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PSA LEVEL AND ITS CORRELATION WITH PROSTATE PATHOLOGY

Pathology

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ABSTRACT

Introduction: Incidence of various Prostate pathologies like Prostatitis, Benign prostatic hyperplasia(BPH), and carcinoma increases with age. Serum PSA(S.PSA) level also increase in BPH, prostatitis, cancer etc. S.PSA level is widely used as a tumor marker for screening of prostate cancer. Gleason's microscopic grading and S.PSA level are important for diagnosis, management and prognosis of Prostate carcinoma. **Aims & Objectives:** The principle aim of this study was

- To correlate S.PSA levels with microscopic diagnosis of prostate biopsy & Gleason's grade

Materials and methods: The present study included total 500 prostate biopsies. Tissue fixation was done in 10% Neutral buffered formaline. Routin paraffin processing was done, 5u thick sections were cut from paraffin block and statined with H&E for microscopic diagnosis. S.PSA level was obtained by using Beckman Coulter UnicelDxl 600- access immunoassay system. S.PSA level, prostate biopsy microscopic diagnosis with Gleason's grading and their correlation was done. **Results:**In present study, Most of the specimens received were TURP followed by Tru-cut needle core and total prostatectomy. Benign lesions were more common as compared to malignant. The most common benign lesion was BPH. Most common age group for Benign & Malignant prostatic lesions was 61-70 years. Majority prostate adenocarcinoma cases had Gleason's score 7 which were in Gleason's grade group 2&3. Sensitivity of S.PSA cutoff 4 ng/ml for diagnosis of prostate adenocarcinoma is 98.48% and specificity is 46.77%. **Conclusion:** Prostatic lesions are common cause for morbidity and mortality in elderly men worldwide. S.PSA level, prostate biopsy microscopic study and correlation of both is helpful in diagnosis, management as well as prognosis of prostate pathology.

KEYWORDS

S.PSA level, Prostate Lesions, Gleason grade

INTRODUCTION:

The Prostate is a pear shaped glandular organ that weighs up to 20gm in normal adult male.[1] Prostate is involved in 3 main important pathologic processes: prostatitis, nodular hyperplasia and carcinoma.[2]The incidence of prostatic lesions increases with age. Prostate carcinoma is one of the leading cause for death in elderly male patient. Digital rectal examination(DRE) & trans rectal USG are preliminary screening methods but it has low specificity & sensitivity. Transrectal biopsy is essential to confirm diagnosis.[3] Gleason's microscopic grading system is the best predictor of disease progression and outcome.[4]

Prostate specific antigen (PSA) is a glycoprotein serine protease which is produced by secretory cells of prostate.PSA level can increase in BPH, prostatitis, cancer etc. PSA level is widely used tumor marker for screening of prostate cancer.[3]

Gleason's microscopic grading and S.PSA level are important for diagnosis, management and prognosis of Prostate carcinoma.[1,5]

In most laboratories, a S.PSA level of 4 ng/ml is reported as the cutoff between normal and abnormal. Some guidelines consider S.PSA values above 2.5 ng/ml as abnormal. The upper age specific S.PSA reference ranges are 2.5 ng/ml for men 40-49 years of age, 3.5 ng/ml for men 50-59 years, 4.5 ng/ml for men 60-69 years, and 6.5 ng/ml for men 70-79 years.[3]

Aims & Objective:

- To study the Histomorphology of various prostatic lesions with respect to age groups
- To correlate S.PSA levels with microscopic diagnosis of prostate biopsy & Gleason's grade
- To study sensitivity and specificity of S.PSA level in prostatic lesions

Material & Method:

Sample

The present study included total 500 prostate tissue specimen received at Civil Hospital, B.J.M.C., Ahmedabad & S.PSA level for each case.

Clinical history

Age, symptoms, P/R examination, other investigation details like radiological reports, S.PSA level were collected.

S.PSA level

S.PSA level was obtained for each case by using Beckman Coulter Unicel DxI 600- access immunoassay system

Specimen type

In present study, Most of the specimens received were TURP followed by Tru-cut needle biopsy and total prostatectomy.

Tissue fixation, processing & staining

For prostate biopsy , tissue fixation in 10% Neutal buffered formaline, and routine paraffin processing was done, 5 µ thick sections were cut from paraffin block and stained with H&E for microscopic diagnosis.

Reporting

All the prostatic lesions were reported into various categories. The cases of prostatic adenocarcinoma were graded using Gleason scoring system.

Results:

Total 500 prostate biopsies were studied.

Mean age for present study is 65.58 year. A maximum number of cases were in 61-70 years of age group.

Clinically DRE findings showed firm nodule in 434 cases and hard nodule in 66 cases.

Out of 500 cases, maximum specimen received were TURP(334) followed by Tru-cut Biopsy(165) and 1 Radical Prostatectomy.

Table 1:Histopathological Diagnosis

Microscopic Finding	No. of cases	Percentage
BPH	280	56%
BPH with prostatitis (total)	97	20%
BPH with chronic prostatitis	76	15.2%
BPH with chronic prostatitis, eosinophilic infiltration	1	0.2%
BPH with acute prostatitis	1	0.2%
BPH with acute on chronic prostatitis	17	3.4%
BPH with granulomatous prostatitis	2	0.4%
BPH with microabscess	1	0.2%

BPH associated with Basal cell hyperplasia	15	3%
BPH associated with urothelial metaplasia	1	0.2%
BPH associated with squamous metaplasia	3	0.6%
BPH associated with infarction	9	1.8%
BPH associated with Postatrophic hyperplasia	9	1.8%
BPH associated with Atypical small acinar Proliferation (ASAP)	3	0.6%
BPH associated with Prostatic intraepithelial Neoplasia (PIN)	1	0.2%
Prostatitis (total)	14	2.8%
Acute Prostatitis	1	0.2%
Chronic Prostatitis	6	1.2%
Acute on chronic Prostatitis	5	1%
Tuberculous prostatitis	2	0.4%
PIN	1	0.2%
Adenocarcinoma of prostate	60	12%
Adenocarcinoma of prostate with High Grade Prostatic Intraepithelial Neoplasia (HGPIN)	5	1%
Urothelial carcinoma	1	0.2%
Total	500	100%

Histopathological diagnosis was as shown in **Table 1**. Benign lesions were more common as compared to malignant. Among benign lesion, BPH was more common finding.

Table 2: Age-wise Distribution in Benign & Maignant Histopathological Categories

Age (Years)	Histopathological category	
	Benign (%)	Malignant (%)
31-40	3(0.7%)	0(0%)
41-50	27(6.2%)	0(0%)
51-60	98(22.6%)	13(19.7%)
61-70	185(42.6%)	24(36.4%)
71-80	99(22.8%)	21(31.8%)
81-90	22(5.1%)	8(12.1%)
Total	434(100%)	66(100%)

Benign and malignant prostatic lesions were common in 7th decade as shown in **Table 2**.

Table 3: Correlation of S.PSA Level with Histopathological Category

S.PSA (ng/ml)	Benign	Malignant	No. of cases
<4	203	1	204
4-10	148	18	166
>10	83	47	130
Total	434	66	500

Table 4: Correlation of S.PSA level with various histopathological diagnosis

Histodiagnosis	S.PSA level (ng/ml)			
	<4	4-10	>10	Total No. cases
BPH	145	89	46	280
BPH with prostatitis	39	41	17	97
Prostatitis	4	4	6	14
BPH associated with Basal cell hyperplasia	6	3	6	15
BPH associated with urothelial metaplasia	0	1	0	1
BPH associated with squamous metaplasia	3	0	0	3
BPH associated with infarction	3	5	1	9
BPH associated with Postatrophic hyperplasia	3	5	1	9
BPH with microabscess	0	0	1	1
BPH associated with ASAP	0	1	2	3
BPH associated with PIN	0	0	1	1
PIN	0	0	1	1
Adenocarcinoma of prostate	1	18	41	60
Adenocarcinoma of prostate with HGPIN	0	0	5	5
Urothelial Carcinoma	0	0	2	1
	203	166	131	500

Correlation of S.PSA level in various prostatic lesions was done as shown in **Table 3 & 4**.

Table 5: Gleason Grade Group and Score[6] in prostate adenocarcinoma

Gleason Score	Gleason Grade Group	Subscore	No. of Cases	Total cases
6	1	3+3=6	19 (29.3%)	19 (29.3%)
7	2	3+4=7	11 (16.92%)	26 (40%)
	3	4+3=7	15 (23.08%)	
8	4	4+4=8	11 (16.92%)	13 (19.98%)
		3+5=8	2 (3.07%)	
		5+3=8	0 (0%)	
9	5	4+5=9	5 (7.67%)	6 (9.21%)
		5+4=9	1 (1.54)	
10		5+5=10	1 (1.5%)	1 (1.5%)
Total			65(100%)	100%

As shown in **Table 5**, Gleason score 7 (3+4 & 4+3) which includes grade group 2 & 3 was observed in a maximum number of cases.

Table 6:Comparison of Gleason grade and S.PSA level

	No. of cases according to S.PSA level (ng/ml)			
Gleason grade group	<4	4-10	>10	Total no. of cases
1	0	6	13	19
2	1	3	7	11
3	0	4	11	15
4	0	4	9	13
5	0	1	7	7
Total no. of cases of Prostate adenocarcinoma	65			

As shown in **Table 6**, maximum patient with prostate adenocarcinoma were in Gleason's grade group 1. Majority patients in gleason grade group 1 having S.PSA level is >10 ng/ml.

S.PSA cut off point was fixed at 4ng/ml .Sensitivity[7] and Specificity[7] were calculated regarding the diagnostic efficacy of biochemical marker for malignancy. So, Sensitivity was 98.48%, Specificity was 46.77%, Positive predictive value[7] (PPV) was 21.96%, Negative predictive value[7] (NPV) was 99.50%, Accuracy[7] was 53.6 %. χ^2 Value[7] 48.58 with degrees of freedom 1 and P value is less than 0.0001. So, S.PSA cut off 4ng/ml for prostate adenocarcinoma is considered to be extremely statistically significant.

DISCUSSION:

In Present study, total 500 Prostate biopsies were studied. Various prostatic lesions and respective S.PSA levels were correlated. The observed results were compared with other studies as follows.

Out of 500 cases, maximum 42.2% cases were in 61-70 years of age group. This was comparable with other study: by Gil et al[8] maximum no. of cases 42.9% in 61-70 years age group.

In present study, maximum number of cases were found in 7th decade which was comparable to other studies by: Gil et al study[8], Anushree&Venkatesh[9] and Wadgaonkar*et al*[10] .

In present study, mean age is 65.6 years. This was comparable with other studies by: Josephine A et al[11]median age was 65.5years, Mansoor I et al[12]median age was 65.55years, Lakhey M et al[13]et al. median age was 67.6years.

Higher percentage of TURP biopsy(66.8%) followed by trucut biopsy(33%) were received. This was comparable with other studies

by: Mittal etal.[14]and Shakya et al.[15]

Out of 500 cases, 87% were benign and 13% were malignant. Benign lesions were more common as compared to malignant. This was comparable with other studies by: Sathyavathi Alva etal[16] 86% benign & 13.3% malignant, Arum chital[17] 89% benign & 11% malignant, Choi JH et al study[18] 82.8% benign & 17.2% malignant, Jean et al[19] 83% benign & 17% malignant.

In present study, most common age group presenting with benign lesions and BPH was 61-70years. This was comparable with other studies by: Anushree&Venkatesh[9] and Wadgaonkar*et al*[10]and Kumar M et al[20]

In present study, Malignant prostatic lesions were mostly found in 7th decade. This was comparable with other studies: by Anushree&Venkatesh[9] and Wadgaonkar*et al*[10],Deshmukh BD et al.[21], Kasliwal N et al[22]

In present study, BPH (56%) was most common benign lesion. This was comparable with other studies by: Jasani JH. etal [23] 56%, AzmiHaroun et al[24]64.48%.

Chronic prostatitis is most commonly observed in BPH. This was comparable with other studies by: Kohnen et al[25]and Anim et al[26].

In Benign cases, 46.44% had S.PSA <4ng/ml, 34.48 % had S.PSA 4-10 ng/ml and 19.08% had S.PSA level >10ng/ml. This was comparable with other study by Kumari K. etal[27] 47.1% had S.PSA <4ng/ml, 28.6% had S.PSA 4-10 ng/ml and 24.3% had S.PSA level >10ng/ml.

In Prostate adenocarcinoma, 1(1.54%) had S.PSA <4ng/ml, 19(29.23%) had S.PSA 4-10 ng/ml and 45 (69.23%) had S.PSA level >10ng/ml. It is comparable with other studies: Alva etal[16] 0% had S.PSA <4ng/ml, 25 % had S.PSA 4-10 ng/ml and 75% patients had S.PSA level >10ng/ml. Sladana Zivkovic et al[28]2.5% had S.PSA <4ng/ml, 27.5 % had S.PSA 4-10 ng/ml and 70% patients had S.PSA level >10ng/ml.

In prostate adenocarcinoma, majority had gleason score 7, Which was comparable with other studies by Jayapradeep et al[29] and Babaian et al[30]

In present study, Sensitivity 98.46% is comparible with other studies by: Lakhey. M et al[13]100%, Kumari k et al[27]93.75% .

In present study, specificity 46.67% is comparible with other studies by: Lakhey. M et al[13]45%, Kumari k et al[27]46.15%% .

In present study, PPV 21.62% is comparible with other studies by: Alva S et al[16] 18%, Akhtar et al[31] 16.6%.

In present study, NPV 99.5% is comparible with other study by Jayapradeep et al[29] 96.43%.

In present study, Diagnostic accuracy[7] 53.6% is comparible with other study by Jayapradeep DP et al[29] 56%.

CONCLUSION

From our study, we can conclude that Most common types of specimens received were TURP. Most common age group for benign as well as malignant prostatic lesions was 61-70 years (7th decade).

Benign lesions were more common as compared to malignant. The more common benign lesion was BPH.

Majority benign cases had S.PSA <4 ng/ml.

Majority malignant cases had S.PSA >10 ng/ml.

Gleason's score 7 was the commonest in prostate adenocarcinoma.

S.PSA, PSA indices like fPSA, proPSA, density, velocity and prostate health index are used in diagnosis, management and follow up of prostatic lesions.

A constellation of architectural, cytoplasmic, and nuclear features along with ancillary studies is essential for diagnosing Prostate Adenocarcinoma.

Conflicts of interest: Nil

Source of funding: Self

Ethical Clearance: Ethical clearance is taken from The Institutional Ethics Committee, B.J. Medical College & Civil Hospital, Ahmedabad. All procedures performed were in accordance with the ethical standards of institution.

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