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Clinico-pathologic spectrum of Prostatic lesions with correlation between androgen receptor staining and Gleason's Score - A 5 year study.

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Introduction

The common lesions affecting the prostate that lead to prostatic enlargement or growth include benign prostatic hyperplasia (BPH), prostatitis, prostatic intraepithelial neoplasia (PIN) and prostatic adenocarcinoma[1]. All these conditions arise in males after 50 years of age and are due to the effect of androgen released from testis. Carcinoma of the prostate is the most common malignant tumour in men over the age of 65 years[2]. The vast majority of these malignant neoplasms are of epithelial origin and differentiation and are carcinomas. There are rare malignant neoplasms in the prostate such as malignant mesenchymal neoplasms (sarcomas) and hematolymphoid neoplasms (lymphomas) of the prostate[3]. Carcinoma prostate is the most frequently diagnosed cancer in men next to carcinoma lung and according to national cancer registries in India it is the second leading site of cancer[4]. The incidence of prostate cancer is low in the Asian countries; however, the incidence is rising by 1% every year. Study of age-specific incidence curves reveals that prostate cancer risk begins to rise sharply after age OF 55 years and peaks at age of 70–74 years, declining slightly thereafter[5]. Androgens play an important role in prostate cancer. Like their normal counterparts, the growth and survival of prostate cancer cells depends on androgens, which bind to the androgen receptor (AR) and induce the expression of pro-growth and pro-survival genes[6]. Since the prostatic diseases both benign and malignant are common and there is evidence of rise in prostate cancer among Asian countries it was felt worthwhile to undertake the present study, our purpose was to analyze

the various clinicopathological spectrum of various prostatic lesions in our tertiary hospital, to study the correlation between the prostatic lesions, patient age and serum PSA, to evaluate the expression of Androgen receptor (AR) in prostatic Carcinomas and its relationship with Gleason score.

Materials And Methods

A combined retrospective and prospective study was conducted in Sher-I- Kashmir Institute of Medical Sciences, Srinagar. A comparison of various clinicopathological parameters was done and a total of 453 patients were included, among which youngest patient was 30 years old and the oldest patient was 85 years old. 262 benign cases and 191 malignant cases were identified on histopathological diagnosis. Serum PSA levels were correlated with age and the prostatic lesions. Among the cases of malignant lesions 40 were subjected to androgen receptor immunohistochemical staining to evaluate its expression and correlation with the Gleason's grading system. Samples from all the Transrectal ultrasound guided (TRUS) biopsies, Transurethral resection of prostate (TURP) chips and radical prostatectomy specimens were included in our study. In retrospective part of the study**,** slides and paraffin blocks were retrieved from archives of the Department of Pathology, SKIMS. Immunohistochemical staining was performed manually according to the instructions provided in the manual attached to the primary antibody**.** The number and intensity of immunoreactive nuclei were assessed by two observers. Owing to the heterogenous content of positive staining cells in the tumors, each slide was scanned at X 40 to identify the areas of highest staining. The intensity of staining was evaluated on a scale of 0-3, where 0= no staining, 1= weak staining, 2= moderate staining and 3 = strong staining. The intensity grades were reported by two pathologists and in concordance a third opinion was taken. Considering the nature of heterogenous staining of PCa, we also used histological score (HSCORE), which is a measure of both the intensity and distribution of staining. The H score was calculated using the equation: HSCORE= $\Sigma Pi\ (i+1)$, where (i) is the intensity score and Pi is the percentage of stained epithelial cells for each intensity. This method of scoring has shown to have low intraobservor and interobserver error. The data collected from patients and retrieved from the RCC section of the hospital was entered in a Microsoft Excel spreadsheet. The data was then compiled by using Statistical package for social sciences (SPSS 27) and relevant tables and charts were generated.

Results

In this study a total of 453 patients were included, with an age range of 30 to 85 years. Out of the total, majority of patients were in the age group of 60-80 years. Out of 453 cases, 262 were benign and 191 were malignant, hence benign cases were found to be more common than malignant cases. Out of the 262 benign cases, 103(39.3%) were in the age group of 60-70 years, followed by 70-80 years age range. Out of the 191 malignant cases 80(41.9%) were seen in the age group of 70-80 years. The mean age of presentation of benign cases was 65.97±8.781 and that of malignant cases was 69.08±7.891. On sub classifying the prostatic lesions, out of the 262 benign cases, 197 were found to be BPH and of the 191 malignant cases, 163 were Adenocarcinoma. Following BPH; Chronic prostatitis was found to be the most common benign prostatic disease Mean age of presentation of patients with chronic prostatitis, BPH with prostatitis, PIN was

66.21±8.991, 66.69 ±8.044 and 69.30±6.530 respectively. The distribution is shown in table 1.

Age group	Sub-Distribution of Prostatic Lesions						Total
	BPH	Adeno	BPH With Prostatitis	Adenocarcinoma With HGPIN	Chronic Prostatitis	Others	
<40	0	0	0	0	0	1	1
	0.0%	0.0%	0.0%	0.0%	0.0%	5.3%	0.2%
40-50	3	0	0	0	0	0	3
	1.5%	0.0%	0.0%	0.0%	0.0%	0.0%	0.7%
50-60	39	7	3	1	7	2	59
	19.8%	4.3%	11.5%	5.0%	25.0%	10.5%	13.0%
60-70	81	70	13	7	6	5	182
	41.1%	42.9%	50.0%	35.0%	21.4%	26.3%	40.2%
70-80	58	66	7	10	12	9	162
	29.4%	40.5%	26.9%	50.0%	42.9%	47.4%	35.8%
>=80	16	20	3	2	3	2	46
	8.1%	12.3%	11.5%	10.0%	10.7%	10.5%	10.2%
Total	197	163	26	20	28	19	453
	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

Table 1; Age wise distribution of various histological types of prostatic lesions

An overlap of symptoms was seen in most of the patients. Frequency (409, 90.3%) was the most common presenting complaint among both benign, and malignant prostatic lesions followed by difficulty in voiding (230, 50.8%). The distribution of clinical symptoms is shown in table 2.

Clinical symptoms	Benign (n=262)	Malignant (n=191)	Total (n=453)
1. Frequency	235 (89.7)	174 (91.1%)	409 (90.3%)
2. Difficulty In Voiding	125 (47.7%)	105 (55.0%)	230 (50.8%)
3. Urgency	120 (45.8%)	34 (17.8%)	154 (34.0%)
4. Hesitancy	98(37.4%)	27(14.1%)	125 (27.6%)
5. Poor Stream	66 (25.2%)	69 (36.1%)	135 (29.8%)
6. Urinary Retention	96 (36.6%)	5 (30.9%)	155 (34.2%)
7. Dysuria	2 (0.8%)	97 (50.8%)	99 (21.9%)
8. Hematuria	5 (1.9%)	10 (5.2%)	15 (3.3%)
9. Nocturia	51 (19.9%)	13 (6.8%)	64 (14.1%)
10. Bone Pain	0 (0%)	4 (2.09%)	4 (0.88%)

11. Flank Pain	2 (0.76%)	0 (0%)	2 (0.44%)
12. Burning Micturation	12 (4.5%)	2 (1.04%)	14 (3.09%)
13. Dribbling of Urine	23 (8.77%)	3 (1.57%)	26 (5.73%)

Table 2; clinical presentation of prostatic lesions

The PSA values were distributed into 4 categories (<4, 4-10, 10-20, >20) ng/ml. 162 cases had a serum PSA value of <4ng/mL, out of which 148 cases were reported to have BPH on histology. 115 cases had a serum PSA level of >20ng/mL, of which 92 cases were reported as Adenocarcinoma. (Table 3)

Histological Type of Prostatic Lesion	PSA VALUES				Total
	<4 ng/ml	4-10 ng/ml	10-20 ng/ml	>20 ng/ml	
BPH	148	47	2	0	197
BPH With Prostatitis	6	10	6	4	26
Chronic Prostatitis	2	17	7	2	28
Granulomatous Prostatitis	0	1	0	1	2
ADENOCARCINOMA	0	15	56	92	163
PIN (HGPIN)	0	3	4	13	20
Adenocarcinoma With Neuroendocrine Differentiation	0	0	0	1	1
Prostatic Abscess	0	1	0	0	1
BPH With Basal Cell Hyperplasia	4	0	1	0	5
Adenocarcinoma With Hyper nephroid Pattern	0	4	0	0	4
Adenocarcinoma With Clear Cell Change	0	0	0	2	2
BPH With Squamous Metaplasia	1	1	1	0	3
Pleomorphic Rhabdomyosarcoma	1	0	0	0	1
Total	162	99	77	115	453

Table 3: Serum psa values among the various prostatic lesions

Benign lesions are more common than their malignant counterpart. Amongst the benign lesions, BPH (197; 43.4%) was the most common followed by Chronic Non-Specific Prostatitis (28; 6.1%) and BPH with Prostatitis (26; 5.7%). Amongst the malignant prostatic lesions, Adenocarcinoma (163; 35.9%) was found to be the most common followed by PIN (20; 4.4%) and Adenocarcinoma with hyper nephroid pattern (4; 0.88%). (Table 4)

Sn.	Benign Prostatic Lesions		Total (n=453)
I)	Inflammation andInfection	Chronic Non-specific Prostatitis	28 6.1%
		Granulomatous Prostatitis	2 0.44%
		Prostatic Abscess	1 0.22%

II)	Metaplasia	Squamous cell	3 0.66%
III)	Hyperplasia	BPH	197 43.4%
		BPH with Basal cell hyperplasia	5 1.10%
		BPH with prostatitis	26 5.7%
	Malignant Prostatic Lesions		
IV)	Epithelial lesions-Carcinoma	Adenocarcinoma	163 35.9%
		Adenocarcinoma with Neuroendocrine differentiation	1 0.22%
		Adenocarcinoma with hyper nephroid Pattern	4 0.88%
		Adenocarcinoma with clear cell change	20.44%
v)	PIN	PIN	20 4.4%
VI)	Mesenchymal lesions	Rhabdomyosarcoma	1 0.22%

Table 4; Histopathological spectrum of prostatic lesions.

Out of the 191 malignant prostatic lesions, 66 cases had a Gleason's score of (4+4=8) constituting 34.74% of the total malignant lesions. 44(23.16%) cases had a Gleason's score of (4+3=7). (Table 5)

Gleason score	(primary+ secondary)	Total no cases	Percentage
Score 6	3+3	21	11.05
Score 7	3+4	22	11.58
	4+3	44	23.16
Score 8	4+4	66	34.74
	5+3	7	3.68
Score 9	5+4	16	8.42
	4+5	10	5.26
Score 10	5+5	4	2.11

Androgen Receptor Score	No of Cases (n=40)
0	0
1+	3
2+	21
3+	16

Table 5; Gleason's score of the malignant prostatic lesions

Out of the 191 malignant cases of the prostate, the expression of AR was evaluated in 40 cases of Prostatic Adenocarcinoma. The expression of AR was scored based on the intensity of nuclear positivity on a scale of 0 to 3+. It was noted that 21(52.5%) cases expressed 2+ nuclear positivity of AR. The intensity of AR expression was heterogenous. (Table 6)

Table 6**:** Androgen receptor expression in 40 cases of prostatic adenocarcinoma – AR scoring (IHC)

The Gleason's score was evaluated of the same 40 cases of prostatic adenocarcinoma in which AR expression was studied. 10(25%) cases revealed a gleason's score of

(4+3=7) and 8(20%) cases revealed a score of (4+4=8). Rest of the cases revealed distributed scoring from 6 to 10.

The maximum intensity of AR score (3+) was seen in 16 cases of prostatic adenocarcinoma. But majority (6) of them had a Gleason score of 7. Hence an increased Gleason score was not associated with increased AR expression. Likewise, even though the minimum AR SCORE (1+) was seen in 3 cases all of which had a Gleason score of 9 or 10. However, a higher number of cases with Gleason score 9 or 10 were observed to show a stronger AR expression. This infers that no correlation could be established between the AR scoring and Gleason scoring in our study. (Table 7)

Gleason Score	Androgen Receptor Score				Total
	0+	1+	2+	3+	(N=40)
6	0	0	2	2	4
7	0	0	9	6	15
8	0	0	5	4	9
9 or 10	0	3	5	4	12
Total	0	3	21	16	

Table 7; Association between androgen receptor scoring and Gleason scoring. p value: 0.14 (not significant)

In order to minimize interobserver variation the cases of prostatic adenocarcinoma on which AR expression was studied, were grouped into 3 categories based on the H score that was calculated using the intensity score of AR expression on the tumour cells. Maximum number of cases were in the H score group of 101-200 and these cases were almost equally distributed among the various Gleason's grade group. Similar observations were noted while studying the correlation between cases in the other H score groups and the Gleason grade groups. Hence no correlation was established between the H score group and the Gleason grade group in our study.

Gleason Grade Group	H Score Group			Total(n=40)
	≤100	101-200	201-300	
1	3	1	0	4
2	0	3	2	5
3	2	5	3	10
4	0	5	4	9
5	3	4	5	12
Total	8	18	14	40

Table 8: Association between H score group and Gleason grade group. P value: 0.145(not significant)

Discussion

The study was an observational study conducted over a period of 5 years out of which $3^{1/2}$ years of the study was retrospective and $1^{1/2}$ years of the study was prospective, comprising of a total of 453 cases. Among the 453 cases, on sub-classifying the prostatic lesions, 197 were found to be BPH and 163 were adenocarcinomas. Similar observations were seen by Banerjee B et al[7], their study showed BPH to be the most common prostatic lesion accounting for 75% of the total cases. Various studies conducted also found BPH to be the most common histological lesion accounting for 74.52% of the total lesions[8].

Majority of the patients in our study had presented with urinary complaints, increased frequency of micturition being the most common followed by difficulty in voiding, urgency, hesitancy poor stream , urinary retention, nocturia, burning micturition and dribbling of urine. The less common symptoms found were dysuria, hematuria, flank and bone pain which were mostly associated with malignant lesions and was statistically significant. Various studies, found frequency of

micturition followed by difficulty in voiding to be the most common presenting complaint[9,10]. In our study amongst the benign lesions we observed mild (4-10ng/ml), moderate (10-20 ng/ml) and marked elevation (>20 ng/ml) in PSA values among 20 cases of BPH with prostatitis, 26 cases of chronic prostatitis, 2 cases of granulomatous prostatitis, 1 case of prostatic abscess and 2 cases of BPH with squamous metaplasia. Although serum PSA levels in combination with TRUS and DRE to a certain extent indicate benign or malignant nature, they are not absolute indicators for the same. Hence histologic examination of the prostatic lesion is mandatory to classify the lesions as benign or malignant. Benign lesions were more common (57.8 %) than malignant cases (42.1%). Our observations were in concurrence with various studies[11-14].

Histological grading of prostatic adenocarcinoma was done according to the Gleason's system. According to the architectural pattern present, Gleason scores were determined and on the basis of Gleason's pattern, grade grouping was done. In the present study Gleason's score 8 was the most common constituting 38.42% followed by Gleason's score 7(34.74%). Several studies have been conducted to evaluate the expression of AR, its role in progression of prostate cancer and its relation with various parameters like the Gleason's score and grade. A finer comprehension of the role of the androgens, androgen receptors, their expression and its relationship with the other clinical parameters would probably help us in having a refined protocol for androgen ablation treatments and prevention of castration resistant prostatic carcinomas. In our study out of the 191 malignant cases of the prostate, the expression of AR was evaluated in 40 cases of prostatic adenocarcinoma. Most of these cases had a Gleason's score of 7(4+3). The intensity of nuclear staining for AR was scored as 0= no staining, 1+= weak equivocal staining, 2+= unequivocal moderate staining, 3+= strong staining. The tumour cells were counted within the hot spots. Majority of our cases revealed an AR intensity score of 2+. All the cases in our study, showed AR expression but with varying intensity. AR expression was selectively nuclear in the tumour cells, cytoplasm was not stained. Also, within same fields both AR positive tumour cells, AR negative tumour cells and less intensely stained areas were identified denoting the heterogeneity of AR expression within prostatic carcinoma. Within the same tumour sections few foci of benign counterparts were observed where the staining was more homogenous and less intense. On correlation of Androgen receptor staining with the Gleason's score, varied intensity distribution was seen among the different Gleason scores. The maximum intensity of AR score (3+) was seen in 16 cases of prostatic adenocarcinoma but majority (6) of them had a Gleason score of 7. Hence an increased Gleason score was not associated with increased AR expression. Likewise, even though the minimum AR score (1+) was seen in 3 cases all of which had a Gleason score of 9 or 10, a higher number of cases with Gleason score 9 or 10 were observed to show a stronger AR expression. On statistical correlation, no significant correlation was observed. There are studies where they have found a significant correlation between AR expression and Gleason score[15-17]. There is another line of opinion based on the studies who have established an inverse correlation between AR expression and tumour differentiation[18,19].

Conclusion

A diversity of benign and malignant lesions is seen in the prostate. The benign lesions were more common

than malignant lesions. Both the spectrum of lesions was common in the elderly age group. Serum PSA values even though were found to be a significant predictor of malignancy, was not an absolute marker because some benign lesions mostly associated with inflammation also revealed raised PSA values. Serum PSA along with imaging and digital rectal examination were useful modalities towards identifying benignity and malignity of the lesions. Among the malignant lesions, Adenocarcinoma of the prostate was the most common. The most common Gleason score found in our study was score 8. In our study most of the cases were in a higher-grade group, a proper screening protocol along with proper awareness among the vulnerable elderly population has become very important. A correlation between AR expression and tumour differentiation was done and no significant correlation was found, restricting the role of AR as a prognostic marker.

Ethics Statement

The study was approved by Institutional Ethical Clearence (IEC) board, SKIMS Soura.

References

1. Husain I, Shukla S, Soni P, Husain N. Role of androgen receptor in prostatic neoplasia versus hyperplasia. Journal of cancer research and therapeutics. 2016;12(1):112
2. Chauhan SC, Sarvaiya NA. Study of clinicomorphologic spectrum of prostatic lesions and correlation with prostate specific antigen levels in a tertiary care center. Indian J Pathol Oncol. 2017;4(2):328
3. Humphrey PA. Histopathology of prostate cancer. Cold Spring Harbor Perspectives in Medicine. 2017;7(10):a030411.
4. Jain S, Saxena S, Kumar A. Epidemiology of prostate cancer in India. Meta gene. 2014;2:596-605.
5. Gann PH. Risk factors for prostate cancer. Reviews in urology. 2002;4(Suppl 5):S3.
6. Robbins & Cotran Pathologic Basis of Disease, 10e:SAE.
7. Banerjee B, Iqbal BM, Kumar H, Kambale T, Bavikar R. Correlation between prostate specific antigen levels and various prostatic pathologies. Journal of Medical Society. 2016;30(3):172.
8. Josephine A. Clinicopathological study of prostatic biopsies. Journal of clinical and diagnostic research: JCDR. 2014;8(9):FC04.
9. Farooq S, Bilal S, Khaliq BI, Sidieq F, Aslam H, Shah I. The spectrum of histopathological patterns observed in prostate specimens in a tertiary care hospital in Kashmir.2019
10. Anushree CN, Kusuma V. Morphological spectrum of prostatic lesions-a clinicopathological study. Med Innov. 2012;1(2):49-54.
11. Satyasri K, Sinha S, Kartheek BV. SPECTRUM OF PROSTATIC LESIONS IN A TERTIARY CARE HOSPITAL--A 5 1/2-YEAR RETROSPECTIVE. Journal of Evolution of Medical and Dental Sciences. 2018;7(36):3991-6.
12. Godbole CR, Bhide SP. Study of histopathological correlation of prostate lesions with serum prostate specific antigen levels in a tertiary care hospital.2020
13. Vani BR, Kumar D, Sharath BN, Murthy VS, Geethamala K. A comprehensive study of prostate pathology in correlation with prostate-specific antigen levels: An Indian study. Clinical Cancer Investigation Journal. 2015;4(5):617.

14. Birare SD, Mahule SK, Dalve KT, Patil NR, Naigaonkar NV. Clinicopathological study of neoplastic and non-neoplastic lesions of prostate-two years study. Indian Journal of Pathology and Oncology. 2017;4(4):622-8.
15. Chodak GW, Kranc DM, Puy LA, Takeda H, Johnson K, Chang C. Nuclear localization of androgen receptor in heterogeneous samples of normal, hyperplastic and neoplastic human prostate. The Journal of urology. 1992;147(3):798-803.
16. Lai CY, Chen CM, Hsu WH, Hsieh YH, Liu CJ. Overexpression of endothelial cell-specific molecule 1 correlates with Gleason score and expression of androgen receptor in prostate carcinoma. International Journal of Medical Sciences. 2017;14(12):1263.
17. Hashmi AA, Mudassir G, Irfan M, Hussain ZF, Hashmi SK, Asif H, Nisar L, Naeem M, Faridi N. Prognostic significance of high androgen receptor expression in prostatic acinar adenocarcinoma. Asian Pacific Journal of Cancer Prevention: APJCP. 2019;20(3):893
18. Theodoropoulos VE, Tsigka A, Mihalopoulou A, Tsoukala V, Lazaris AC, Patsouris E, Ghikonti I. Evaluation of neuroendocrine staining and androgen receptor expression in incidental prostatic adenocarcinoma: prognostic implications. Urology. 2005;66(4):897-902.
19. Miyamoto KK, McSherry SA, Dent GA, Sar M, Wilson EM, French FS, Sharief Y, Mohler JL. Immunohistochemistry of the androgen receptor in human benign and malignant prostate tissue. The Journal of urology. 1993;149(5):1015-9.