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Age Related Lesions of Prostate in Men above 40 Years. An Autopsy Study

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Abstract
Introduction: *Prostate enlargement occurs in elderly men due to two causes, benign prostatic hyperplasia and prostatic carcinoma, which are sources of considerable morbidity and mortality. These two conditions are significant public health issues throughout the world. BPH is extremely common in men above 40years and its incidence is nearly 95% in men above 70 years. A rising incidence of microscopic foci of prostate cancer is found in men with increasing age. Results of autopsy studies have shown that almost 30% of men over the age of 50 have histological evidence of prostate cancer.*
Materials and Methods: *This study involved 50 prostate specimens obtained by autopsy and their histological analysis.*
Results: *The mean age in this study was 57.5years. Non neoplastic lesions studied were benign prostatic hyperplasia, atypical adenomatous hyperplasia, chronic prostatitis.*
Premalignant lesions were low grade prostatic intraepithelial neoplasia, and high prostatic intraepithelial neoplasia.
The incidence of latent carcinoma was 12%.
Conclusion: *The lesions categorised in our study were non neoplastic, premalignant, and carcinoma. Non neoplastic lesions included benign prostatic hyperplasia, chronic prostatitis, basal cell hyperplasia, and atypical adenomatous hyperplasia, The incidence of was BPH (74%), basal cell hyperplasia (6%), atypical adenomatous hyperplasia (10%), and Chronic prostatitis was seen in (24%), low grade PIN (24%), high grade PIN (8%) in the total 50 specimens. The incidence of carcinoma is 12%.*
Keywords: *prostate, autopsy, histopathology, age, non neoplastic, neoplastic, premalignant,latent.*

Introduction

Prostate cancer is the most common malignancy among elderly men and is the second leading malignancy in the Western world.[1] The incidence of prostate cancer has steadily increased over the last decade. A rising incidence of microscopic foci of prostate cancer is found in men with increasing age. Results of autopsy studies have shown that almost 30% of men over the age of 50 have histological evidence of prostate cancer.[2]

Individual cancers show substantial variation in its outcome. It is important to stage the disease because of its variable biological potential. The various prognostic indicators include clinical staging, serum PSA levels, percentage of biopsy core involved and histological grade. The

histological grade correlates both with local invasiveness and the metastatic potential[3].

Prostate enlargement occurs in elderly men due to two causes benign prostatic hyperplasia and prostatic carcinoma, which are sources of considerable sources of morbidity and mortality. These two conditions are significant public health issues throughout the world. BPH is extremely common in men above 40years and its incidence is nearly 95% in men above 70 years.

Prostate cancer is one of the commonest malignancies and a leading cause of cancer related deaths in western world. At present morphology remains the gold standard to assess the status of carcinoma. Various subtypes of prostate cancer are of clinical relevance and have specific clinicopathologic features and prognosis. They include small-cell neuroendocrine, adenoid cystic and basal cell (basaloid), squamous cell, urothelial, and sarcomatoid carcinomas. Other primary malignant prostate lesions that are not adenocarcinomas are exceedingly rare and include primary prostate sarcomas, germ cell tumors, rhabdoid tumors, phyllodes tumors, malignant peripheral nerve sheath tumors, nephroblastoma, primary malignant melanoma, as well as primary hematopoietic malignancies.

Carter and colleagues[4] showed that 50% of men between 70 and 80 years of age showed histological evidence of malignancy. A lifetime risk of 42% for developing histological evidence of prostate cancer in 50-year-old men has been calculated.[5] In men at this age, however, the risk of developing clinically significant disease is only 9.5%, and the risk of dying from prostate cancer is only 2.9%.[5]

Prostate cancer rarely causes symptoms until it is advanced. Abnormalities found on digital rectal examination (DRE) or by serum prostate-specific antigen (PSA) elevations can result in recommending a prostatic biopsy. Transrectal ultrasound (TRUS)-guided, systematic needle biopsy is the most reliable method.

The most valuable adjunctive study for the diagnosis of minimal adenocarcinoma is immunohistochemistry using antibody 34betaE12 [6].

Objectives

1) To estimate the prevalence of benign lesions in the prostate in men above 40years
2) To estimate the prevalence of prostatic carcinoma and protatic intraepithelial neoplasia in autopsy material of prostate.
3) To study the other age related pathological lesions in the prostate.

Materials and Methods

Study Design: Descriptive study.

Setting: Study involves two departments in TD Medical College, Alappuzha, Department of Pathology and Department of Forensic Medicine.

Duration of Study: January 2014 to July 2015.

Case Selection: Specimen of prostate will be collected from 50 consecutive postmortem cases of men above 40years done in the TD Medical College, Alappuzha during the period of January 2014 to July 2015.

Inclusion Criteria

All autopsy specimens of prostate in men above 40years during the period of January 2014 to July 2015.

Exclusion Criteria

Autopsies of those residing outside Alappuzha and those whose consent is not received.

Sample Size: 50 autopsy prostate glands

Study Procedure: After obtaining an informed consent from the relative of deceased, the bladder and prostate will be removed enmasse during autopsy and prostate will be dissected out .The dissected out specimen will be fixed in 10% formalin. Grossly the size, weight, and obvious gross pathology will be noted. Multiple bits including whole cut surface area will be taken from prostate. Haematoxylin-eosin stained sections will be studied. All sections will be studied for age related non neoplastic lesions and other lesions

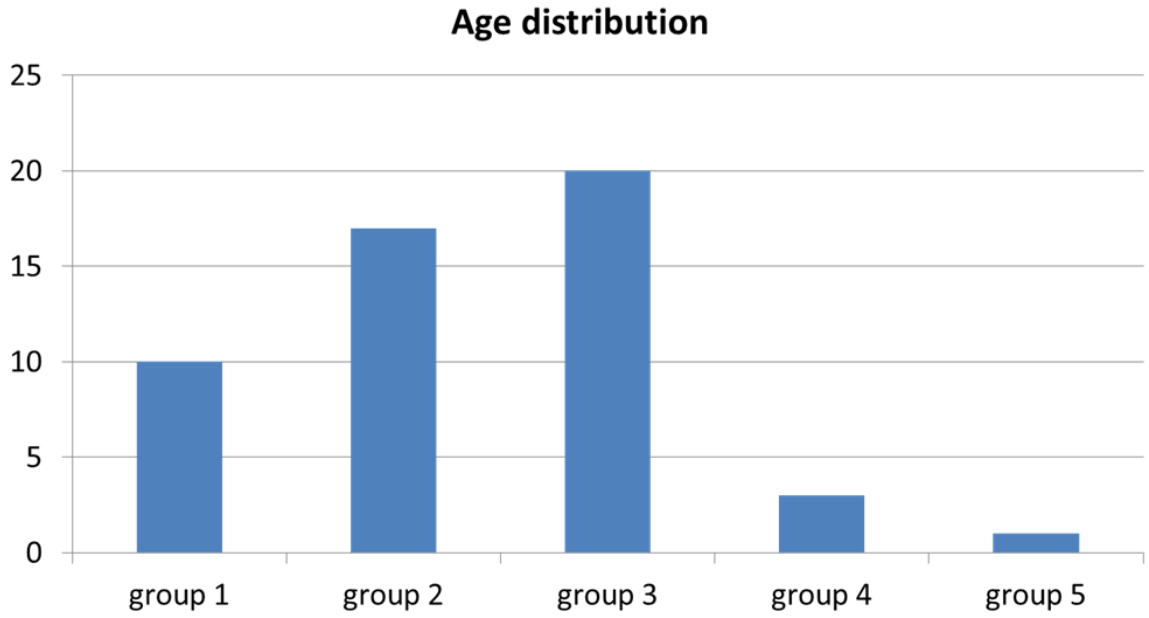
Analysis: Data obtained was entered in open office spread sheet and analysed using appropriate statistical tests.

Observation and Results

A total 50 cases which met the inclusion criteria were included in the study and analysed.

The mean age in our study was 57.5years ranging from 40-82 years.

The associations of carcinoma, precancerous conditions, and benign conditions of prostate were analysed.



The 5 cases of carcinoma was seen in the 6 th decade, 7th decade and 7th decade. All the cases of carcinoma were of lower grade. Gleason scoring was done for the malignant cases. All of them had a gleason score of 6 (3+3). There is increased incidence of carcinoma as the age progresses. One of the carcinoma cases showed perineural invasion.

Table 1 Distribution of prostate carcinoma in various age groups

Age group	Total No.	Positive specimens	Percentage
1. 40-49	10	0	0%
2. 50-59	17	0	0%
3. 60-69	20	2	10%
4. 70-79	2	2	100%
5. 80-89	1	1	100%

Incidence of carcinoma in our study was found to be 12%. There was no significant association between carcinoma and age more than 50years. (fischer exact test 0.07)

Image 1.low power view of the malignant foci

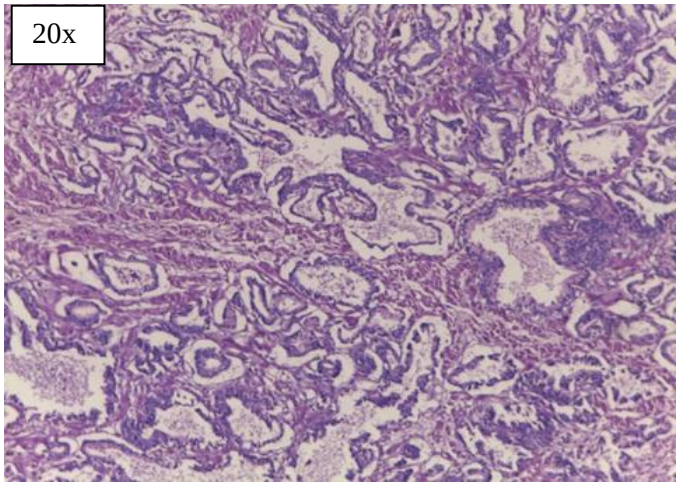
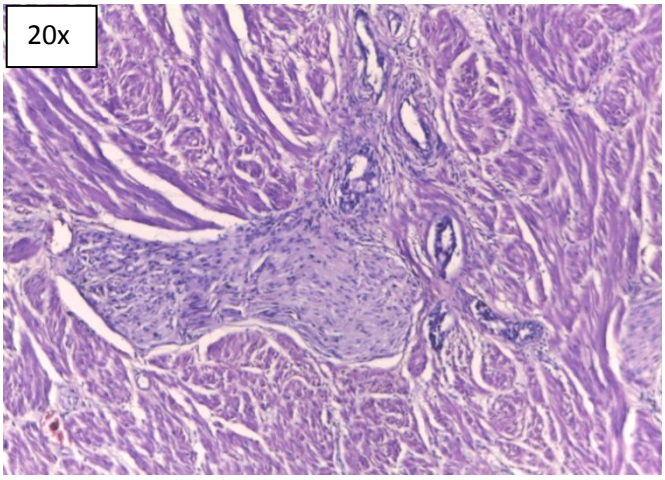


Image 2: showing perineural invasion of neoplastic glands



Age and Benign Prostatic Hyperplasia: BPH was the most common lesion encountered in this study. The lesion showed a linear progression with age. But BPH was seen from the 4th decade onwards. 4 out of 10 cases had BPH in the 4thdecade (40%), 11 out of 17 cases (64.17%) in the 5th decade, 17 out of 20 cases.85%) in the 6th decade, and 1 case each in the 7th and 8th decade

Prostatic carcinoma and BPH

out of the 5 cases of carcinoma 3 also showed BP

Image 3: low power view of benign prostatic hyperplasia

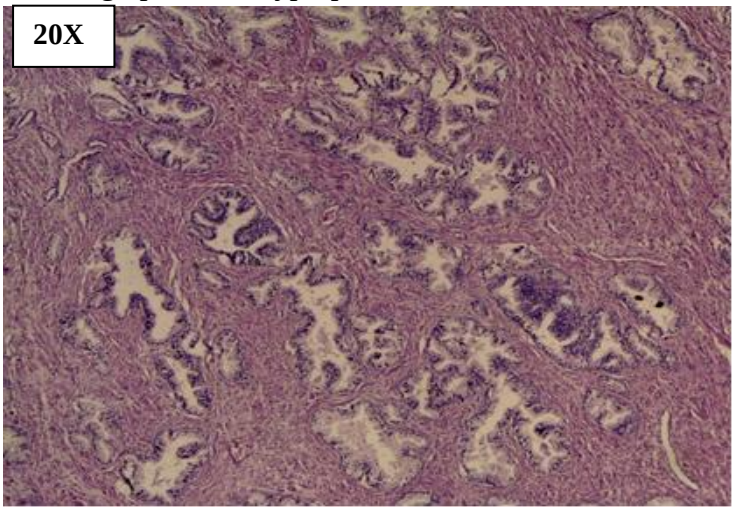


Table 2 Distribution of benign prostatic hyperplasia (BPH) in various age groups

Age group	Total specimens	Positive specimens	Percentage
1. 40 - 49%	10	4	40%
2. 50-59%	17	11	64.71%
3. 60-69%	20	17	85%
4. 70-79%	2	1	50%
5.80-89 %	1	1	100%

Prostatic Intraepithelial Neoplasia (PIN) Prostatic intraepithelial neoplasms were divided into 2 groups, low grade and high grade. There were 16 cases of intraepithelial neoplasms.of these 12 were had low grade PIN, and 4 cases had high grade PIN. Maximium number (6) of low grade PIN were seen in the 6th decade, 5 cases in the 5th decade showed low grade PIN, 1 case in the 4th decade. All the cases of high grade PIN were in the 6 th decade.

Image 4 shows a gland with high grade prostatic intraepithelial neoplasia (HGPIN).Epithelial hyperplasia with nuclear hyperchromasia and nuclear enlargement with tufting and papillary pattern

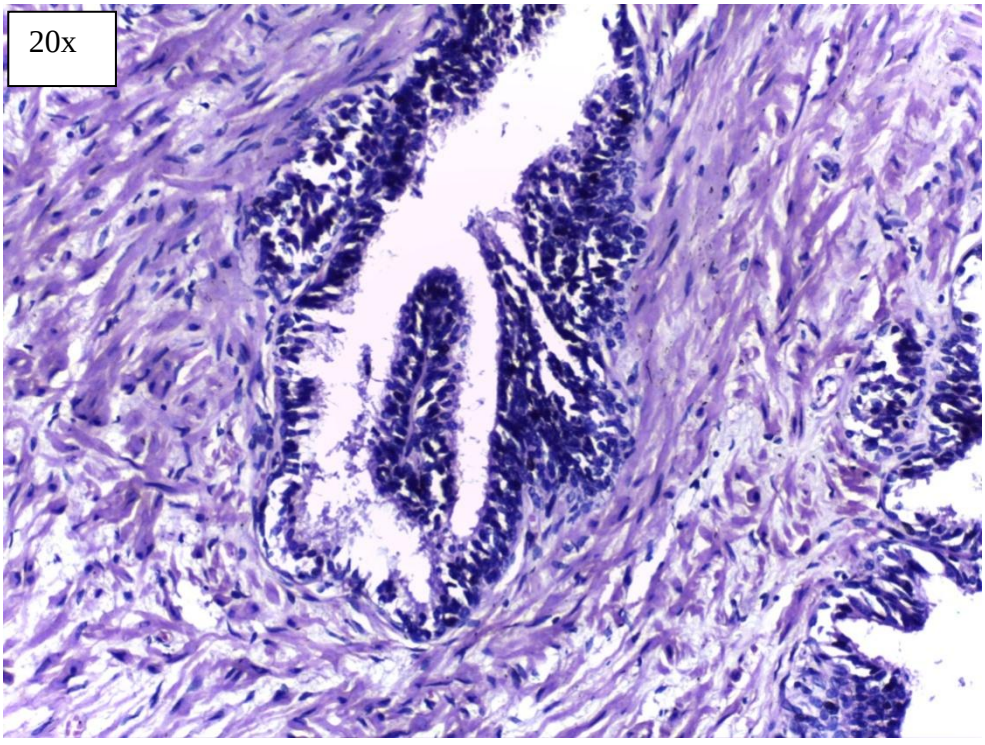
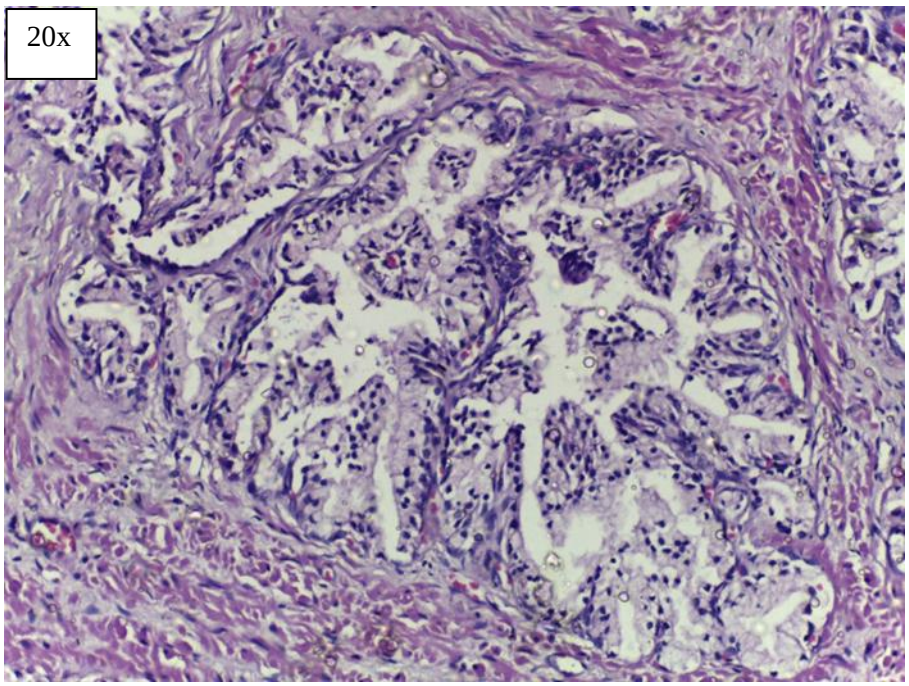


Image 5 shows glands with low grade prostatic intraepithelial neoplasia (LGPIN) lined by cells with mild atypia



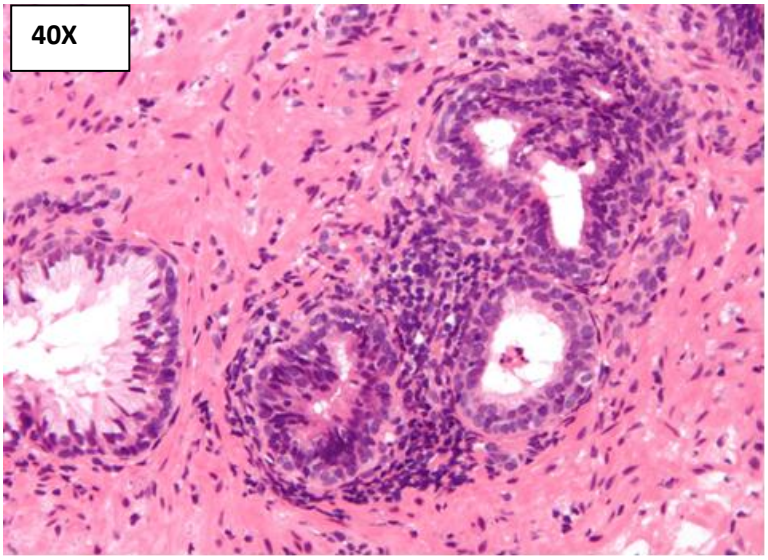
Chronic Prostatitis 12 cases in our study showed evidence of chronic prostatitis with dense lymphocytic infiltrate. 3 cases in the 4th decade showed chronic prostatitis, 2 in the 5th decade, and maximum number of 6 in the 6th decade and 1 case in the 8th decade.

Only one case with carcinoma had evidence of chronic prostatitis. There was no statistically significant association between carcinoma and chronic prostatitis

Table 3 : Distribution of chronic prostatitis in various age groups

Age groups	Total number	Chronic prostatitis +	Chronic prostatitis -
1.40-49	10	3	6
2. 50-59	17	2	15
3. 60-69	20	6	14
4.70-79	2	0	2
5.80-89	1	1	1

Image 6: microphotograph of chronic prostatitis with dense lymphocytic collection



Atypical Adenomatous Hyperplasia (AAH): 5 cases of atypical adenomatous hyperplasia were seen in our study and 3 cases were in the 6th decade and 2 cases in the 5th decade.

Image 7: foci of atypical adenomatous shyperplasia

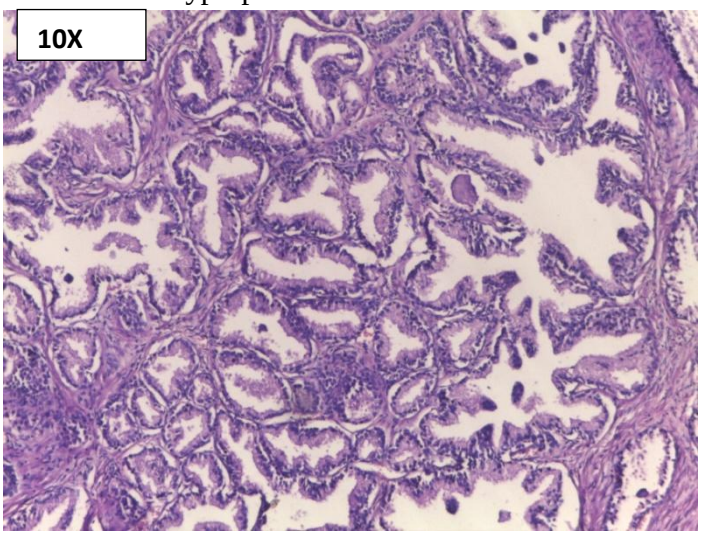
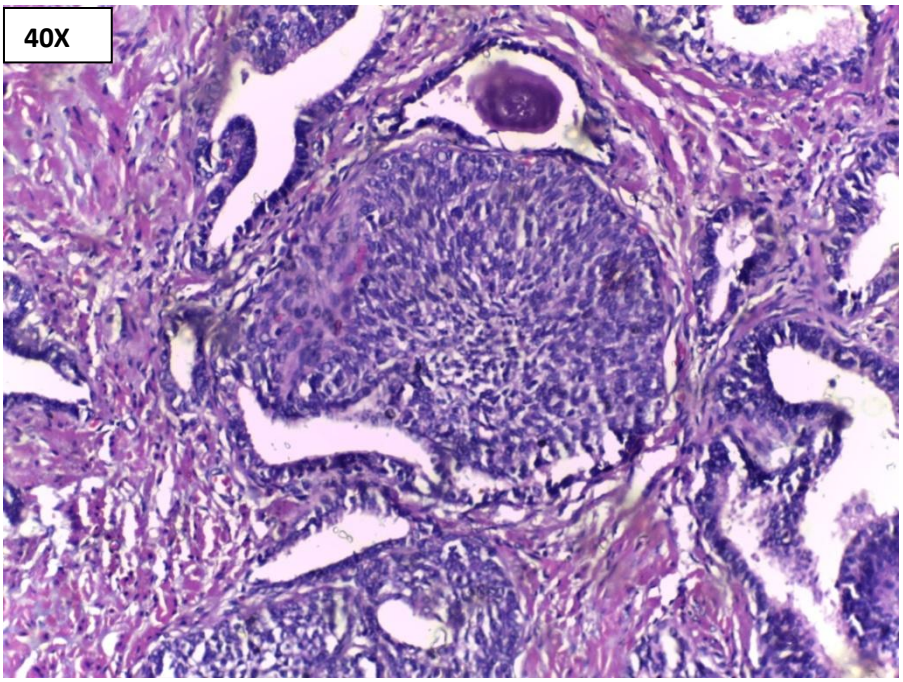


Table 3: Distribution of atypical adenomatous hyperplasia in various age groups

Age group	Total no.	Positive specimens	Percentage
1.40-49	10	0	0%
2.50-59	17	2	34%
3.60-69	20	3	6.6%
4.70-79	2	0	0%
5.80-89	1	0	0%

Basal Cell Hyperplasia: 3 cases in our study had basal cell hyperplasia. None of those cases had PIN or carcinoma. All the cases showed benign prostatic hyperplasia. 2 cases were associated with chronic prostatitis.

Table 3: Distribution of atypical adenomatous hyperplasia in various age groups



Discussion

Three pathological processes affecting the prostate gland with sufficient frequency to merit discussion: inflammation, benign nodular enlargement, and tumours. The burden of prostate cancer falls on men who are elderly or black. The median age at diagnosis is approximately 71 years, and the median age at death is 78 years. More than 75% of all cases of prostate cancer are diagnosed in men older than 65 years of age, and 90% of deaths occur in these patients.

The mean age of the 50 cases in our study was 57.5 years with a range of 40 to 82 years. Maximum number of cases were seen in the sixth decade. Prostatic carcinoma is a tumour of old age and our results were comparable with other studies. In our study out of 50 cases, all the cases which showed prostatic adenocarcinoma, had low gleason grading of (3+3). Less is known about the cause of prostate carcinoma than about any other common cancer in the human body. A number of risk factors for Prostate cancer have been proposed, although the findings are often weak and controversial. The well-established risk factors include: increasing age, race, and family history of prostate cancer. Risk factors that have not been well elucidated include: dietary, obesity, physical inactivity, hormonal, occupational, smoking, infections and/or inflammation, and sexual factors.

Heredity appears to be one of the most consistent and strongest risk factors for the development of prostate cancer.[6] Genetic studies suggest that a strong familial predisposition may be responsible for as many as 5-10% of malignant cases.[7]

Perineural invasion (PNI) was noted in one specimen with adenocarcinoma. The finding of PNI is a potential preoperative predictor of extraprostatic tumor extension. PNI is defined as the presence of prostate cancer tracking along or around a nerve within the perineural space. . PNI is a major mechanism of prostate cancer extension from prostatic parenchyma to periprostatic soft tissue and so PNI extensive enough to be sampled on needle biopsy may signal an increased likelihood of extraprostatic extension of cancer or

cancer recurrence. In a study by Trpkov, no significant differences were found between the patients with and without perineural invasion regarding the organ-confined disease, positive margins, tumor volume, and prostatectomy Gleason score[8].

Prostatic intraepithelial neoplasia (PIN) is the most established precursor of prostatic carcinoma. The presence of prominent nucleoli within an existing duct structure is an easy way to identify the disorder. Four main patterns of high-grade PIN (HGPIN) have been described: tufting, micropapillary, cribriform, and flat. In addition to exhibiting similar cytologic features, both HGPIN and prostatic carcinoma are associated with increased incidence and severity with age, and with high rates of occurrence in the peripheral zone of the prostate. HGPIN and prostate cancer share genetic and molecular markers as well, with PIN representing an intermediate stage between benign epithelium and invasive malignant carcinoma. The clinical significance of HGPIN is that it identifies patients at risk for malignancy.

In a study by Hyung L. Kim, Ximing J. Yang, the incidence of isolated high-grade PIN was 63% and was associated with elevated serum PSA values.[9]

The incidence of PIN in our study was 12%. Low grade lesions being 16%,and high grade being 8%. The PIN was associated with higher age (> 60years) and the association was statistically significant (p value- 0.035).

Benign lesions

Benign prostatic hyperplasia

The incidence of BPH in our study was 74% and was seen in all the age groups . 14% were seen in age group between 40 and 50. Maximum number of cases was seen in 6th decade with 34%.

BPH refers to the increase in size of the prostate in middle-aged and elderly men. It occurs almost exclusively in the transitional and periurethral zones. It is characterized by hyperplasia of prostatic stromal and epithelial cells, resulting in the formation of large, fairly discrete nodules in the periurethral region of the prostate

The prevalence of BPH rises markedly with age. Autopsy studies have observed a histological prevalence of 8%, 50% and 80% in the 4th, 6th and 9th decades of life, respectively.[10] Multiple observational studies from Europe, the US and Asia have demonstrated older age to be a risk factor for BPH onset and clinical progression by several different metrics

Atypical adenomatous hyperplasia

Atypical adenomatous hyperplasia (AAH) is a localized proliferation of small glands within the prostate that may be mistaken for carcinoma. Features that could not reliably separate AAH from carcinoma included lesion shape, circumscription, multifocality, average gland size, variation in gland size and shape, nuclear shape, chromatin pattern, and amount and tinctorial quality of cytoplasm. Although the biologic significance of AAH is uncertain, its light microscopic appearance and immunophenotype allow it to be distinguished from carcinoma in most cases. It is usually a microscopic finding, but occasionally it presents as a mass lesion.

In a study by Bostwick, David G et al, AAH was more common in older patients and in those with greater prostatic weight, higher prostatic volume, and higher serum prostate-specific antigen level.[11]

Our study showed 5 cases of atypical adenomatous hyperplasia (10%). None were associated with carcinoma. There was no significant association with age more than 50years.

Basal cell hyperplasia

Thorsun characterized the incidence and histomorphological attributes of basal cell hyperplasia in a series of 500 consecutive sextant needle core biopsy samples and in 26 completely embedded prostate glands from radical prostatectomy specimens. Comparative proliferation indices (by MIB-1 staining) and apoptotic indices (by TUNEL labeling) were quantitated for peripheral zone versus transition zone basal cell hyperplasia versus normal basal

cells. The incidence of basal cell hyperplasia in prostate needle biopsy tissue was 10.2% (51 of 500 cases)

Our study showed 3 cases with basal cell hyperplasia (6%), 2 in the 4th decade and 1 in the 6th decade. One of the cases was associated with chronic prostatitis. No association with PIN or carcinoma were detected. Though the literature states that a significant association is seen with chronic lymphocytic prostatitis, as the number of positive specimens are few there is no statistically significant association in our study.

Conclusion

1) The mean age in our study is 57.5.
2) The incidence of carcinoma is 12%.
3) All the cases of carcinoma were of low grade, gleason's score (3+3=6).
4) Intraepithelial neoplasms were categorised as low grade and high grade.
5) The incidence of premalignant lesions (PIN) was 12%, low grade being 16% and high grade 8%.
6) PIN was associated with age >50years and was statistically significant (p value- 0.035).
7) The benign lesions categorised in our study were benign prostatic hyperplasia, chronic prostatitis, basal cell hyperplasia, and atypical adenomatous hyperplasia.
8) BPH (74%), basal cell hyperplasia (6%), atypical adenomatous hyperplasia (10%)
9) Chronic prostatis was seen in 12 cases (24%).
10) There was no statistically significant association between chronic prostatitis and carcinoma.
11) There was no association between chronic prostatitis and basal cell hyperplasia in our study.

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