ORIGINAL RESEARCH

To study the histopathological spectrum of prostatic lesions and to classify them as benign, with associated inflammation, premalignant and malignant

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ABSTRACT

Background: Gleason's system is now widely being utilized as the histologic grading system for prostatic cancer and is a powerful predictor of cancer behaviour.The present study was conducted to analyse the histopathological spectrum of prostatic lesions and to classify them as benign, with associated inflammation, premalignant and malignant.

Material and methods: The sample size was 302. Collected data was analyzed with descriptive statistics followed by chi- square test. Tests were used to analyze diagnosing benign and malignant prostatic lesions. p value was calculated and considered statistically significant when p value was less than 0.005.

Results: Out of 302 specimens, 72.5% were of BPH, 1% of PIN and 26.5% were of Adenocarcinoma. Majority (40.1%) of patients were in 7th decade (BPH) followed by in 8thdecade (33.4%) in adenocarcinoma. Of the total cases, majority of the specimens received were of TURP chips (74.8%). Most of the patients had grade II prostatomegaly on clinical examination in benign cases and grade IV in malignant cases. Out of 85 benign cases, majority (83 cases) had firm prostate. Of the 39 malignant cases, 33 prostates were hard and 6 were firm in consistency. Most of the patients (63.6%) in our study presented with acute and chronic urinary retention, increased frequency, poor urinary stream. Most common Gleason score in our study was 7(33.7% cases).

Conclusion: The present study concluded that out of 302 prostatic specimens studied, benign lesions were common, accounting for 72.5% and malignant lesions accounted for 26.5%.

Keywords: malignant lesions, prostatic lesions, histopathological.

INTRODUCTION

In males, the prostate is pyramidal fibromuscular gland which surrounds the prostatic urethra from the bladder neck to the membranous urethra and is itself surrounded by a thin but tough connective tissue capsule. It lies at a low level in the lesser pelvis, behind the inferior border of the symphysis pubis and pubic arch and anterior to the rectal ampulla, through which it may be palpated. By age of 20 years, prostate approximately weighs 20 gms but almost invariably enlarges with the development of benign prostatic hyperplasia (BPH), weighing

usually 40 gms, but sometimes as much as 150 gms or even more after the first five decades of life.[1]The prostate consists of stromal and glandular components. Smooth muscle cells, fibroblasts and endothelial cells are present in the stroma. The glandular component is composed of acini and ducts. The glands show a convoluted pattern with the epithelium thrown up into folds, sometimes into almost a papillary pattern. It has double layered epithelium- Tall columnar secretory type and flat basal type cells.

The epithelial cells of prostate are:-

a) Epithelial Cells

b) Basal cells(quiescent/reserve cells)

c) Neuroendocrine cells.[1]

The prostate has got 3 main functions, as a gland of external secretion, as a muscle and as a sensory organ.[1]

Digital Rectal Examination is the mainstay of examination of the prostate.When conducting a DRE, it is necessary to detect hard nodules that vary in size, depth and hardness or prostate enlargement that varies in volume change and stiffness. The former typically relate to carcinoma, the latter signal benign prostatic hyperplasia (BPH) or prostatitis. The size, depth, and hardness of nodules and relative stiffness of a given prostate contribute to the perceptible range of abnormalities.[22]Lesions of the prostate such as hyperplasia, non-specific inflammation, infarcts, abscess, premalignant condition and tumors lead to increase in serum PSA levels.[3-6] Gleason's system is now widely being utilized as the histologic grading system for prostatic cancer and is a powerful predictor of cancer behaviour.[4,7]The present study was conducted to analyse the histopathological spectrum of prostatic lesions and to classify them as benign, with associated inflammation, premalignant and malignant.

MATERIAL AND METHODS

This descriptive study was conducted in the Histopathology section of Department of Pathology, Christian Medical College and Hospital, Ludhiana, done over a period of 3 years which included 2 years of retrospective and 1 year of prospective study. The retrospective period was from 1st January 2012 till 31th December 2013 and prospective study period was from 1st January 2014 till 31st December 2014.The study was done on prostatic tissue obtained either by trucut biopsy, transurethral resection (TURP) or open prostatectomy. The sample size was 302.

INCLUSION CRITERIA

All the prostatic tissue specimens sampled either by trucut biopsies, transurethral resection (TURP) and/or via open prostatectomy procedure and which had serum PSA estimation done.

EXCLUSION CRITERIA

- Prostatic tissue with no serum PSA level.
- Repeat biopsy specimen of the same patient.

The clinical details of all the retrospective and prospective cases were noted down from the histopathology forms available in the Pathology Department and/or from patient's records as per protocol.

PROCESSING OF THE PROSTATIC BIOPSIES

For prospective cases, specimens were received and detailed macroscopic examination was done. The tissue received was fixed in 10% neutral buffered formalin and processed. In case of TURP specimen, tissue was taken in a minimum of four cassettes (each cassette hold approx.2gms) and in case of excess tissue, one additional cassette for each additional 10 gm of tissue was taken. In cases of prostatectomy specimens, multiple sections were made at a

distance of 3 to 5 mm. Trucut biopsy specimens were grossed entirely. After grossing, representative tissue sections were processed overnight for 15½ hours in an automated tissue processor (Leica TP 1020) which involved dehydration done by use of graded alcohols beginning with 70% ethanol in water then progressed through 95-100%. This was followed by clearing done by xylene, and later embedding of tissues into paraffin blocks. The sections were cut at 3-5 micron thickness and subsequently stained by haematoxylin and eosin stain.
For retrospective cases, the slides and data were taken out from the pathology records. Clinical and gross details were noted down as per protocol. Microscopic examination of both the retrospective and prospective cases was done personally and classified as BPH, BPH with associated prostatitis, premalignant (adenosis, PIN- low and high grade) and malignant. The malignant lesions were further graded as low, intermediate and high grade based on Gleason's score. Fresh sections were cut from available paraffin blocks if required for retrospective cases. Immunohistochemistry (CK5/6, P63 and AMACR) was done in doubtful cases to differentiate premalignant from malignant lesions.

MODIFIED GLEASON GRADING SYSTEM[8,9]

SCORE DESCRIPTION

1. Single, separate, uniform glands in closely packed masses with a definite, usually rounded, edge limiting the area of tumor.
2. Single, separate, slightly less uniform glands, loosely packed (separated by small amounts of stroma), with less sharp edge.
3. a. Single, separate, much more variable glands, may be closelypacked but usually irregularly separated; ragged, poorly defined edge.
   b. Like 3a, but very small glands or tiny cell clusters
   c. Sharply and smoothly circumscribed rounded masses ofPapillary or loose cribriform tumor(papillary intraductal tumor)
   a. Ragged outlined, ragged infiltrating, fused glandular tumor
   b. Like 4a, with large pale cells(hypernephroid)
4. a. Sharply circumscribed, rounded masses of almost solid Cribriform tumor, usually with central necrosis (Comedocarcinoma)
   b. Ragged masses of anaplastic carcinoma with only enough gland formation or vacuoles to identify it as adenocarcinoma.

GLEASON SCORE

Primary grade is assigned to the dominant pattern and secondary to the sub-dominant pattern. The two numeric grades are added to obtain the combined Gleason score. In tumors with one pattern, the number is doubled.

WHO HISTOPATHOLOGICAL GRADING

GX Grade cannot be assessed
G1 Well differentiated tumor (Gleason score 2-5)
G2 Moderately differentiated tumor (Gleason score 6)
G3-4 Poorly differentiated tumor/undifferentiated (Gleason score 7-10).

STATISTICAL ANALYSIS

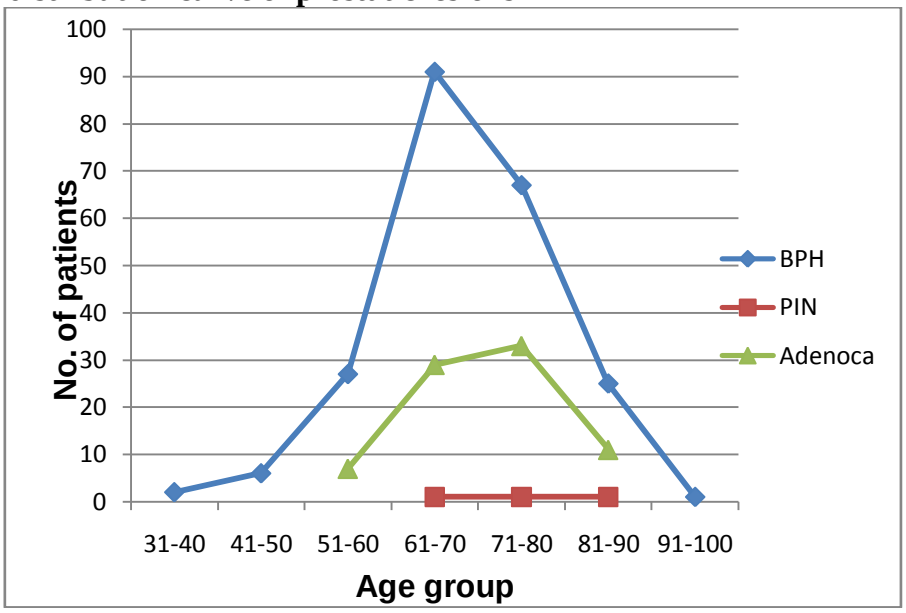
Collected data was analyzed with descriptive statistics followed by chi- square test.Tests were used to analyze the benign and malignant prostatic lesions. p value was calculated. Values were considered statistically significant when p value was less than 0.005.

RESULTS

Out of 417 prostatic specimens were received for histopathological examination, only 302 specimens were evaluated. Out of 302 specimens, 72.5% (n=219) were of BPH, 1% (n=3) of PIN and 26.5% (n=80) were of Adenocarcinoma. Nine cases of adenocarcinoma had foci of PIN.

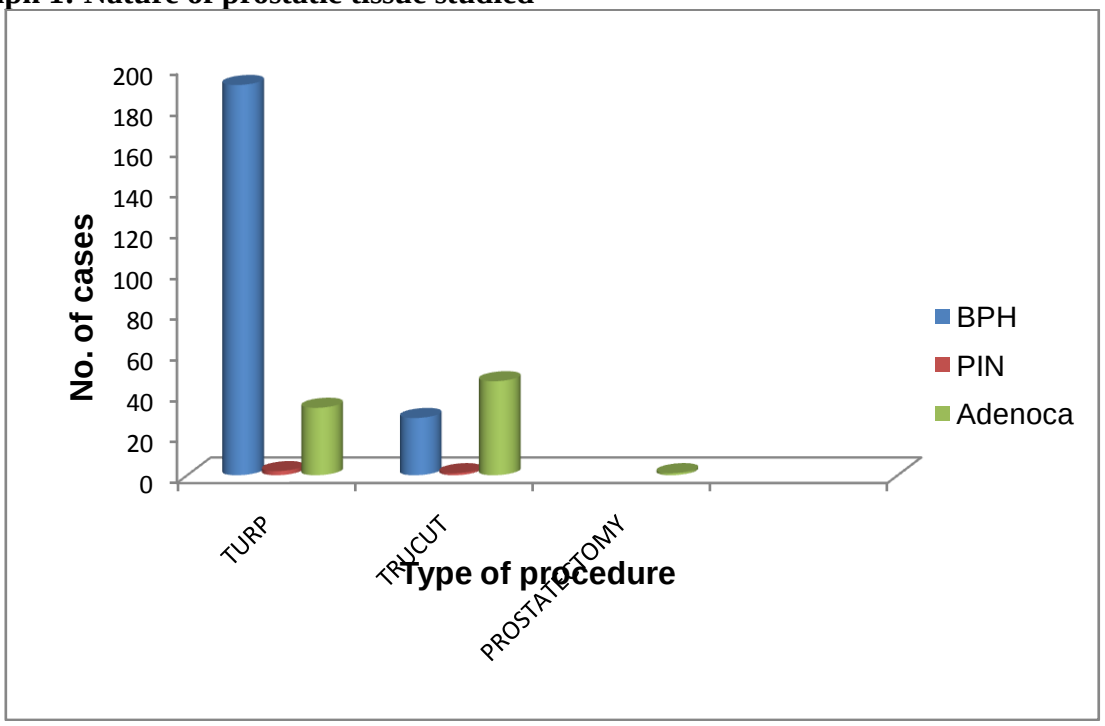
The age of the patients included in the study ranged from 35 to 94 years with a mean age of 70.1 years. Majority (40.1%) of patients were in 7th decade (BPH) followed by in 8th decade (33.4%) in adenocarcinoma. The mean age of presentation for BPH and Carcinoma was 69.4 years and 71.7 years respectively.

Fig 1: Age distribution curve of prostatic lesions



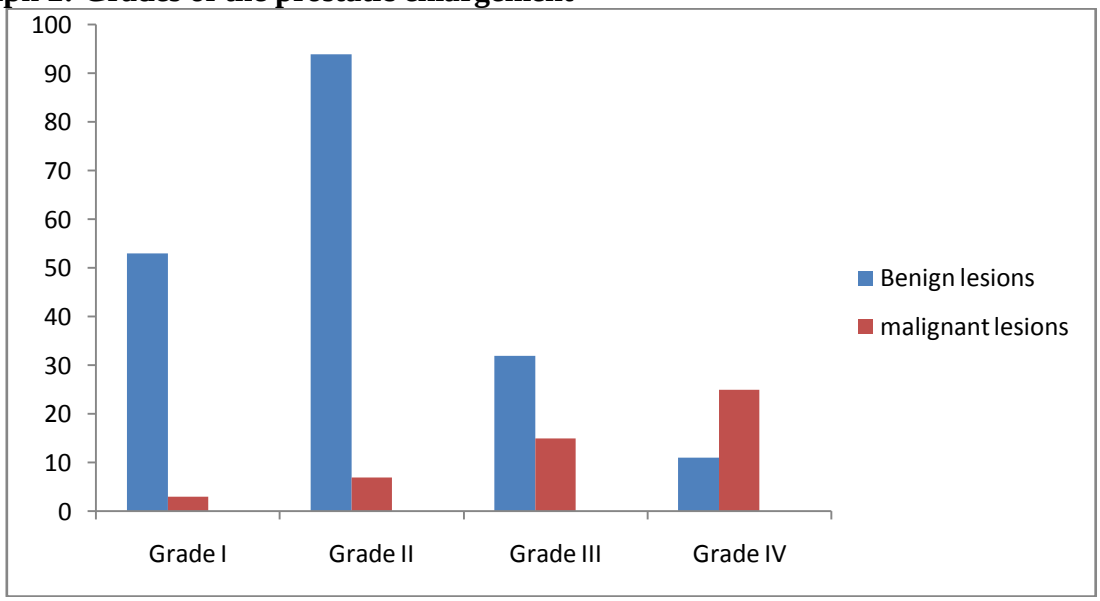
Of the total cases, majority of the specimens received were of TURP chips (74.8%), followed by trucut biopsy (24.8%); prostatectomy specimens were only 0.3% of the total specimens.

Graph 1: Nature of prostatic tissue studied



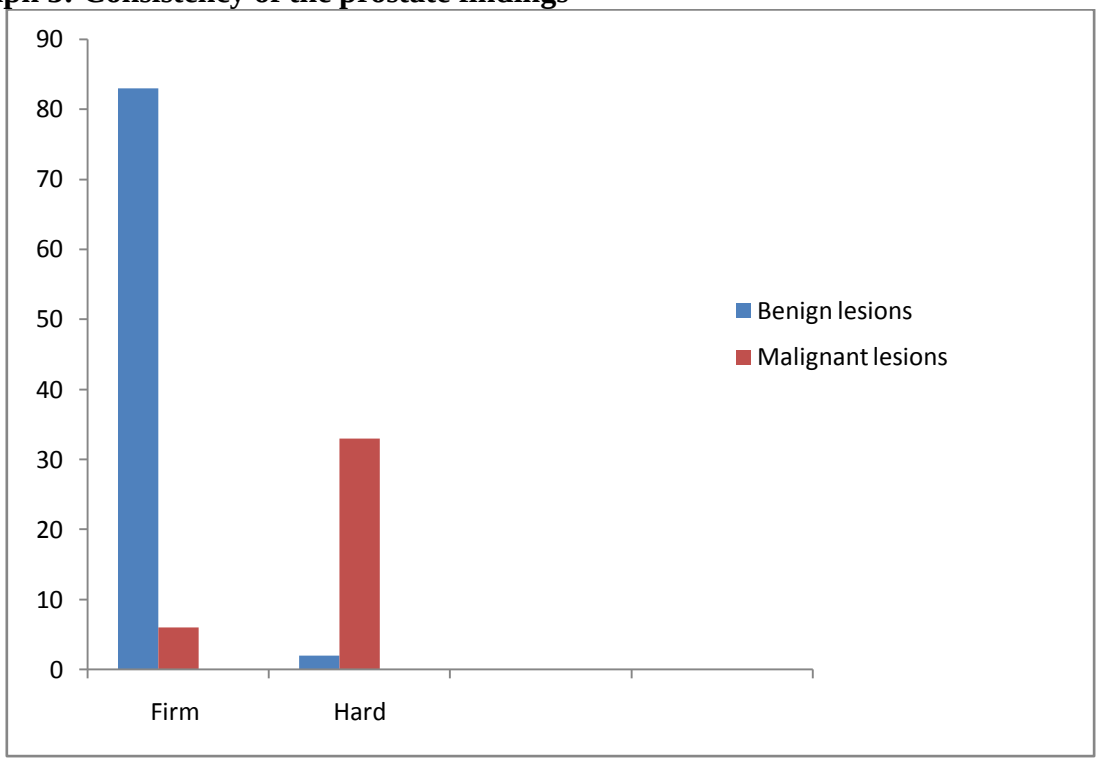
DREwas done in 240 cases out of 302 in our study. Of these, most of the patients had grade II prostatomegaly on clinical examination in benign cases and grade IV in malignant cases.

Graph 2: Grades of the prostatic enlargement



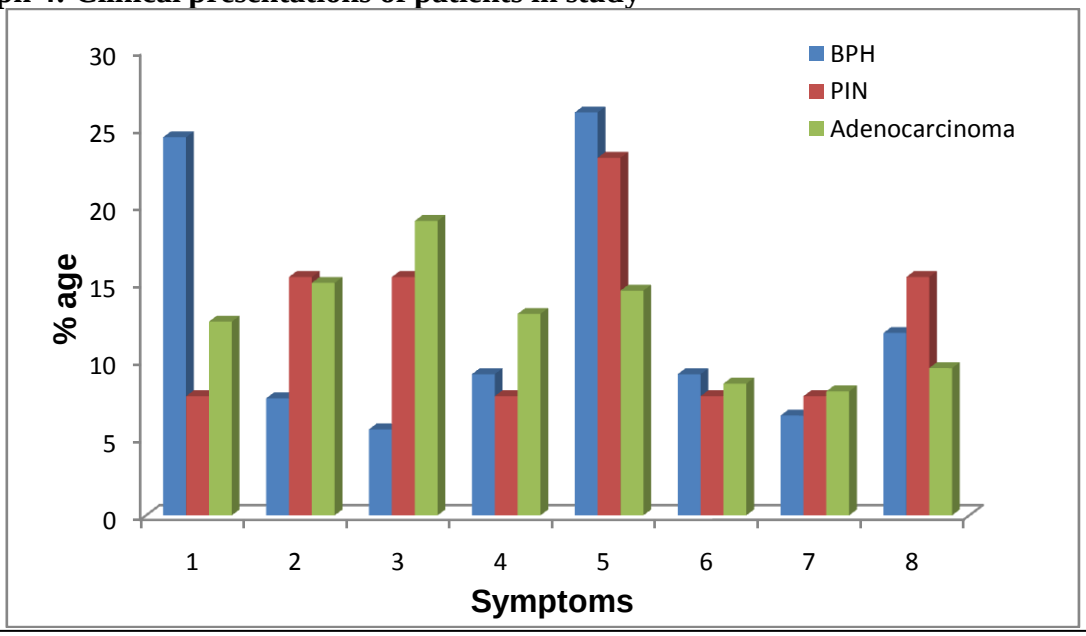
Of the 240 cases, the consistency of the prostate was mentioned in only 124 cases of which 85 were benign and 39 were malignant. Out of 85 benign cases, majority (83 cases) had firm prostate whereas 2 cases had prostate with hard consistency which were associated with inflammation. Of the 39 malignant cases, 33 prostates were hard and 6 were firm in consistency. Hard prostatic nodule was significantly associated with malignant cases in our study.

Graph 3: Consistency of the prostate findings



Most of the patients (63.6%) in our study presented with acute and chronic urinary retention, increased frequency, poor urinary stream while 38% had nocturia, burning micturition and incomplete voiding.

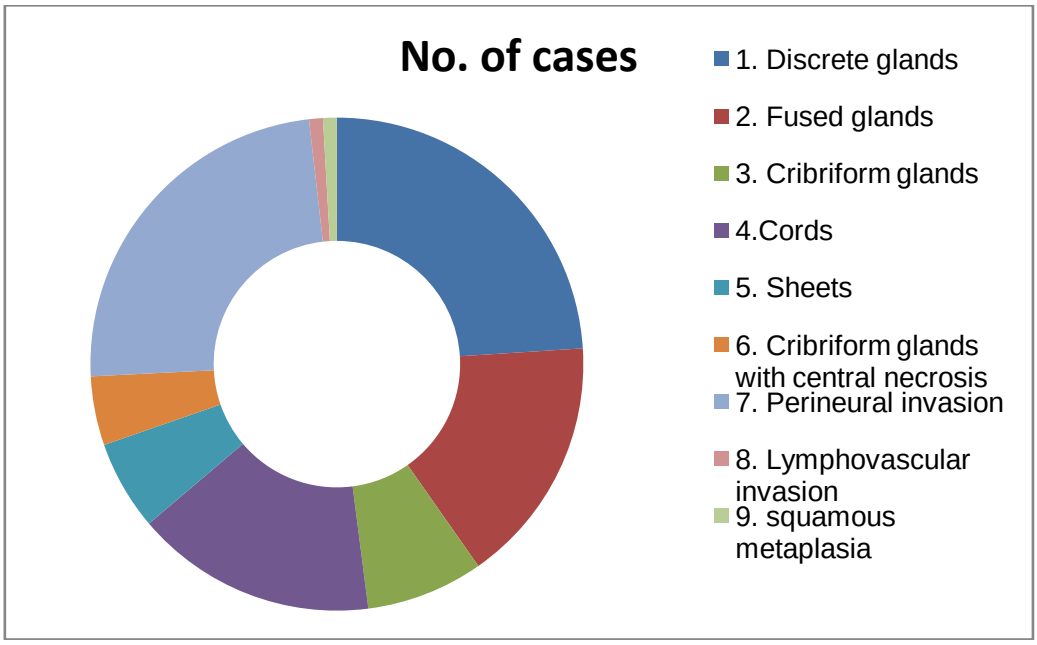
Graph 4: Clinical presentations of patients in study



1. Increased freq	2.Nocturia	3.Poor urinary stream	4.incomplete voiding
5. Urinary retention	6.Dysuria	7.Hematuria	8.Burning micturition

Various morphological patterns were seen with majority of the cases showing one or more than one of the different growth patterns. The tumour was categorized depending on the predominant growth pattern. Majority of the lesions showed discrete glandular pattern. In addition to this, other patterns seen were fused glands, cribriform glands, sheets, cords and tumour with central necrosis pattern. Fifty three cases had showed discrete glandular pattern**.** Fused glandular pattern was seen in 36 cases**.** Cribriform glandular pattern were found in 17 cases. Very few cases showed histology of sheets and cribriform glandular pattern with central necrosis. Perineural invasion were seen in 53 cases of which 2 cases showed presence of ganglion cells**.**Lymphovascular invasion and squamous metaplasia were seen in 2 cases respectively**.** Brisk mitotic activity with abnormal mitotic figures are also seen in high grade tumor**.**

Fig 2: Case distribution of Adenocarcinoma cases

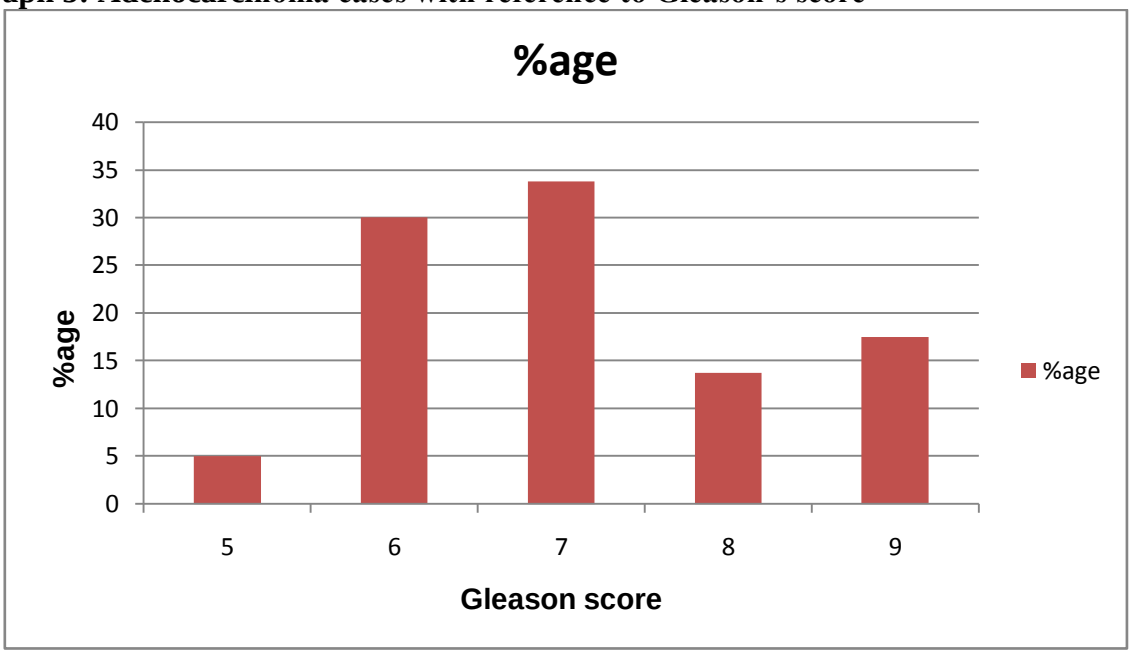


GLEASON SCORE

All of the 80 malignant cases were graded using Gleason's scoring system. Primary grade was assigned to dominant pattern and secondary grade to subdominant pattern. The two numeric grades are added to obtain the Gleason's score. Lowest Gleason score was 5 and highest score was 9 in the present study.

Most common Gleason score in our study was 7(33.7% cases). We also found 11 cases (13.7%) with Gleason score of 8 and 14 cases (17.5%) with Gleason score of 9. All these cases (Grade 7,8& 9) fell under poorly differentiated adenocarcinoma category according to WHO classification. Twenty four cases (30%) were categorised under moderately differentiated adenocarcinoma by WHO with Gleason score of 6 and 4(5%) were described as well differentiated adenocarcinoma with Gleason score of 5.

Graph 5: Adenocarcinoma cases with reference to Gleason's score



DISCUSSION

In our study majority of the patients of BPH presented in the age group of 61-70 years of age and adenocarcinoma in the age group of 71-80 years. The mean age of presentation for BPH and Carcinoma was 69.4 years and 71.7 years respectively. Majority of the patients were found to be 7th (BPH) and 8th (adenocarcinoma) decade.

These findings are comparable with studies done by Lakhey et al,[4]Shirish et al[10] whereas Murthy et al[11], Jasani et al[12] found maximum cases in 6th and 7th decade.

The TURP chips formed bulk of the specimens in our study accounting for 74.8% of total specimens. Our findings were in concordance with few other studies.[10,13]

Most commonest lesion in our study was BPH (72.5%) followed by adenocarcinoma prostate (26.5%) which was in concordance with studies done by Arora et al[14], Jasani et al[12], Anushree et al[15], Shirish et al[10],. Out of 80 cases of adenocarcinoma, 9 were associated with PIN which was also documented in the studies done by Lakhey et al[4] and Maru AM et al[16] however the incidence of PIN in these studies were much higher compared to the present study.

Most common clinical presentation (63.6%) in our study was urinary retention, increased frequency and poor urinary stream while 37.9% had nocturia, burning micturition and incomplete voiding. Our findings were in accordance to various other studies.

BPH is a heterogenous disease that is characterised histologically by a variable degree of stromal and epithelial hyperplasia. Less than half of the cases [31.5% (n=69)] showed

epithelial and stromal hyperplasia without prostatitis. Similar findings were noticed by Lakhey et al[4].

Squamous metaplasia was only seen in 01 case (0.4%) in the present study. A study conducted by Shirishet al[10] found higher incidence (9.6%) of BPH showing squamous metaplasia.

Chronic inflammatory cells of varying degree were found in 35.2%(n=77) of the cases in our study which was comparable with studies done by Lakhey et al[4] whereas it was much lower when compared to study done by Shirish et al (87.9%)[10].

In our study, acute and chronic inflammation was much higher (30.1%) when compared to other studies. One case of acute and chronic inflammation in our study showed presence of squamous metaplasia and granulomatous inflammation.

Seven cases (3.2%) of granulomatous prostatitis were found in our study. Barazkai etal[17] in their study showed 7.1% cases of granulomatous prostatitis.

Most common Gleason score in our study was 7(33.7% cases). We also found 11 cases (13.7%) with Gleason score of 8 and 14 cases (17.5%) with Gleason score of 9. All these cases fell under poorly differentiated adenocarcinoma category as per WHO classification. Our findings were almost similar with various other studies.[80,81,150]while in the study done by Barakzai et al[17] and Babaian et al[18] most common Gleason score was found to be 8.

CONCLUSION

The present study concluded that out of 302 prostatic specimens studied, benign lesions were common, accounting for 72.5% and malignant lesions accounted for 26.5%.

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