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HISTOPATHOLOGICAL STUDY OF CARCINOMA OF THE PROSTATE

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ABSTRACT

Adenocarcinoma is the most common malignancy of the prostate and one of the leading causes of death in males. Prostate cancer accounts for 14% of cancer deaths, the second highest in men after lung cancer. Serum PSA, Fine Needle Aspiration cytology (FNAC) and core biopsy integration of these methods into diagnostic triad has enhanced the early detection of prostate cancer at early stage which is curable. Gleason's grading and serum PSA level are important markers for estimating prognosis of prostatic cancer. **Methods and Material:** 70 cases of prostatic malignancy, admitted to department of urology were included in this study. Serum PSA level of prostate was record in all cases. Needle Core Biopsy and TURP specimens were examined for histopathological diagnosis and Gleason grading was done according to Gleason grading system where ever possible. **Results:** In the present study 70 cases of prostatic carcinoma were study out of which 68 cases were adenocarcinoma (63 cases were conventional adenocarcinoma and 5 cases were adenocarcinoma foamy cell variant) and 2 cases were transitional cell carcinoma. Prostatic carcinoma was most common in 7th decade. Maximum No. of patient has serum PSA level >10ng/ml (92.85% cases of carcinoma). The sensitivity (92.3%) were maximum for serum PSA level > 4 ng/ml for prostatic carcinoma. Transitional cell carcinoma (2.9%) is a less common type of carcinoma other than adenocarcinoma which occur primarly in prostate. According to Gleason grading system maximum no. of cases of

adenocarcinoma (65.71%) were found moderately differentiated adenocarcinoma which have Gleason score 5-7. Followed by poorly differentiated adenocarcinoma (28.6%) which have Gleason score 8-10. 2 cases were found well differentiated adenocarcinoma (2.9%) which have Gleason score 2-4. **Conclusion:** Integration of DRE serum PSA level and Biopsy is the best method for detection of Prostate carcinoma. All prostate carcinoma should be graded by Gleason grading system to know the prognosis of carcinoma.

KEYWORDS: Prostate adenocarcinoma, Gleason grading, PSA level, Transitional cell carcinoma.

INTRODUCTION

Prostate cancer accounts for 14% of cancer deaths, the second highest in men after lung cancer. Both incidence and mortality have decreased in the past few years.[1] The mechanism of prostate carcinogenesis is multifactorial and believed to involve a combination of dietary, environmental, lifestyle and hormonal causes. The Highest frequency of BPH, PIN and adenocarcinoma cases occurred between 50 and 70 years.

The integration Serum PSA, Fine Needle Aspiration cytology (FNAC) and core biopsy are enhanced the early detection of prostate cancer at early stage which is curable. Malignant lesions of prostate are predominantly adenocarcinomas along with other variant.[2] The grading of these carcinomas is performed using Gleason's score.

This study intended to do the incidence in the population, age incidence, typing and grading of this cancer in the Bikaner region of Rajasthan.

MATERIAL AND METHODS

The study was carried out in the department of Pathology, Sardar Patel, medical college and associated group of hospitals, Bikaner. The study was hospital based prospective study, including all the patients with prostate cancer who attended hospital. Gleason grading was done according to Gleason grading system.

Data were collected in a pre-set proforma. Detailed history with clinical presentation, Digital Rectal Examination findings and Ultrasonographic findings and serum prostate-specific antigen (PSA) levels, whenever possible were recorded.

All surgical pathology specimens, including transurethral resection of the prostate (TURP) and prostate needle biopsy specimens were studied by conventional haematoxylin and eosin (H&E) sections and special stains were done wherever it was indicated.

Inclusion Criteria

All in patients clinically suspected of having obstructive uropathy of prostatic origin who underwent cystoscopy and transurethral resection prostate (TURP) or trucut needle biopsy.

Exclusion Criteria

1. Those who had undergone surgical intervention earlier.
2. Inadequate biopsies.
3. Patients on therapy for malignancy.

Grading Systems

Currently the only accepted system and the one recommended by WHO is the Gleason scoring system. The Gleason system has been accepted widely by urologists and medical and radiation oncologists throughout the world as the preferred grading system for prostate adenocarcinoma.

The Gleason scoring system is based on

1. Degree of glandular differentiation.
2. Growth pattern of the tumor in relation to the stroma on low-power magnification.

The predominant tumor pattern (referred to as ‘primary’) is graded from 1 to 5, and the ‘secondary’ pattern (if present) is graded similarly, with the two numbers being added to obtain the Gleason score or sum.

If the tumor has the same pattern throughout (i.e., it has only a ‘primary’ pattern), the number is multiplied by 2 in order to obtain the final score.

Some tumors have a tertiary pattern. This is to be reported only if it is a grade 5. In general, Gleason high score tumors (8–10) are usually abundantly represented in the biopsy cores.

Gleason’s Score

Score - 2-4 - Well differentiated

Score - 5-7 - Moderately differentiated

Score - 8-10 - Poorly differentiated

Table 1- Gleason Grading

STAGE	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
3a	Single, separate, much more variable glands; may be closely packed but usually irregularly separated; ragged, poorly defined edge
3b	Like 3a, but very small glands or tiny cell clusters
3c	Sharply and smoothly circumscribed rounded masses of papillary or loose cribriform tumor (‘papillary intraductal tumor’)
4a	Raggedly outlined, raggedly infiltrating, fused glandular tumor
4b	Like 4a, with large pale cells (‘hypernephroid’)
5a	Sharply circumscribed, rounded masses of almost solid cribriform tumor, usually with central necrosis (‘comedocarcinoma’)
5b	Ragged masses of anaplastic carcinoma with only enough gland formation or vacuoles to identify it as adenocarcinoma

Results- Maximum no. of biopsy specimen received were core needle biopsy (77.1%) followed by TURP CHIPS (22.9%).

In the present study 70 cases of prostatic carcinoma were study out of which 68 cases were adenocarcinoma (63 cases were conventional adenocarcinoma and 5 cases were adenocarcinoma foamy cell variant) and 2 cases were transitional cell carcinoma.

Distribution of cases according to age

Maximum no. of patients of carcinoma was found in age group of 61-70 years (30 cases, 42.85%) followed by 71-80 years age group which make (22 cases, 31.42%) of total cases and 51-60 years age group (9 cases, 12.85%).

>80 year age group have low incidence of cases makes only (5 cases, 7.14%) of total cases. Minimum no of patient was found in 41-50 years age group (4 cases, 5.71%). Mean age group of carcinoma - 69.43 years.

Table: **2**. **Distribution of cases according to clinical complaints.**

Clinical complaints	No. of cases	Percentage
Frequency	43	61.42%
Decreased stream of urine	35	50.0%
Hesitancy	25	35.71%
Urgency	27	38.57%
Residual urine	26	37.14%
Nocturia	21	30.0%

Only 2 (2.85%) cases out of 70 cases of carcinoma were showing serum PSA level <4ng/ml. Only 3 (4.28%) cases out of 70 cases of carcinoma were showing serum PSA level 4-10ng/ml. 65 (92.85%) cases out of 70 cases of carcinoma were showing serum PSA level >10ng/ml.

Table: 3. Distribution of cases according to type of carcinoma

Type of carcinoma	Frequency	Percent
Adenocarcinoma	63	90.0
Adenocarcinoma(foamy)	5	7.1
Transitional cell ca.	2	2.9
Total	70	100.0

Table: 4. Distribution of cases according to Gleason score

Gleason score	Frequency	Percent	Grade of Adenocarcinoma
4	2	2.9	Well diff. adenocarcinoma
5	3	4.4	Moderately diff. adenocarcinoma
6	11	16.2	
7	32	47.1	
8	11	16.2	Poorly diff. adenocarcinoma
9	9	13.2	
Total	68	100.0	

Only 2 (2.9%) cases out of 70 cases of adenocarcinoma have Gleason score 4 and graded as well diff. adenocarcinoma.

46 (67.47%) cases out of 70 cases of adenocarcinoma have Gleason score 5-7 and graded as moderately diff. adenocarcinoma.

20(29.41%) cases out of 70 cases of adenocarcinoma have Gleason score 8-9 and graded as poorly diff. adenocarcinoma.

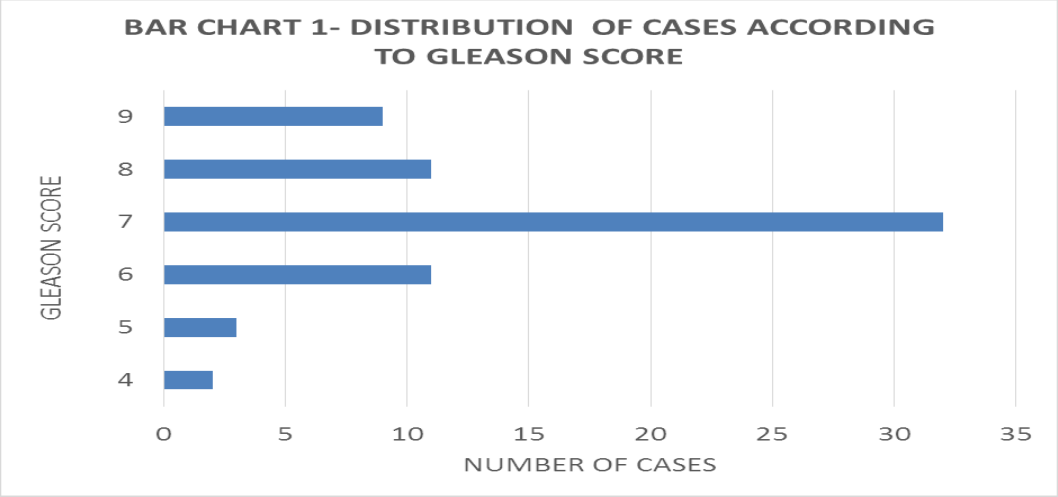

Table: 5. Distribution of cases according to final histopathological diagnosis

Diagnosis	Frequency	Percent (%)
Well diff. Adenocarcinoma	2	2.9
Moderately diff. Adenocarcinoma	46	65.71
Poorly diff. Adenocarcinoma	20	28.6
Transitional cell carcinoma	2	2.9
Total	70	100.0

According to Gleason grading system maximum no of cases of adenocarcinoma (46 cases, 65.71%) were found moderately differentiated adenocarcinoma which have Gleason score 5-7. Followed by poorly differentiated adenocarcinoma (20 cases, 28.6%) which have Gleason score 8-10. 2 cases were found well differentiated adenocarcinoma (2 cases, 2.9%) which have Gleason score (2-4). 2 Cases (2.9%) were found Transitional cell carcinoma which is not graded by Gleason grading system.

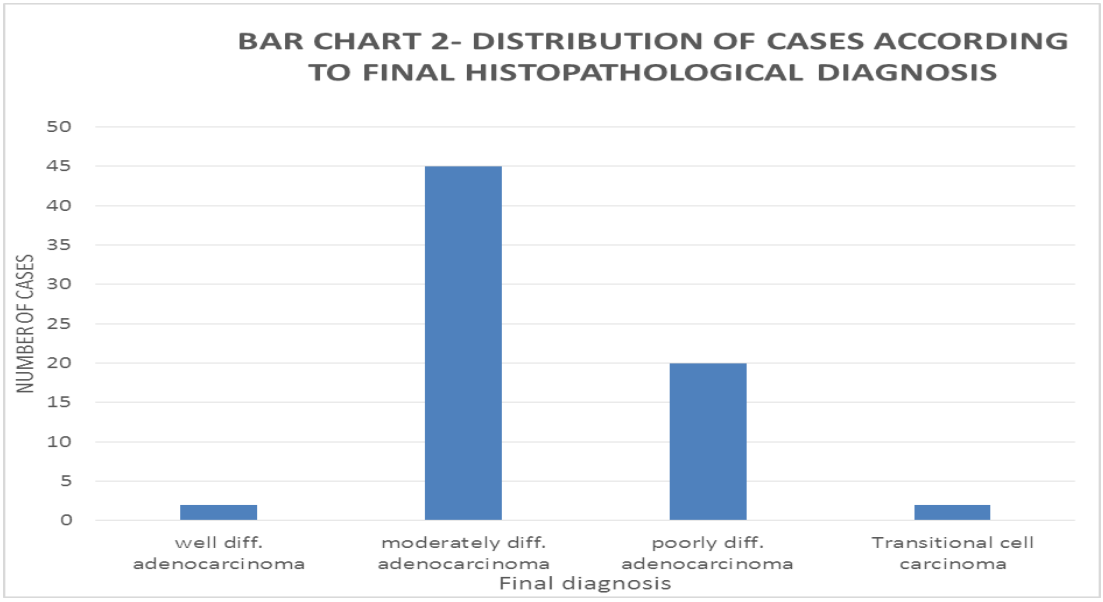

TABLE: 6. Distribution of serum PSA level according to Type and Grade of carcinoma

Serum PSA value (ng/ml)	Well diff. Adenocarcinoma	Moderately diff. Adenocarcin--oma	Poorly diff. Adenocarci-noma	Transiti-onal cell carcinoma	Total	Percent
<4	0	1	1	0	2	2.85
4-10	0	3	0	0	3	4.29
>10	3	41	19	2	65	92.85
Total	3	45	20	2	70	

FIGURE WITH LEGEND-

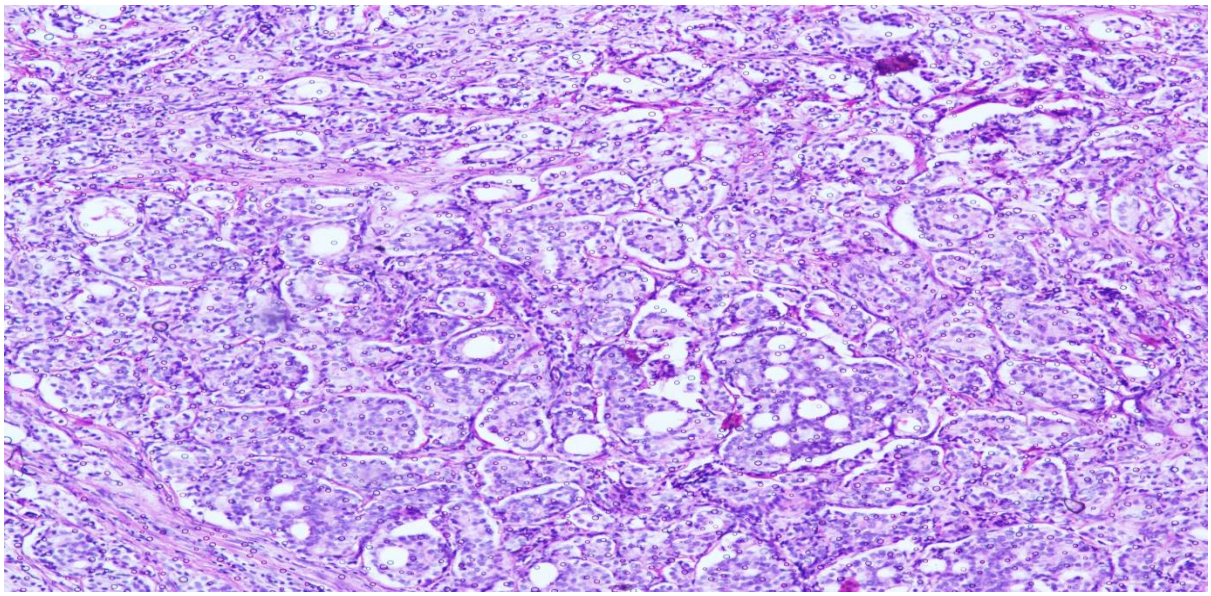

Figure 1: Adenocarcinoma prostate Gleason Grade 2 showing single and separate non uniform glands (H&E, 10x).

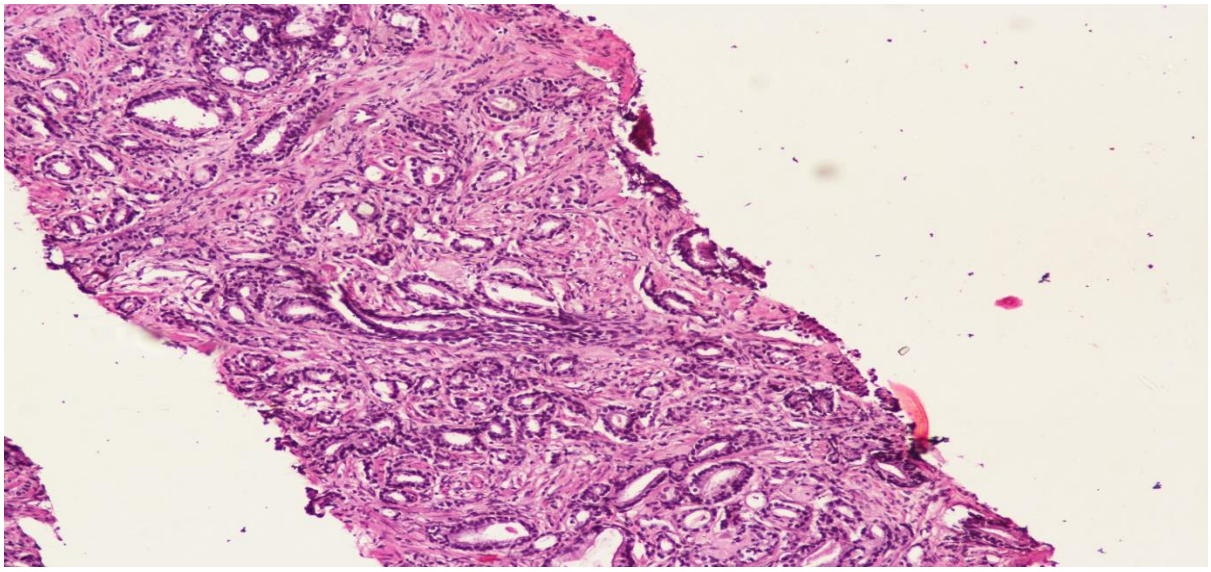

Figure 2: Adenocarcinoma prostate Gleason Grade 3 showing single and separate glands having marked variation in size and shape and increased stromal component in between glands (H&E, 10X).

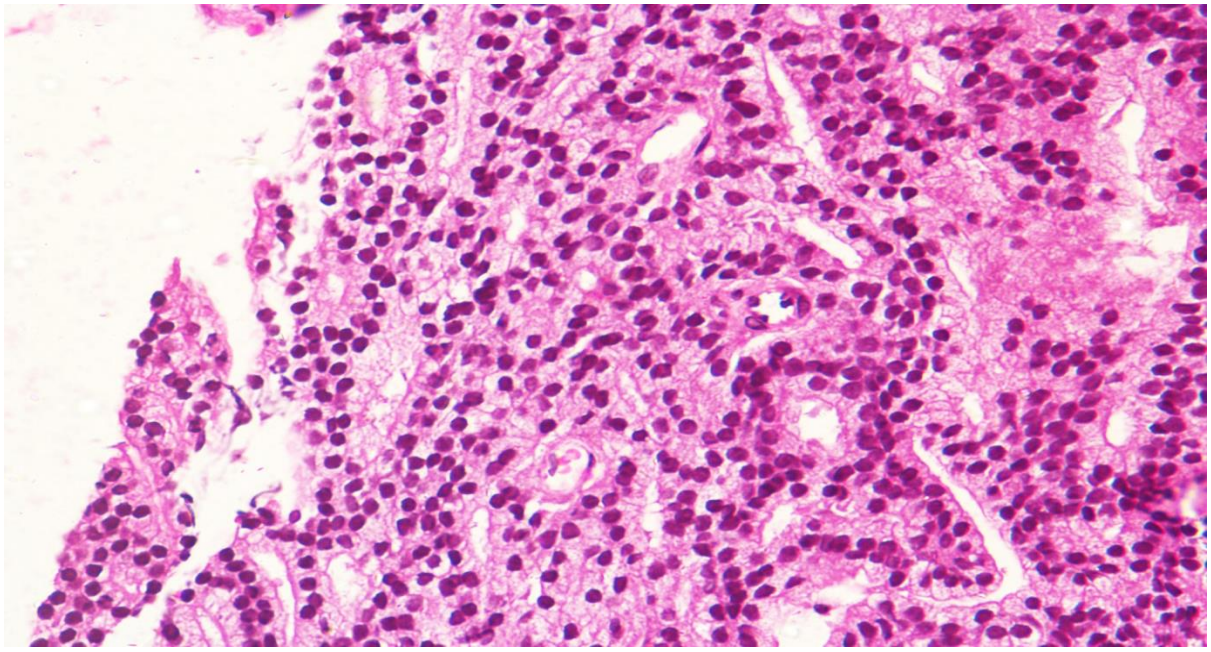

Figure 3: Adenocarcinoma prostate Gleason Grade 4 High power view showing fused glands, no single and separate glands (H&E, 40x).

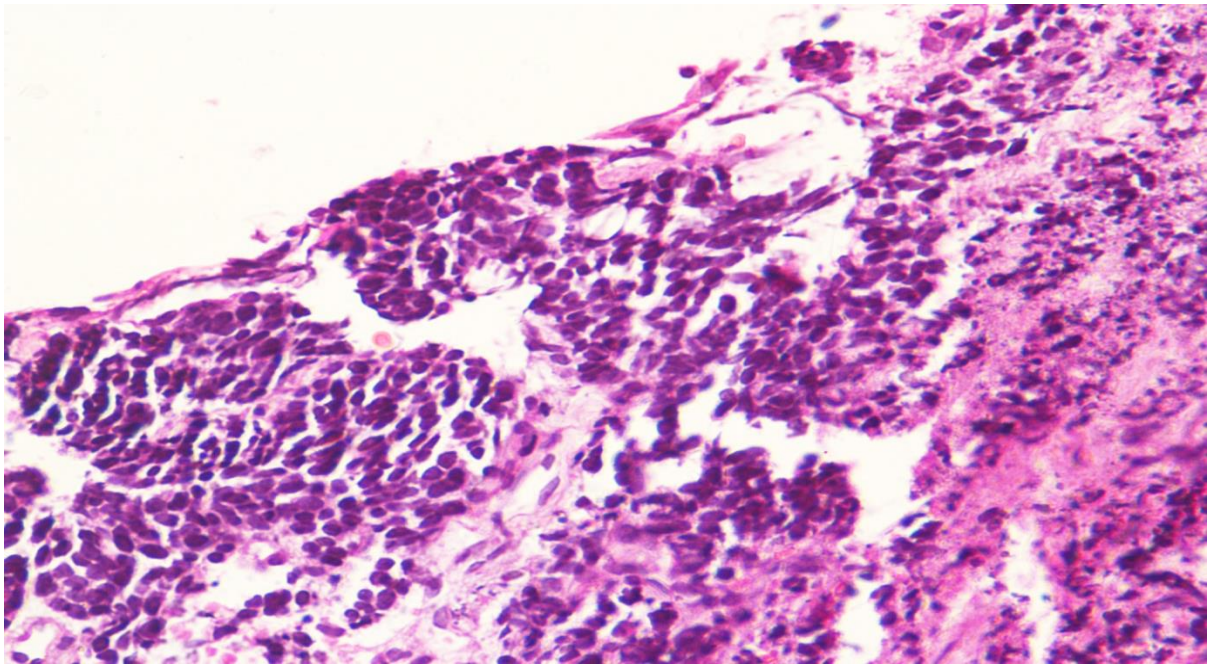

Figure 4: Adenocarcinoma prostate Gleason Grade 5 high power view showing no glandular differentiation with solid masses of highly pleomorphic cells (H&E, 40X).

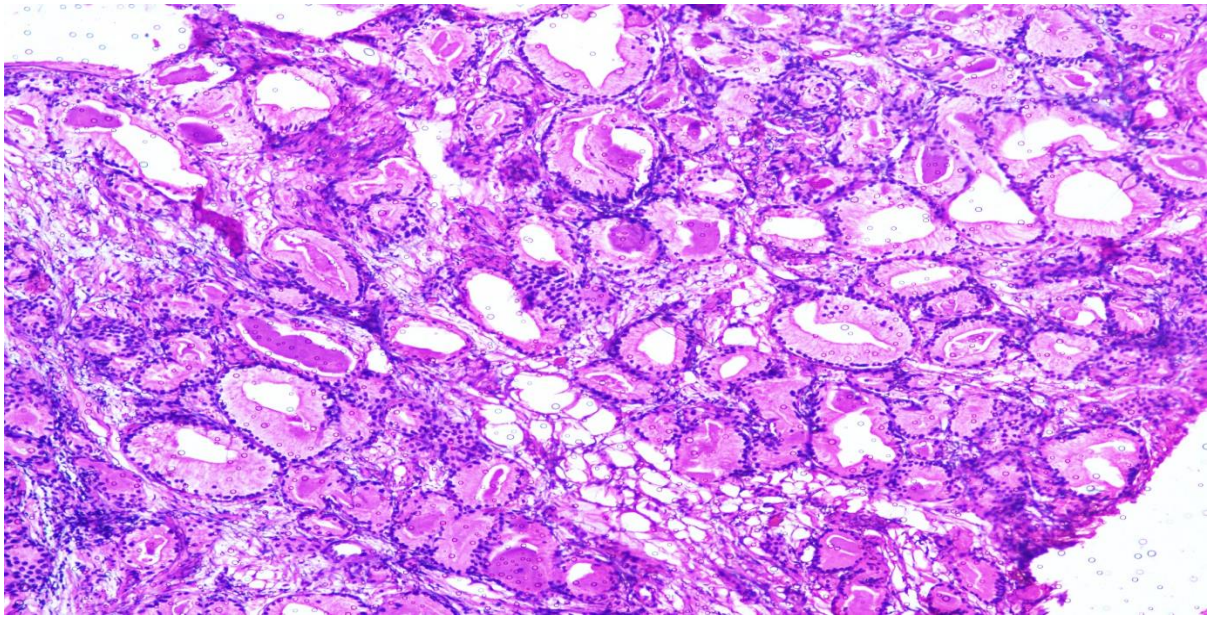

Figure 5: Adenocarcinoma prostate (foamy gland variant), Glands show little cellular & nuclear pleomorphism with abundant foamy eosinophilic cytoplasm (H&E, 10x).

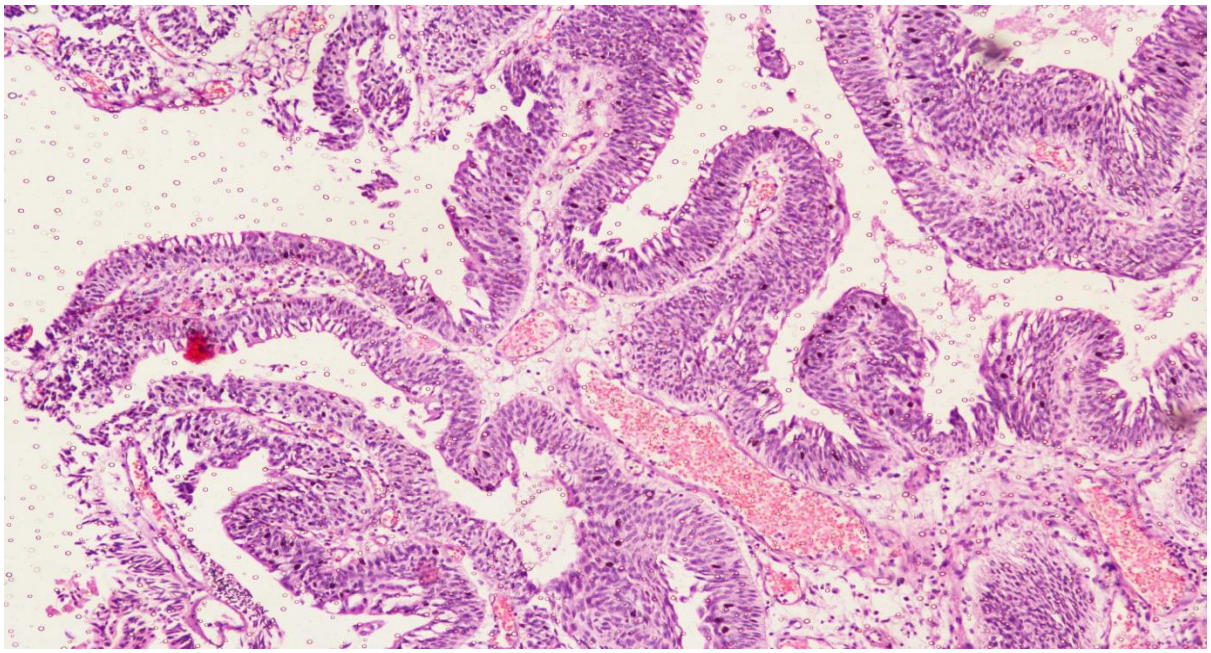

Figure 6: Transitional cell carcinoma prostate- Showing papillae lined by transitional epithelium with fibro-vascular core (H&E, 10x).

DISCUSSION

Adenocarcinoma is the most common malignancy of the prostate gland, accounts for more than 25% of all malignancies in men. As a result of aggressive screening and better treatment, both the incidence and mortality have significantly decreased in the past few years.[3]

Prostate cancers are relatively rare in Asian populations, but recent data indicate that the incidence is rapidly increasing.[4]

Conventional acinar adenocarcinoma represents over 90% of prostate carcinomas. The majority are multifocal (60%-90%)[5] and exhibit an acinar or mixed acinar and ductal growth pattern.[6-7] The remaining 10% are composed of variants of adenocarcinoma. Carcinomas may arise in any zone of the prostate, but the relative distribution is different in each zone; 68% of the carcinomas arise in the peripheral zone, 24% in the transition zone, and 8% in the central zone.[8] Adenocarcinoma rarely can arise from the ectopic prostate tissue.[9]

Distant metastatic spread occurs when carcinoma invades into lymphovascular spaces. The most common sites of metastasis are regional pelvic lymph nodes, bone, and lung.[6, 10]

The principle criteria for diagnosis of well differentiated adenocarcinoma include a small-gland proliferation recognized as being discrete or focally infiltrative on low-power examination, the presence of a single cell lining with complete absence of the basal cell layer, nucleomegaly, and presence of large nucleoli.[11]

Several other features have been shown to be helpful for diagnosis of carcinoma—intraluminal crystalloids, blue mucin, glomerulations, mucinous fibroplasia (collagenous micronodules), and circumferential perineural invasion.

Among a survey of genitourinary pathologists, features that were considered to be pathognomonic for cancer were glomeruloid bodies (58%), collagenous micronodules (64%), circumferential perineural invasion (84%), and glands in fat (36%). When none of these features were present, 39% of pathologists required a minimum of 2 to 10 glands (median 3) to diagnose cancer, whereas the others had no lower limit.[12]

Although several grading systems have been proposed for prostatic carcinoma in the past, such as those from the MD Anderson Cancer Center, Gaeta, and Mostofi [13,14] currently the only accepted system and the one recommended by WHO is the Gleason scoring system.
The Gleason scoring system is based on

1. Degree of glandular differentiation.
2. Growth pattern of the tumor in relation to the stroma on low-power magnification.

The rules of applying Gleason's system according to the association of Directors of Anatomic and Surgical Pathology are as under:

The predominant tumor pattern (referred to as 'primary') is graded from 1 to 5, and the 'secondary' pattern (if present) is graded similarly, with the two numbers being added to obtain the Gleason score or sum.

If the tumor has the same pattern throughout (i.e., it has only a 'primary' pattern), the number is multiplied by 2 in order to obtain the final score.

Some tumors have a tertiary pattern. This is to be reported only if it is a grade 5.In general, Gleason high score tumors (8–10) are usually abundantly represented in the biopsy cores

Gleason's Score.

Score - 2-4 - Well differentiated

Score - 5-7 - Moderately differentiated

Score - 8-10 - Poorly differentiated

The tumor is divided into 5 patterns based on the tumor differentiation, with 1 being best differentiated and 5 being worst differentiated. Because of the frequent heterogeneity of tumor differentiation, prostate cancers often have more than one pattern. In the original Gleason grading system, the most common patterns (primary and secondary) are recorded. However, in the revised Gleason grading system, the score has been revised to the primary and worst patterns instead of the second most common pattern for biopsy grading. The sum of these patterns constitutes a score that ranges from 2 to 10.[15-17]

Gleason grading has been proved as a reliable and clinically significant prognostic factor in numerous studies. It correlates with extraprostatic extension, seminal vesicle invasion, and regional lymph node metastases.[18] It is one of the key variables in several well-established prognostic models.

PSA recurrence-free survival of 2 years and 4 years was 62% and 35%, respectively, for patients with a radial distance of less than 0.75 mm, compared with 35% and 18%, respectively, for those with a radial distance of 0.75 mm or greater.[19]

Variants of prostatic adenocarcinoma account for 5% to 10% of all adenocarcinomas. Recognition of these variants is important because many have a poorer prognosis than conventional acinar prostate adenocarcinoma. By convention, Gleason grading is often

applied to these variants and is almost always pattern 3 or higher.[20] Variants of adenocarcinoma with their proposed Gleason grading recommendations are listed in Table given below.

Table: 7. Variants of Prostate Carcinoma with Gleason Grading and Patterns of Prostate Cancers

Histologic Type or Pattern	Gleason Grade
Mucinous carcinoma	4, may be 3 (graded by underlying architectures)
Ductal–endometrioid	4, 5 with necrosis
Signet ring cell carcinoma	5
Foamy gland carcinoma	3-5, graded by underlying architectures
Pseudohyperplastic carcinoma	3
Atrophic carcinoma	3
Adenosquamous/squamous carcinoma	Not graded
Sarcomatoid carcinoma	Not graded
Small cell carcinoma	Not graded
Transitional cell carcinoma	Not graded
Adenoid cystic/basaloid carcinoma	Not graded
Glomeruloid patterns	3 or 4 (no consensus)
Collagenous micronodules	3 (subtract collagen from analysis)
Vacuoles Mucin	
Subtract vacuoles from analysis	
Subtract mucin from analysis	

The prognosis of prostatic TCC is generally very poor, and it does not respond to hormonal therapy.[21,22] Although TCC may arise de novo in the prostate, most cases are associated with TCC of the urinary bladder.[21, 23]

CONCLUSION

Prostate adenocarcinoma are important clinicopathological entity in elderly people. Integration of DRE serum PSA level and Biopsy is the best method for detection of Prostate carcinoma. All prostate carcinoma should be graded by Gleason grading system to know the prognosis of carcinoma.

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