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Original Research Article

Histopathological Study of Prostatic Diseases in B.P.K.I.H.S, Nepal: A Hospital Based Study

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ABSTRACT

Introduction: Carcinoma of prostate is one of the common tumors of elderly men causing significant morbidity and mortality. Other prostatic pathology ranged from inflammatory lesions to benign prostatic hyperplasia (BPH). Gleason score (GS) combined with grade and pathological stage for prostate carcinoma correlates with clinical behavior and is best marker for predicting prognosis.
Objective: To evaluate the histopathological spectrum of various prostatic lesions in biopsy specimen at B.P.K.I.H.S
Methods: A hospital based descriptive cross sectional study over a period of one year was carried out on biopsy specimen received at histopathology laboratory in the department of pathology. Histopathology slides were assessed and categorized into different groups. Prostate carcinoma was graded according to new grading system.
Results: BPH was the commonest encountered lesion seen in the prostate (62.79%). Prostatitis in 13.9%. Prostatic adenocarcinoma was found in about 23.3%, no cases of PIN were documented. Majority of these cases were of high grade adenocarcinoma (Grade Group 4 and 5) with frequent Gleason score 8-10. (P <0.0001)
Conclusion: Various spectrums of prostatic lesions in different age groups were determined. Histopathological study with thorough examination of biopsy section is mandatory to detect malignancy. Increase awareness of prostate malignancy with advancing age and timely mass screening of prostatic lesion is recommended to reduce mortality.

Key words: Benign prostatic hyperplasia, Gleason score, Prostatic adenocarcinoma.

INTRODUCTION

Prostatic diseases are common causes of morbidity in adult males and shows varying incidence in different geographical locations worldwide. [1] Benign prostate hyperplasia (BPH), prostatitis and prostate carcinoma are diseases primary affecting the prostate gland. Of these three, BPH is the most common and often seen in an advanced age. Enlargement of prostate gland causes urinary symptoms like hesitancy, retention, urgency and dribbling. [2,3] Worldwide BPH affects 210 million males and is common over the age of 50 years. [4]

Prostatitis is third most common urinary tract problem for men older than 50 years age. Prostatitis may be acute, chronic or granulomatous. [5,6] Histologic evidence of BPH can be seen in approximately 20% of men by 40 years of age and this percentage increases to 70% by age 60 and to 90% by age 80. [6] Considerable risk factors for BHP include advancing age and

an intact androgen supply. [7] Other Additional risk factors include modifiable factors such as obesity, diabetes, high levels of alcohol consumption, and physical inactivity. [8] Although pathophysiology of BPH is unknown, most accepted mechanism suggests appearance of nodular hyperplasia of prostate is due to action of testosterone and its active metabolite, dihydrotestosterone on prostate gland. [9] Studies have shown that the appearance of prostatic intraepithelial neoplasia (PIN), a dysplastic lining epithelium of prostate gland may precede carcinoma by 10 or more years. [10]

Carcinoma of the prostate is second leading cause of cancer death among men. Carcinoma is a disease of elderly men occurring at age 65 years and above, with increasing trend in Asian countries in last 25 years. [11] The worldwide incidence of prostate carcinoma has been rising rapidly due early detection and screening programmes. [12] Majority of prostate carcinomas are adenocarcinomas constituting more than 95% of total prostatic malignancies. These adenocarcinoma develops from duct acini. Other less common histological subtypes include transitional cell carcinoma, neuroendocrine tumor, small cell carcinomas, signet ring carcinoma, basal cell carcinoma which account for about 5%. [5,10]

The strongest risk factors for prostate malignancy development are advancing age, race, family history, hormonal activity and premalignant conditions such as PIN and atypical adenomatous hyperplasia. [13] Other suggested possible risk factors include association with bladder neoplasm, cigarette smoking, vasectomy, food habits and environmental factors. [12] Prostate carcinoma rates in different studies were in the range of 12.5-30.9% of prostatic lesions [1,4,11,14] Gleason's grading system is superior and the best predictor of disease progression and outcome. [15,16] The aim of the current study was to determine the various histopathological patterns of the prostatic lesions in our set up, where less commonly such studies have been done and to grade and score prostatic adenocarcinomas according to new grading system.

AIM AND OBJECTIVES

1. To evaluate the histopathological spectrum of various prostatic lesions in biopsy specimen at B.P.K.I.H.S
2. To grade prostatic tumors according to microscopic grading system.

MATERIALS AND METHODS

Cases of prostate biopsy including Trans urethral resection of prostate (TURP) with histological diagnosis retrieved during period of one year April 2017 to March 2018 were studied in histopathology lab, department of pathology at B.P. Koirala Institute of Health Sciences (B.P.K.I.H.S), Dharan, Nepal. Hospital based, descriptive cross sectional study was carried out. Ethical clearance was obtained from the institutional ethical review board BPKIHS to conduct the study. Patients who do not give consent for the study, biopsies with inadequate material and patient already diagnosed and undergone treatment for carcinoma prostate were excluded.

The specimens were fixed immediately in 10% formalin for 24 hours. Gross features of specimens were noted. For TURP specimens, approximately 5-7 gm of tissues were processed in one cassette and embedded. The blocks were sliced into 3-5 micron thickness using standard microtome and the sections were further stained with hematoxylin and eosin stain. Special stains were applied in necessary slides. Sections were examined under light microscopy.

Diagnostic criteria followed for diagnosing benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia (PIN), and adenocarcinoma were adapted from guidelines laid down by World Health Organization (WHO).

For carcinoma of the prostate, considering the glandular differentiation and growth pattern of tumor cells in relation to stroma, a new grading system in

conjunction with the Gleason system was applied. Gleason's score is obtained by the sum of predominant tumor pattern with next common pattern. This new grading system has been accepted by the World Health Organization (WHO) for the 2016 edition of Pathology and Genetics, Tumours of the Urinary System and Male Genital Organs. [17,18] Prostate adenocarcinoma was assigned one of the four grades: 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. Grade Group 4 (Gleason score 8), only poorly-formed/ fused/cribriform glands or predominantly well-formed glands with a lesser component lacking glands or predominantly lacking glands with a lesser component of well-formed glands. Grade Group 5 (Gleason scores 9-10), Lacks gland formation (or with necrosis) with or without poorly-formed/fused/cribriform glands. [17,18]

Statistical methods Data obtained from case sheet and slide review were entered in Microsoft Excel 2007 and checked for consistency. They were further entered into SPSS version 11.5 for statistical analysis. Tables containing data distribution were kept in various formats. For descriptive statistics Percentage, range for quantitative data, arithmetic mean, Standard deviation and standard error were applied .For inferential statistics Chi-square test, linear by linear correlation were applied for determination of significant differences between analyzed groups. χ^2-test estimate the degree of association between the selected variables. Level of significance was set at $p<0.05$.

RESULTS

86 specimens were received for histopathological examination, 79 (91.9%) were transurethral resection of prostate (TURP) and 7 (8.1%) were needle biopsies. TURP specimens were grey white to tan colour and received in multiple small tissue bits size ranging from 0.3cm to 1.8 cm in diameter. Seven needle biopsy specimens were strips of gray-white tissue ranging from 0.4 to 1.2 cm in length. The histopathological findings of each case were also noted down. Various prostate pathology was broadly classified into BHP, prostatitis and prostatic carcinoma. BPH was microscopically characterized by proliferation of glandular and fibromuscular component, these glands were lined by two layer of cells comprising of inner columnar and outer cuboidal to flattened epithelium. Papillary infloldings, cystic changes, calcification and corpora amylacea were also seen (figure 1). Benign prostate hyperplasia comprises 54 cases (62.79%). Peak occurrence of BPH was seen in the age group 60-69 years. youngest case of BPH was seen in 53 yrs and oldest in 87 yrs of age with mean age of 67.7±8.1. Maximum number of benign cases 28 (32.5%) were seen also seen in the age group 60-69 years (Table 1, 2).

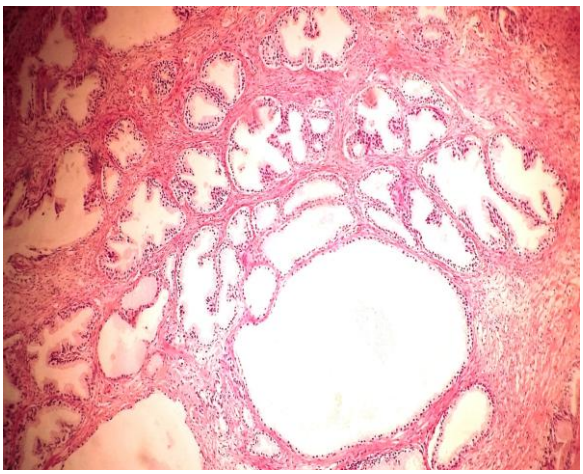

Fig: 1 Photomicrograph showing proliferation of cystically dilated gland and stromal proliferation. (100X H & E Stain) Benign Prostatic Hyperplasia.

Prostatitis accounts 12 cases (13.9%). Microscopically Prostatitis reveals dense inflammatory aggregates of lymphocytes and few plasma cells around glandular and in stromal component (figure 2).Two cases of granulomatous prostatitis was also seen.

These prostatitis were mostly chronic and were associated with BPH.

Table1. Distribution of various prostate diseases on histopathology by age groups in years.

Age Group	Histopathology			Total N (%)
	BPH	**Prostatitis**	**Adenocarcinoma**	
50-59	8	0	0	8 (9.3%)
60-69	26	2	4	32 (37.2%)
70-79	15	6	12	33 (38.4%)
80-89	5	4	3	12 (13.9%)
90-99	0	0	1	1 (1.1%)
Total N (%)	54 (62.79%)	12(13.9%)	20(23.3%)	86 (100%)

(Linear by linear association X^2 12.71, df 1, P <0.0001)

Table 2. Mean age in years of various prostate diseases

Type of Dx category	N	Mean age in years	Std. Deviation	Confidence Interval for Mean at 95%		Minimum	Maximum
				Lower Bound	Upper Bound		
Prostate adeno-carcinoma	20	74.90	8.078	71.12	78.68	61	92
Prostatitis	12	74.50	5.947	70.72	78.28	64	82
BPH	54	67.76	8.196	65.52	70.00	53	87
Total	86	70.36	8.521	68.53	72.19	53	92

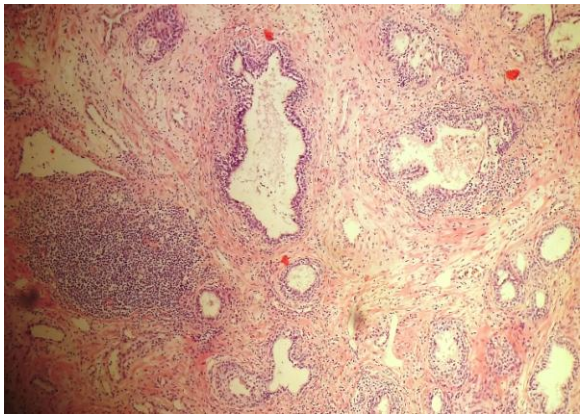

Fig: 2 Photomicrograph showing densely inflamed prostatic tissue with lymphocytes. (100X H & E Stain). Chronic Prostatitis.

Out of 86 cases, 20 cases (23.3%) were diagnosed as prostate carcinoma. All twenty diagnosed malignant cases were of prostatic adenocarcinoma. Peak occurrence of adenocarcinoma was distributed in age group 70-79 years, 12/20 cases. (Table 1). Youngest patient with prostate carcinoma was 61 years and oldest patient was 92 years old with mean age of 74.9 ± 8.07. (Table 2). All case of prostate adenocarcinoma was graded according to new microscopic grading system in conjunction with Gleason system. Gleason's score is obtained by the sum of predominant tumor pattern with next common pattern. The Gleason score 3 + 3 = 6 (Grade Group 1) which represents differentiated tumors to Gleason score 5 + 5 = 10 (Grade Group 5) representing undifferentiated tumors was assigned accordingly to each carcinoma case according to its histologic features. No cases prostatic intraepithelial neoplasia (PIN) was encountered in the study.

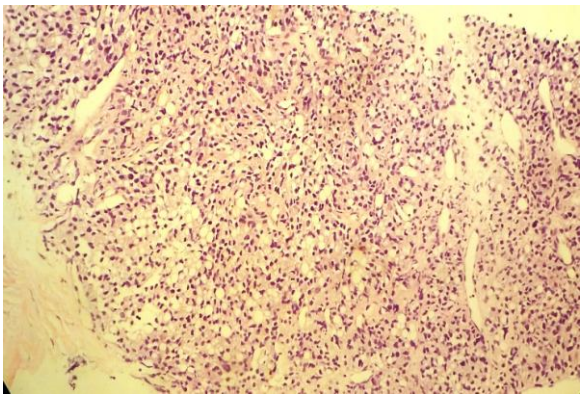

Fig: 3 Photomicrograph showing solid sheets of tumor cells Pattern 5, and poorly formed gland next predominant pattern 4. Gleason score 9 (5+4). Grade Group 5 (100X H & E Stain) **Prostatic adenocarcinoma.**

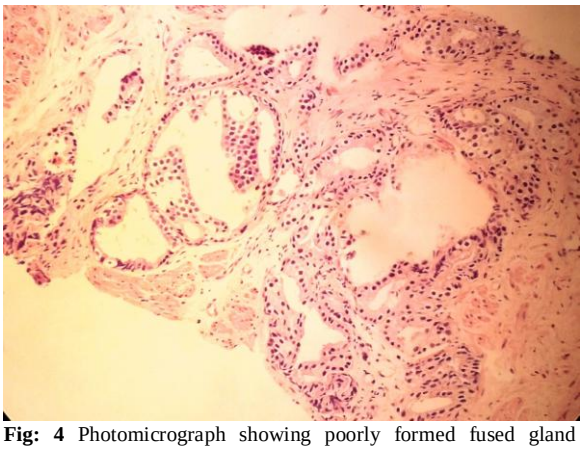

Fig: 4 Photomicrograph showing poorly formed fused gland Pattern 4, cribriform gland pattern 4. Gleason score 8 (4+4). Grade Group 4 (100X H & E Stain). **Prostatic adenocarcinoma.**

We found prostatic adenocarcinoma with Gleason score 9 (Figure 3) were most

common, representing 8 cases (40.0%). Next most common Gleason score was 8 (Figures 4) representing 6 cases (30.0%). 4/20(20%) case with Gleason score 7 and one case each with Gleason score 6 and 10. Table 3 shows distribution of prostate adenocarcinomas with reference to their Gleason score.

Table 3: Distribution Gleason score in prostate adenocarcinoma.

Gleason Score	6	7	8	9	10	Total
Number of cases	1	4	6	8	1	20
Percentage	5.0	20.0	30.0	40.0	5.0	100

9/20 (45%) case of adenocarcinoma were in Grade Group 5, next most common grade we encounter during study was Grade Group 4 with six(6) cases (30%). No adenocarcinomas were seen in grade 3. Similarly 4/20 (20%) malignant cases were in grade 2 and 1/20 (5%) cases was grade 1. (Table 4)

Table 4: Distribution of Grade Group in prostate adenocarcinoma.

Grade Group	1	2	3	4	5	Total
Number of cases	1	4	0	6	9	20
Percentage	5.0	20.0	0	30.0	45	100

DISCUSSION

Prostate diseases are common in the elderly age group. Prostate hyperplasia and malignancy are increasingly frequent with advancing age. BHP is the most common seen lesion. In the present study of 86 cases of prostatic lesions, 54 (62.79%) cases were diagnosed as BHP, 12 (13.9%) cases as prostatitis and 20 (23.3%) cases were diagnosed as of prostatic cancer. In a similar study done by Puttaswamy *et al.*, [19] a total of 62 prostate biopsies were studied over a 2-year period. The most common pathology encountered was benign lesions constituting 80.6% (n = 50). In our study, BHP was seen most common affecting age group 60-69 years. This finding is similar to the study done by Bhat *et al* [20] and Vani *et al.* [2]

Chronic prostatitis was seen in 12 prostatic biopsies, and in the majority of cases was of moderate intensity. Granulomatous prostatitis was seen in 2 cases. These findings are similar to most of the studies on prostatitis, like the study of Anim *et al.* [21] and Mohammed *et al.*, [22] which also found chronic prostatitis as the most common inflammatory lesion affecting prostate followed by granulomatous prostatitis. In a study by Shakya *et al.*, [23] found two cases of PIN among 106 cases (1.88%). Similar studies of Banerjee et al., [24] Maru *et al.* [25] found 10.99% of cases with PIN. In our study no case of PIN encountered.

Prostate cancer is one of most common malignancies in the world. More than 75% cases of all prostate cancers occur in males more than 60 years age. In present study Prostate cancer was found to be affecting 20 (23.3%) cases of all the 86 cases studied. These 20 cases were of prostatic adenocarcinoma histologic type. These findings were in agreement with the studies of Wadgaonkar *et al.*, [3] Puttaswamy *et al.*, [19] Deshmukh *et al.* [26] and Jatav *et al.* [27] who also found, 19.4 %, 15%, 9% and 9.7% of all prostatic lesions as prostatic adenocarcinoma, respectively. These studies also found adenocarcinoma as the principal variant of prostatic cancer, constituting more than 90% of all prostatic cancer cases.

Not a single case of transitional cell carcinoma, small cell carcinoma, neuroendocrine tumors, or secondary tumor was identified in our study due to rarity of these tumors, however a study by Albasri *et al* [4] reported adenocarcinoma in 95.9% and rare incidence of squamous cell carcinoma and transitional cell carcinoma in less than 3%. [4]

We found in our study prostatic adenocarcinoma affecting later decades of life, with the youngest patient affected being 61 years of age. Maximum percentages of patients were seen in their 8th decade of life which was in close concordance with the studies of Bhat et al, [20] Vani et al. [2]

The Gleason grading system is based on histologic pattern of prostate tumor cells and is the most widely used grading method for prostatic adenocarcinoma. It determines microscopic heterogeneity of tumor cell

present in prostate biopsy specimen through primary and secondary pattern of tumors cell. These patterns are added to obtain Gleason score ranging from ≤6 to 10, and group grade is assigned. [17,18,28,29,30] Grade group I represents the most well differentiated tumors, in which neoplastic glands are uniform and round in appearance. By contrast, grade 5 tumors show no glandular differentiation and tumor cell infiltrates stroma into sheets, nest and cord. Our studies showed 75 % cases (15/20) were in Grade Group 4 and 5. Twenty five (25%) 5/20 cases were in Grade Group 1 and 2. Patient with high Grade Group have increase risk of mortality. Studies have shown that patients with a pathological GS of ≤6 have an excellent prognosis with free survival, which can be up to 90%. However, men with a GS ≥7 adenocarcinoma have a 29-43% risk of death from prostate cancer. [30] The Gleason system in conjunction with new grading system and stage correlates with clinical behavior and is best marker for predicting prognosis. [17,18,31] This score helps urologist in decision making for prostate adenocarcinoma treatment. [31]

Present study showed 15 /20 cases (75%) commonest Gleason score of 8-10. In study done by Albasri et al [4] found most common Gleason score 5-7 followed by next common score 8-10. Similarly Angurana et al [32] study reveal 64.3% of carcinoma case with score between 6-10. According to study Bhat et al [20] and Vani et al [2] most of the prostate carcinoma has score 8-9 which is comparable to our study.

CONCLUSION

The most common pathology encountered in prostate specimens is benign prostatic hyperplasia. Only a few cases of prostatitis and no cases of PIN were documented. Most of the benign diseases of prostate occur in the age group of 60-69 years. Histopathological study of biopsy specimen is mandatory to detect malignancy. Most of the prostate carcinoma 75% (15/20 cases) have a high Gleason score 8-10, that correlates with high mortality in patients. Increase awareness of prostate malignancy with advancing age and timely mass screening of prostatic lesion is recommended for early detection and to reduce mortality.

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