presenting complaints

Presenting Complaints	No. of Cases (%)
Micturition: (Burning, Increase in frequency, Increase in frequency and burning)	60 (80)
Abdominal pain	4 (5.33)
Incontinence	10 (13.33)
Urinary retention	20 (26.66)
Inguinal swelling	6 (8)
Dribbling hematuria	4 (5.33)

Table 3: Histopathological distribution of various prostatic lesions

Histopathological Diagnosis	No. of Cases (%)
Benign prostatic hyperplasia	56 (74.66)
Benign prostatic hyperplasia with Chronic prostatitis	6 (8)
Benign prostatic hyperplasia with Granulomatous prostatitis	1 (1.33)
Benign prostatic hyperplasia with basal cell hyperplasia	2 (2.66)
Benign prostatic hyperplasia with Squamous metaplasia	1 (1.33)
Benign prostatic hyperplasia with Cystitis glandularis	1 (1.33)
Prostatic Intraepithelial Neoplasia 1	1 (1.33)
Post operative spindle cell nodule	1 (1.33)
Adenocarcinoma	5 (6.66)
Undifferentiated carcinoma	1 (1.33)
Total no. of cases	75 (100)

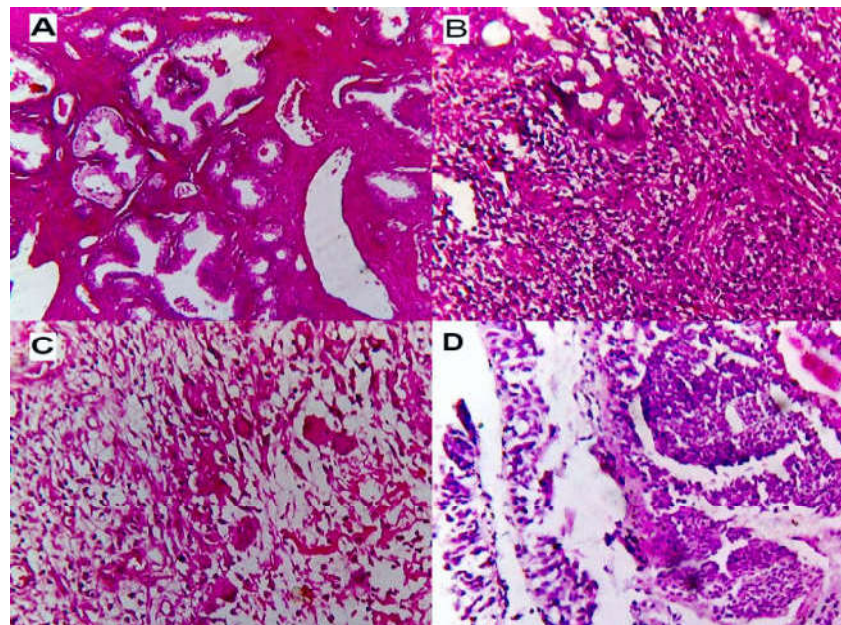


Fig. 1A: BPH: Photomicrograph showing intraluminal papillary infolding and corpora amylacea. (H&E, 40X) **B:** Chronic prostatitis: Photomicrograph showing dense lymphoplasmacytic inflammatory infiltrate in the stroma as well as in glandular lumina. (H&E, 40X) **C:** Granulomatous Prostatitis: Photomicrograph showing scattered Langhans' giant cells in the stroma. (H&E, 40X) **D:** Basal cell Hyperplasia: Photomicrograph showing a focus of small group of acini filled with proliferating small darkly stained basal cells having scanty cytoplasm and oval nuclei. (H&E, 40X)

Table 4: Comparison with various previous studies

Histopathological diagnosis	Mittal <i>et al.</i> ^[18]	Anjorin <i>et al.</i> ^[9]	George and Thomas ^[21]	Monika Garg <i>et al.</i> ^[6]	Present study
Total no. of cases	185	801	1,163	364	75
Benign prostatic Hyperplasia	40.00	71.6	88.5	34.62	74.66
With prostatitis	38.39	11.2	-	32.69	8
With Granulomatous prostatitis	1.62	-	-	3.57	1.33
- Nonspecific				3.57	1.33
- Tubercular				-	-
With Basal cell Hyperplasia	5.4	-	-	3.85	2.66
With Squamous metaplasia	3.24	-	-	0.82	1.33
Prostatic intraepithelial neoplasia (LGPIN)	-	-	0.6	0.55	1.33
Adenocarcinoma	7.02	17.2	10.9	20.05	6.66
Post operative spindle cell nodule	-	-	-	-	1.33
Undifferentiated carcinoma	-	-	-	-	1.33

*Values are presented as percentage unless otherwise indicated

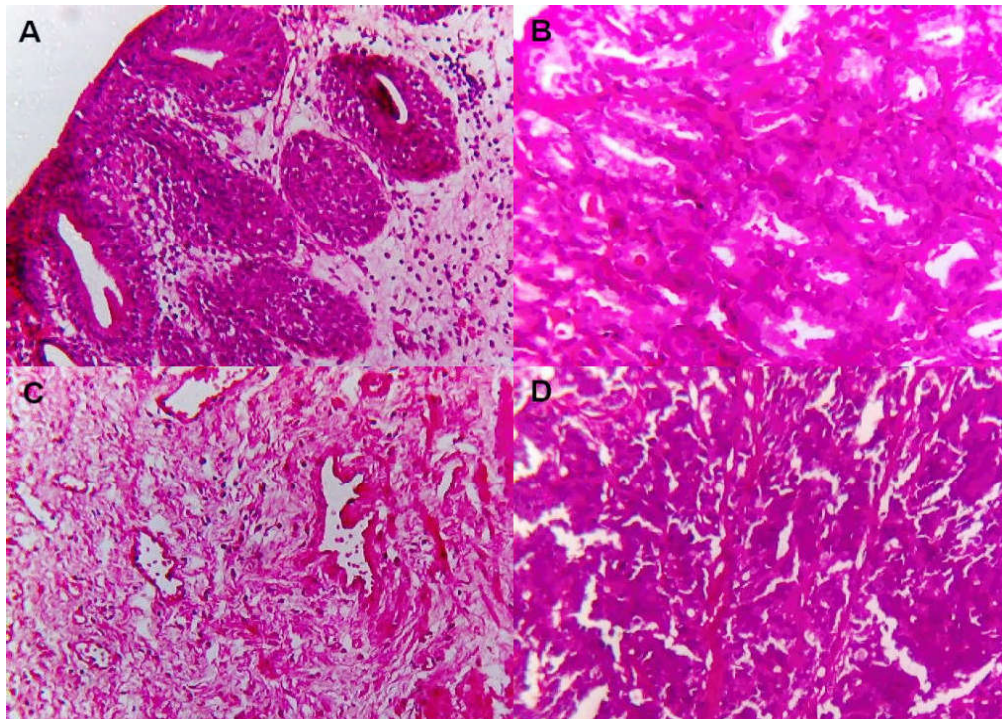


Fig. 2A: Benign Prostatic Hyperplasia with Cystitis Glandularis showing Brunns' nests. (H&E, 40X) **B:** Low Grade Prostatic Intraepithelial Neoplasia: Photomicrograph showing increased cellularity seen as crowding of glands with irregular spacing along with anisonucleosis and small nucleoli. (H&E, 40X) **C:** Post operative spindle cell nodule: Photomicrograph showing bland looking spindle cells arranged in irregular fascicles in myxoid stroma with scattered inflammatory cells and dilated blood vessels. (H&E, 40X) **D:** Adenocarcinoma with Gleason score 9: Photomicrograph showing solid growth of tumor cells with papillary architecture of glandular proliferation (Gleason Pattern 5B with Pattern 4). (H&E, 40X)

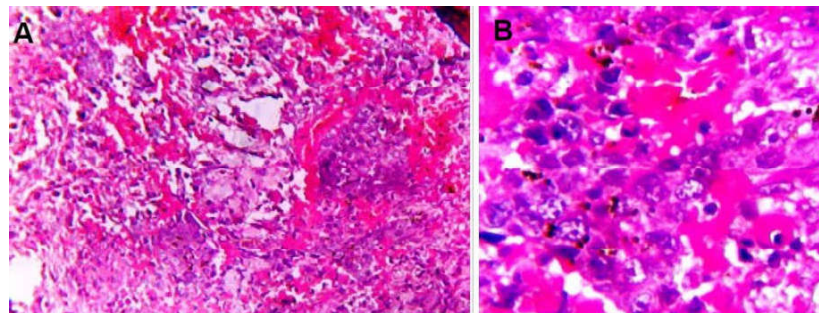


Fig. 3A: Undifferentiated Carcinoma: Photomicrograph showing highly pleomorphic tumor cells arranged in small non-cohesive sheets and also as single cells. (H&E, 40X), **B:** Undifferentiated Carcinoma: Photomicrograph showing pleomorphic tumor cells with highly dysplastic nuclei with prominent nucleoli. ((H&E, 100X)

One (1.33%) case each of Prostatic intraepithelial neoplasia 1, Undifferentiated carcinoma, and post operative spindle cell nodule were also noted. Amongst the 5 cases of Adenocarcinoma, the Gleason scores were 4 (1 case), 5 (2 cases), 7 (1 case), and 9 (1 case) (Table 3).

Discussion

Prostatic specimens constitute a good percentage of the surgical pathology workload. Prostate gland is a retroperitoneal organ encircling the neck of bladder and urethra and is devoid of distinct capsule. Prostatic parenchyma can be divided into four biological and anatomical zones: peripheral, central, transitional and anterior fibromuscular stroma. Two important histopathological prostatic lesions are BPH and Prostatic carcinoma causing enlargement of prostate gland. Most hyperplasia occur in transitional zone while most carcinoma originate in the peripheral zone. BPH is the non-malignant adenomatous overgrowth of prostate gland. Enlarged prostate gland leads to urethral constriction and thus causing various urinary symptoms such as weak stream, hesitancy, frequency, urgency, nocturia, incomplete emptying, terminal dribbling, overflow or urge incontinence and complete urinary retention [2].

BPH is characterized pathologically by a cellular proliferation of the epithelial and stromal elements in the prostate gland, resulting in the formation of large discrete nodules in peri-urethral region of prostate. (Figure 1A) These histological changes begin in the 3rd decade of life and clinically in the 5th decade of life, resulting in increased resistance to urinary flow during micturition [5].

In India the incidence of BPH is estimated to be 92.97% [3]. It is currently estimated that in United States of America approximately 200,000 new cases are detected every year, of which approximately one fifth prove to be lethal [16]. In India the incidence of carcinoma of prostate is estimated at 8/100,000 persons [17]. In the present study BPH alone and BPH associated with non-neoplastic lesions were 67 (89.33%) cases and the Adenocarcinoma prostate 5 (6.66%) cases. Mittal et al. in their study comprising of 185 biopsies, reported BPH in 172 (92.97%) cases and carcinoma prostate in 13 (7.02%) cases [18].

Chute, Panesar and Girman [19] in their study of BPH patients reported obstructive voiding in 36.45% of the patients as the chief complaint followed by frequent urination in 34.75% of the patients. Dysuria, slow stream, increased urinary frequency and complete

retention of urine are the most common symptoms in patients with carcinoma prostate. In the study done by Hafiz Muhammad Aslam et al. the commonest complaints of patients of BPH were urinary retention 21 (95.5%) and, dribbling and hematuria 10 (83.3%) [2]. In our study, common presenting complaints were increase in frequency and burning micturition 60 (80%) whereas urinary retention was present in 20 (26.66%) patients, followed by incontinence in 10 (13.33%).

In present study mean age of patients was 63.04 years and mostly cases were present in the age group of 60-69 years (34.66%). Hafiz Muhammad Aslam et al. study reported 65.7 ± 7.6 years mean age and mostly cases were in the age group of 60-70 years (58.3%) [2]. These findings were similar with studies conducted in Pakistan, Oman, India and Saudi Arabia [20,21,22]. In Monika Garg et al. study the age of patients ranged from 7 years to 93 years; however, the predominant population was in the 6th to 7th decade with a mean age of 68.6 years [6].

In the present study BPH alone 56 (74.66%) and BPH associated with non-neoplastic lesions were 11 (14.66%) cases. All the 67 (89.33%) cases were most frequently found in the age group of 60-69 years closely followed by 50-59 years. Mean age for benign prostatic lesions was 63.29 years and adenocarcinoma prostate patients was 65.6 years and mostly seen in the similar age group as for BPH. No significant difference was noted in the mean age of the non-neoplastic and neoplastic groups. Hafiz Muhammad Aslam et al. reported most common prostatic lesion in their study as BPH 42 (87.5%) which was frequently found in the age group of 60-70 years [2]. Their study showed that after BPH, Prostatic Adenocarcinoma was the commonest lesion (12.5%), occurring mostly in the same age group as BPH [2]. A study done by Manjit Singh Bal SK et al. had 87% cases of BPH and also the same age group being affected [22]. Lokuhetty et al. in their study reported that maximum incidence of both benign and malignant prostatic lesions were in the seventh decade of life [23]. The mean age for BPH patients in their series was 68.1 years and mean age for carcinoma prostate patients was 71.3 years [23]. Ibrahim et al. in their study reported mean age for benign prostatic lesions as 64.3 years and for carcinoma prostate the mean age was 66.8 years [24]. In the study done by A. Josephine the mean age for prostatic lesions was 65.5 years with a mean age of 63.8 years for benign prostatic lesions and a mean age of 68.8 years for carcinoma patients [5]. Chukwuemeka Charles Nwafor et al. reported BPH cases accounted for 62.8% of all prostatic lesions, and most cases were in the 7th and 8th decade [1]. The results of the present

study agree with the studies by George and Thomas [21], in which the mean age was 66.81 years, and by Barakzai et al [14], in which the mean age was 66.9 years.

In present study of 75 cases, 68 (90.66%) were non-neoplastic lesions, whereas neoplastic lesions were 7 (9.33%). In Monika Garg et al. study, of 364 cases, 285 (78.3%) were non-neoplastic lesions, whereas neoplastic lesions constituted 79 of the total cases (21.7%). Decline in the number of cases beyond the age of 80 years reflects the average life span of people in our country. This agrees with the studies conducted by Mittal et al.[18], Anjorin et al.[9], and George et al.[21], in which non-neoplastic lesions formed the bulk of the cases (Table 4).

Chronic prostatitis 6 (8%) accounted for most of the non-neoplastic histological change associated with BPH in our study (Figure 1B). In Monika Garg et al. study prostatitis lesions were 132 (36.3%) [6]. In the study of Mittal et al. prostatitis constituted 38.4% of the cases, of which 26.3% of cases were chronic prostatitis [18]. Prostatitis is seen in about 11-98% of prostatic specimens and its diagnosis is dependent on the criteria used by the assessor [1]. Since the major reason for the removal is either BPH or Carcinoma Prostate, some pathologist may not emphasis the presence of inflammatory cells except in rare cases such as tuberculosis or schistosomiasis.

In the present study we had 1 (1.33%) of Granulomatous prostatitis associated with BPH which showed ill defined non caseating granulomas with Langhans' giant cells in stroma as well as intraluminal. (Figure 1C) Ziehl Nelsen (20%) staining for acid fast bacilli was negative in this case. Monika Garg et al. study showed Granulomatous prostatitis in 13 of 364 cases (3.6%) [6].

Basal cell hyperplasia (BCH) (Figure 1D) was the second most common entity in the non-neoplastic group and accounted for 2 (2.66%) of the total cases. All cases had associated BPH. Study conducted by Monika Garg et al [6] accounted for 14 (3.9%) of the similar cases. Thorson et al [25] study found the incidence of BCH along with BPH in the range of 3.1% to 8.9%.

Our study revealed 1 (1.33%) case of BPH associated with Squamous metaplasia. Study of Monika Garg et al [6] and Mittal et al [18] had 3 (0.8%) and 3.24% similar cases respectively.

The present study revealed 1 (1.33%) case of BPH associated with Cystitis glandularis in the TURP tissue bits (Figure 2A). Cystitis glandularis result from chronic inflammation or other causes of mucosal irritation, such as ureteral reimplantation, neurogenic

bladder, or bladder exstrophy. Microscopically, initial change is focal proliferation of the basal layer of transitional epithelium, producing buds that later become solid nodules (von Brunn nests or islands) located within lamina propria. Few nodules develop a central cystica area caused by the accumulation of mucin. Cells lining the cyst show an urothelial appearance, the condition is called cystitis glandularis or cystica. Immunohistochemical marker CK7 shows positivity for cystitis glandularis.

One (1.33%) case of post operative spindle cell nodule (PSCN) in a patient with past history of TURP 6 months back was reported in our study (Figure 2C). PSCN of the prostate and bladder is a rare lesion often misinterpreted as sarcoma, hence it is important to recognize [26]. Nodule consists of a reactive proliferation of spindle cells. PSCN are usually described as histologically identical to inflammatory myofibroblastic tumors, except that a history of prior instrumentation can be elicited.

In the present study we had 1 (1.33%) of Prostatic Intraepithelial neoplasia 1 [i.e. Low-grade Prostatic intraepithelial neoplasia (LGPIN)]. (Figure 2B) Chukwuemeka Charles Nwafor et al. reported HGPIN accounted for 1% of cases. Similar low rates were reported in Jos and India [5]. High-grade Prostatic intraepithelial neoplasia (HGPIN) is accepted as a precursor lesion of carcinoma [6]. The presence of prominent nucleoli within an existing duct structure is an easy way to identify the disorder [27,28]. Clinical studies suggest that PIN predates carcinoma by 10 years or more, with low-grade PIN first appearing in men in their thirties [28]. The finding of PIN indicates the need for repeat biopsy and follow-up, especially in patients with elevated serum PSA concentration [28]. The clinical significance of HGPIN is that it identifies patients at risk for malignancy [27].

In the present study prevalence of adenocarcinoma prostate was 6.66%, i.e., 5 of 75 cases. (Figure 2D) In Monika Garg et al. study prevalence of prostatic carcinoma was 20.1%, i.e., 73 of 364 cases [6]. Similar results were obtained by Mittal et al [18] and Rekhi et al [29] In the present study the age range was 60-79 years with a mean of 65.6 years. Majority of carcinoma prostate cases (n=3, 60%) were seen in the age group of 60-69 years, closely followed by the age group of 70-79 years (n=2, 40%). In Monika Garg et al. study, the age range for prostatic carcinoma was 44-93 years, with a mean of 68.7 years and majority of cases (n=26, 35.6%) were seen in the age group of 71 to 80 years, closely followed by the age group of 61 to 70 years. In their study, 2 cases were seen below the age of 50 years.

One (1.33%) case of undifferentiated carcinoma aged 59 years old was also seen in the present study.

(Figure 3A & B). The patient was an already diagnosed case of carcinoma bladder. In such a scenario, the differential diagnosis is between high-grade urothelial and prostatic carcinoma. For confirmation the immunohistochemical panel to be used is CK34&E12, CK7, P53, for the urothelial carcinoma and PSA, PSAP, and Leu7 for the prostate carcinoma.

Numerous grading systems have been designed for the histopathological grading of prostate cancer. Prostate biopsy Gleason score (GS) correlates with tumour aggressiveness, tumour volume, serum PSA levels, prognosis and influence of the treatment policy. Gleason's grading system recognizes the histologic heterogeneity of tumor present within a single prostate specimen by assigning grades to the primary and secondary patterns and combining this grade into the score (scored as 2-10) [30]. Though reproducible, across different institutions, stage, and grade depend on the subjective assessment of the investigator(s) [31]. Studies have shown that patients with a pathological GS of less than or equal to 6 have an excellent progress-free survival, which can be up to 90%. However, GS more than or equal to 7 adenocarcinoma have a 29-43% risk of death from prostate cancer [32].

The present study had 5 (6.66%) cases of prostatic adenocarcinoma and their Gleason scores were 4 (1 case), 5 (2 cases), 7 (1 case), and 9 (1 case). There were 60% cases with GS 5-7, 20% with GS 8-10 and 20% with GS 2-4. In the study done by Surveillance, Epidemiology, and End Results (SEER) Prostate cancer trends 1973-1995 (1998) 41% of patients had GS 5-7, 23% had GS 2-4 and 21% with GS 8-10 [16]. In the study done by Bing - Yirshen et al. there were 46% of carcinoma prostate patients with GS 5-7 and 33.3% with GS 2-4 [23]. A. Josephine study had 60% of carcinoma cases with GS 5-7, 25% with GS 8-10 and 15% with GS 2-4 [5].

Conclusion

Benign prostatic hyperplasia is the most commonly encountered prostatic lesion. Investigations like digital rectal examination, transrectal ultrasound and serum prostate specific antigen estimation are an adjunct in the diagnosis of prostatic lesions, but a definitive diagnosis of non-neoplastic and neoplastic lesions of prostate can be made by histopathological study only. Biopsies are considered as gold standard for tissue diagnosis of prostate cancer. Prostate carcinoma cases are relatively high and have a high Gleason scores that foretell high mortality. Frequency of prostate cancer is on the rise and measures should be taken for its

early detection. Screening protocols and awareness programs need to be introduced to reduce the mortality.

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