Research Paper

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Study of Histopathological Lesions in Transrectal Ultrasound Guided Biopsies of Prostate in Patients with Raised Serum Prostate Specific Antigen.

Medical Science

KEYWORDS : Transrectal ultrasound (TRUS) Benign Prostate Hyperplasia, Prostatitis, Serum Prostate Specific Antigen (PSA), Adenocarcinoma, Gleason Score

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ABSTRACT

Aims and Objectives: *To determine the age distribution of patients with prostatic lesion, study prevalence of distribution of various prostatic lesions, admitted in Civil hospital, Ahmedabad and to determine histological types related with prostate specific antigen.*

Background: *Carcinoma of prostate is one of common tumors of old age in men. With Digital rectal examination (DRE), prostate specific antigen (PSA) is major screening tool for prostate cancer. While Transrectal Ultra sound (TRUS) guided needle biopsies of prostate are considered gold standard for the diagnosis of prostate cancers*

Materials and methods *The study carried out at tertiary care centre civil Hospital, Ahmedabad from January 2014 to October 2014.The study includes 110 cases.Serum Prostatic specific antigen level and Histopathological examination of prostatic biopsies was done and correlate. Raised serum PSA level were arbitrarily divided into mild(4 to 10 Ng/ml), moderate (10.1 to 20ng/ml) and marked elevations (≥20.1)*

Results *The mean age of patients was 66.9± 9.4 years. Out of 110 cases , 69(62.72%) cases were benign and 41(37.2%)malignant. Among malignant lesions, all cancers were according to Gleason's grading system, 16 patients (39.02%) had grade 3, 17 (41.46%%) grade 4 and remaining 8 (19.51%) patients had grade 5. Mild serum PSA rise was seen in 63(57.27%)patients, among these 53(84.1%)showed benign lesions and 10(15.9%)malignant. Moderate serum PSA rise was seen in 26(23.6%) cases , among 12(46.15%) showed benign and 14(53.8%) malignant. 21(19.1%) patients had serum PSA level > 20.1Ng/ml. Among these 4(19.04%) cases were benign and 17(80.9%) malignant. Malignant lesions includes prostatic adenocarcinoma.Benign lesions includes benign prostatic hyperplasia ,prostatitis.*

Conclusion

- *In present study, the commonest pathology encountered in the prostates studied was Benign lesion (62.72%). Incidence of carcinoma was 41 cases (37.2%).69 (62.72%) cases showed benign lesions with mean age 57.7 ±4.86. and 41 (37.2%) Malignant with mean age 65.70 ± 5.64.*
- *In TRUS biopsies of prostate in patients with symptoms of prostatism and high serum PSA, the mean serum PSA was 24.63±9.4 ng/ml in adenocarcinoma. In Benign prostatic lesion mean serum PSA level was 6.16 ± 2.4 ng/ml.*
- *In present study serum PSA level useful method for assessing and individual's risk of prostate cancer . In addition elevated level more than 4.0 ng/ml with TURS guided needle biopsy is useful and diagnostic method.*

Introduction:

- Prostatic carcinoma is an important growing health problem, presenting a challenge to urologists, radiologists and pathologist (1,2). Incidence of prostatic diseases, benign prostatic hyperplasia, and carcinoma increases with age(3).
- Prostate cancer is the leading cause of new cancer in men and is second only to lung cancer as a leading cause of cancer-related deaths in men(4) .Several factors, including age, race, family history, hormone levels, and environmental influences are suspected to play a role in pathogenesis(5).
- This study includes description of incidence of various lesions of prostate, their clinical manifestations, serum prostate specific antigen (PSA) level, classification and grading of prostate tumors.
- The diagnosis requires careful history, physical examination including digital rectal examination (DRE), serum prostate specific antigen (PSA) estimation and transrectal ultrasound (TRUS) and TRUS-guided needle biopsies of the prostate.

Aims and Objectives:

- To determine the age distribution of patients with prostatic lesion.
- To study prevalence of distribution of various prostatic lesions, admitted in Civil hospital, Ahmedabad.
- To determine histological types related with prostate specific antigen.

Material and Methods:

A study carried out at tertiary care teaching hospital Ahmedabad, from January 2014 to October 2014 . The study includes 110 cases between 50 to 76 years of age group , who presented to with or without complaints of prostatism. Their detailed physical examination and DRE were performed, followed by appropriate laboratory investigations including determination of serum PSA. Serum PSA levels were calculated and correlated with various clinical and biopsy findings.

- **Biopsy technique:**
- TRUS guided needle biopsies of the prostate gland were performed only in those patients who had serum PSA levels ≥ 4 ng/ml and/or abnormal DRE suspicious for prostate cancer. Ultrasound guidance was provided by a diagnostic ultrasound machine with, biplaner transrectal probe. Biopsies were obtained with patient in right or left lateral decubitus position and the prostate was imaged in the sagittal plane(7,8). Only first time biopsies were included. Repeat biopsies were not included in the analysis.

- **Pathologic study:**
- The biopsy specimens were processed and studied at the department of Histopathology, Gross examination of the biopsies included precise length and diameter and color of the cores. The biopsies were processed for paraffin embedding, cut at 3-5 um and stained by haematoxylin and eosin (H&E) for detailed microscopic examination.
- The histopathological grading and scoring by Gleason system was done in all cases of adenocarcinoma of prostate.
- The score biopsies were graded and scored according to revised WHO criteria for the grading and scoring of needle biopsies of the prostate (10).

- **Statistical analysis**
- Simple descriptive statistics such as mean ± SD were used for continuous variables such as age and clinical and laboratory parameters.
- Percentages were used for categorical data.

- **Results:**

ꕥ The main clinical features of all patients are shown in Table-1. in variable combination.

ꕥ Table: 01- Main presenting symptoms of the patients

Sr. No.	clinical features	No. of cases(%)
1.	Retention of urine	30(27.27%)
2	Weak stream	22(20%)
3	Frequency	15(13.63%)
4	Urgency	13(11.81%)
5	Hematuria	12(10.9%)
6	Nocturia	10(10.9%)
7	Hesitancy	8(7.27%)

In present study, the Mean age of all patients 66.9±9.4 years. out of 110 cases, 69 (62.72%) cases showed benign lesions with mean age 57.7 ±4.86 years. and 41 (37.2%) Malignant with mean age 65.70 ± 5.64 years.(Table no -2)

Table: 02- Age wise distribution of cases.

Sr. No.	Age range (years)	Benign lesion No. of cases(%)	Malignant lesion No. of cases(%)
1	50-60	18 (16.36%)	4 (3.63%)
2	61-70	40 (36.36%)	22 (20%)
3	› 70	11 (10%)	15 (13.63%)

Out of 110 cases, 41 (37.2%) revealed adenocarcinoma and the remaining 69 (62.72%) showed adenomyomatous hyperplasia(figure 2) with or without associated active prostatitis(figure 3) .(Table no -3) The six patients with chronic granulomatous inflammation showed no caseation necrosis and negative results for acid fast bacilli on Ziel-Nelson staining and thus were labeled as idiopathic granulomatous prostatitis.(figure 4)

ꕥ Table:03- No. of cases according to histopathology diagnosis

Sr. No.	Histopathological Diagnosis	No. of cases(%)
1	Adenocarcinoma	41 (37.27%)
2	BPH	35 (31.81%)
3	Chronic non specific Prostatitis	15 (13.63%)
4	Acute ; Prostatitis	6 (5.48%)
5	PIN	2 (1.81%)
6	Chronic Granulomatous Prostatitis	6 (5.45%)
7	Others (foreign body granuloma ,Non specific)	5 (4.54%)

ꕥ The mean serum PSA value was 13.36 ± 8.6 ng/ml; total range was 4 to 36 ng/ml. The mean PSA was significantly higher in the cancer group than in the benign. The rate of cancer detection increased significantly with increasing serum PSA level. 21 out of 110 patients (19.09%) had serum PSA ≥ 20.1 ng/ ml. Of these, 17 (80.95%) patients had prostatic adenocarcinoma, and 4 (19.04%) benign changes.(Table no-4).

ꕥ Raised serum PSA level were arbitrarily divided into mild(≥4 to 10 Ng/ml), moderate (≥10.1 to 20Ng/ml) and marked elevations (≥20.1 to highest)

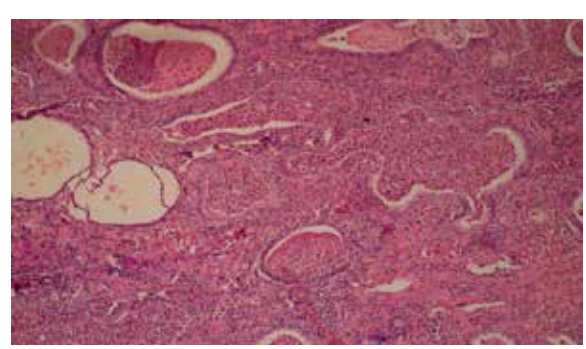
Table:04- No. of cases with raised serum PSA leve

	S.PSA level 4to 10 ng/ml 63 cases	S.PSA level 10.1 to 20 ng/ml 26 cases	S.PSA level >20.1 ng/ml 21 cases
Benign cases	53 (84.1%)	12 (46.15%)	4 (19.07%)
Malignant cases	10 (15.9%)	14 (53.8%)	17 (80.99%)

ꕥ Out of 110,69 (62.72%) showed adenomyomatous hyperplasia with or without associated active prostatitis Among 41 patients with adenocarcinoma, according to Gleason's grading system, 16 patients (39.02%) had grade 3, 17 (41.46%%) grade 4 (Figure 1) and remaining 8 (19.51%) patients had grade 5. Most of the patients having grade ≥ 3 showed markedly high levels of serum PSA.

ꕥ Similarly, on Gleason scoring, eight patients (16.67%) had score 6, twelve (25.0%) score 7, ten (20.83%) score 8, fourteen (29.1%) score 9 and four (8.33%) had score 10 (Table no- 5). Most of the patients having Gleason score ≥ 6 also showed markedly high levels of serum PSA.

ꕥ Chronic prostatitis showing infiltration of lymphocytes, plasma cells, histiocytes in the stroma and secretions and neutrophils in lumen (H & E, 100X)



ꕥ **Table no .5 Histopathological characteristics of prostate cancer observed in 48 patients with raised serum prostate specific antigen levels.**

Patients	No of cases (%)
Biopsy Gleason grade	
3	10 (24.39%)
4	20 (48.78%)
5	11 (26.82%)

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Biopsy Gleason score	
6	6 (14.63%)
7	10 (24.39%)
8	9 (21.95%)
9	13 (31.70%)
10	3 (7.31%)

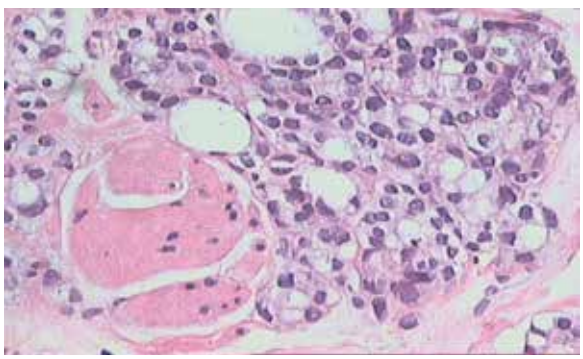

Figure 1. High magnification image showing a few glandular lumina with focal areas of loss of glandular differentiation, a pattern consistent with Gleason grade 4 adenocarcinoma of the prostate (H&E, × 400).

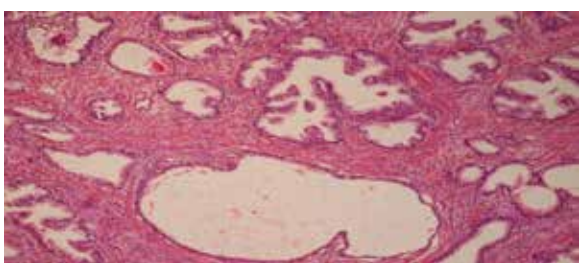

Figure 2: Benign prostatic hyperplasia with glandular and stromal proliferation and dilated gland (H & E, 100X)

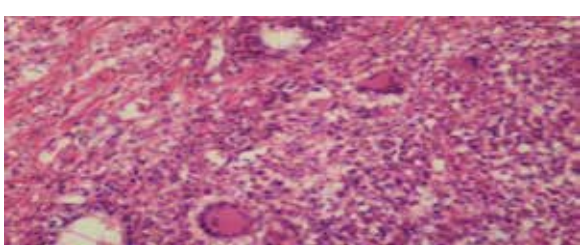

Figure 3: Granulomatous prostatitis showing epitheloid cell granulomas and giant cells (H & E, 400X)

Discussion:

- Carcinoma of prostate is common cancer in India due to increasing life expectancy and relatively better diagnostic method. The gold standard triad for diagnosing prostate cancer comprised DRE, PSA level and transrectal ultrasonography (11).
- It is a report on the spectrum of pathological lesions found in TRUS-guided biopsies of the prostate in men with elevated serum PSA and/or symptoms of prostatism .
- The prostate cancer is seen typically in elderly men and its frequency rises with increasing age (5). In this context, the mean age of our patients is concordant with that reported previously in local and international studies (12). However, significant rise in cancer incidence was seen in our patients with increasing age, as in other studies (5).

In our study, most patients were symptomatic; 92% presented with lower urinary tract symptoms (LUTS) commonly knows as prostatism. Very few patients (8%) presented for screening of the prostate cancer at asymptomatic stage. This is understandable given the low level of awareness of this cancer among the general population.

- In a study from China, cancer detection rate was 40% (6). In the study by Levine et al. (13) cancer was detected in 31% of cases. Presti et al. observed prostate cancer in 42% of the TRUS-guided biopsies (14).
- All these studies included patients with raised serum PSA associated with or without prostatism, as in our study. However, different levels of serum PSA and different biopsy strategies were employed in these studies, which are reflected in slight differences in cancer detection rates. The overall cancer detection rate in TRUS-guided biopsies in our series was 37.2%.
- In a significant number of patients with raised serum PSA,TRUS-guided biopsies showed benign hyperplastic or inflammatory lesions rather than cancer. The proportion of benign lesions was greater in patients with mild or moderate elevations of serum PSA. In contrast, cancer was more frequent in cases with marked elevations in serum PSA.

Table : 06:- Benign and malignant Prostatic lesion: Comparison between PSA level with other study.

PSA Range	Benign Prostatic hyperplasia			Malignant prostatic lesion			
Ng / ml	Kshitij et al18	Ishtiaq Ali Khan et al19	Present study	Kshitij et al18	H.A Mwalyoma et al19	Sladana Zivkovic et al20	Present study
0-4	71.6%		-	10.5%		2.50%	-
4-10	22.6%	74%	76.81%	26.3%	5.3%	27.50%	24.39%
>10	3.0 %	26%	23.18%	63.7%	94.7%	70.0%	75.60%

- Similar observations have been noted in previous investigations as well. These findings show that simply a rise in serum PSA levels ≥ 5 ng/ml does not indicate that a patient has prostate cancer because benign conditions such as hyperplasia and prostatitis can also increase the serum PSA levels (15,16). In our study, 21 (20.1%) patients had PSA levels of ≥ 20 ng/ml, of which 17 (80.99%) patients had adenocarcinoma,4(19.07%) patients had hyperplasia.
- This is an interesting finding which shows that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes, as in previous studies (6).(table no- 6)
- Table no 06- shows cases of BPH most commonly present between PSA level 4-10 ng/ml (76.81%), which is compared with study of Khitij et al. and cases of Adenocarcinoma is more commonly present at PSA level >10.0 ng/ml (75.60%) and it is compared with other study.

Conclusion:

- In present study, the commonest pathology encountered in the prostates studied was Benign lesion (62.72%). Incidence of carcinoma was 41 cases (37.2%).69 (62.72%) cases showed benign lesions with mean age 57.7 ±4.86. and 41 (37.2%) Malignant with mean age 65.70 ± 5.64.
- In TRUS biopsies of prostate in patients with symptoms of prostatism and high serum PSA, the mean serum PSA was 24.63±9.4 ng/ml in adenocarcinoma. In Benign prostatic lesion mean serum PSA level was 6.16 ± 2.4 ng/ml.
- In present study serum PSA level useful method for assessing and individual's risk of prostate cancer . In addition elevated level more than 4.0 ng/ml with TURS guided needle biopsy is most useful and diagnostic method for prostate.

REFERENCE

1. Ries LAG, Eisner MP, Kosary CL, et al. (eds).SEER Cancer Statistics Review, 1975- 2001,National Cancer Institute. Bethesda, MD,2004. 2. Sasagawa I, Nakada T. Epidemiology of prostate cancer in East Asia. Arch Andro 2001;47(3):195-201. 3. Walsh PC. Why make an early diagnosis of prostate cancer. J Uro 1990;147:853-4. 4. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. CA Cancer J Clin. 2010;60(5):277-300. 5. Epstein JI. The lower urinary tract and male genital system. In: Robbins SL, Kumar V, Abbas AK, Cotran RS, Fausto N, editors. Robbins and Cotran pathologic basis of disease. 8th ed. Philadelphia: Saunders/Elsevier; 2010. p. 982-1004. 6. Dai B, Ye DW, Kong YY, Shen YJ, Wang BH. Individualized prostate biopsy strategy for Chinese patients with different prostate-specific antigen levels. Asian J Androl. 2008;10(2):325-31. 7. Hodge KK, McNeal JE, Stamey TA. Ultrasound guided transrectal core biopsies of the palpably abnormal prostate. J Urol. 1989;142(1):66-70. 8. Philip J, Ragavan N, Desouza J, Foster CS, Javle P. Effect of peripheral biopsies in maximising early prostate cancer detection in 8-, 10- or 12-core biopsy regimens. BJU Int. 2004;93(9):1218-20. 9. Gleason DF. Histologic grading of prostate cancer: a perspective.Hum Pathol. 1992;23(3):273-9. 10. Montironi R, Mazzuccheli R, Scarpelli M, Lopez-Beltran A, Fellegara G, Algaba F. Gleason grading of prostate cancer in needle biopsies or radical prostatectomy specimens: contemporary approach, current clinical significance and sources of pathology discrepancies. BJU Int. 2005;95(8):1146-52. 11. Franco O E, Arimak, Yanagwa M and Kawamura J. The usefulness of Power Doppler Ultrasonography for diagnosing prostate cancer: histological correlation of each biopsy site. Br J Urol 2000; 85:1049–52. 12. Gupta NP, Ansari MS, Dass SC. Transrectal ultrasound guided biopsy for detecting early prostate cancer: An Indian experience. Indian J Cancer. 2005;42(3):151-4. 13. Levine MA, Ittman M, Melamed J, Lepor H. Two consecutive sets of transrectal ultrasound guided sextant biopsies of the prostate for the detection of prostate cancer. J Urol. 1998;159(2):471-5; discussion 5-6. 14. Presti JC, Jr., Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. J Urol.2000;163(1):163-6; discussion 6-7. 15. Catalona WJ. Clinical utility of measurements of free and total prostate-specific antigen (PSA): a review. Prostate Suppl. 1996;7:64-9.