

Prognostic Significance of Prostate Specific Antigen in Comparison with Histological Grade of Prostatic Adenocarcinoma: A Hospital Based Study

Mohan Rao. Nandam^{1*}, Vissa Shanthi¹, Bhavana Grandhi¹, Syama Sundara Rao Byna¹,
Vijayalakshmi Muramreddy¹ and Jyothi Conjeevaram²

¹Department of pathology, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh (India)

²Department of Social And Preventive Medicine, Narayana Medical College, Chinthareddypalem, Nellore, Andhra Pradesh (India)

ABSTRACT

Background: Prostate gland disease causes significant morbidity in elderly males. Our objective of the study was to evaluate the histopathological spectrum of prostatic lesions in correlation with prostate specific antigen and compare the prostate specific antigen with histological grade of prostatic adenocarcinoma.

Methods: The present retrospective study was carried in the department of pathology, Narayana Medical College & Hospital, Nellore, and Andhra Pradesh, India from January 2015 to December 2015. 119 Prostatic biopsy specimens were analyzed histopathologically for diagnosis of types of prostatic lesion and correlated with serum PSA level. Prostatic adenocarcinomas were graded according to Gleason histological grading. Gleason's grading of tumors was correlated with serum PSA levels

Result: Out of 119 patients, 95 cases had benign prostatic hyperplasia, 17 cases had prostatic adenocarcinoma, 7 cases had prostatitis. In our study, the maximum number of BPH cases (51.58%) showed PSA levels < 4ng/ml. Most of prostatic adenocarcinoma (82.35%) displayed PSA levels >10ng/ml. 5 cases (71.43%) of prostatitis showed PSA levels of 4 to 10ng/ml. Maximum cases of grade 2 and grade 3 prostatic adenocarcinoma had PSA range of 20-49.99 ng/ml.

Conclusion: Benign prostatic hyperplasia is the most commonly diagnosed prostatic lesions. Investigation like serum PSA level detection can aid in the diagnosis, but accurate diagnosis of non-neoplastic and neoplastic lesions of prostate can be made by histopathological study of prostate biopsy. There is a positive relation was seen between higher levels of PSA and Gleason histopathological grade.

Keywords: Prostate specific antigen, Gleason histopathological grade, Prostatic adenocarcinoma, prostatic lesions

Introduction

Recent reports around the globe suggest that prostate gland disease causes significant morbidity and mortality in elderly male. ^[1] In USA, it has been recorded as the important cause of cancer-related deaths in men after lung cancer. Among the total population, one out of six will be diagnosed with prostate cancer during lifetime. Annual checkup of Prostatic specific antigen levels in the men above 50 years of age was recommended by American cancer society.^[2,3] For the diagnosis of prostatic cancer, PSA acts as an important tumor marker. ^[4] For every gram of malignant tissue, the PSA levels raised by 2-3ng/dl which is 10 times more when compared to rise in PSA level for every gram of hyper plastic tissue.^[5,6] Frequently encountered prostatic lesions are Benign Prostatic Hyperplasia, chronic prostatitis, granulomatous prostatitis and Adenocarcinoma.^[1] Our main aim of this study was to evaluate the histopathological spectrum of prostatic lesions in correlation with PSA levels and prognostic significance

of PSA levels by comparing with histopathological grade of prostatic adeno carcinoma.

Materials and Methods

The present retrospective study was carried in the department of pathology, Narayana Medical College & Hospital, Nellore, Andhra Pradesh, during the period of January 2015 to December 2105. Samples (serum and biopsy) from 119 patients, aged between 35 to 84 years, were examined for the level of serum PSA and histopathology of prostate biopsy was studied.

Serum PSA was done on ACCESS-2 (BECKMAN COULTER) by chemiluminescence method. The range of PSA determination using this equipment is 0.1-150ng/ml. Prostatic biopsy was collected from patients who underwent transurethral resection of the prostate for BPH, open Prostatectomy for prostatic lesion and transrectal ultrasound guided biopsy for suspicious malignancy.

Prostatic biopsy specimens were kept in 10% neutral buffered formalin. Specimens were grossly examined for size/quantity and weight followed by processing, paraffin embedding and section cutting. 3-5 microns section were stained with Hematoxylin & Eosin and reported. Prostatic adenocarcinomas were graded according to Gleason’s histopathological grade.

Statistical analysis: Data collected was entered in MS Excel and analyzed using SPSS-Version 22.0 Percentages and chi-square values were calculated. A P value of 0.05 was taken as significance.

Results

During the period of one year from January 2015 to December 2015, 119 prostatic biopsy specimens were received. The age ranges of patients were 31-90 years. The mean age of presentation was 64.46±10.70 years. Most common prostatic lesion is BPH [95 cases (79.83%)] with mean age 63.67±11.29 years. Second most common lesion is prostatic adenocarcinoma [17 cases (14.28%)] with mean age 68.88±6.49 years and least common is prostatitis [7 cases (5.88%)] with mean age 64.43±7.03 years (Figure1).

In our study of 24 cases of prostatic lesions, 3 cases were prostatic adenocarcinomas, 19 cases BPH and 2 cases were prostatitis and occurred in the age group of 51-60 years. In the Age group of 61-70 years they were 45 cases of prostatic lesions, out of which 7 were prostatic adenocarcinomas, 34 were BPH and 4 cases were chronic prostatitis. The

age group of 71-80 years they were 35 cases of prostatic lesions, out of which 7 were prostatic adenocarcinomas, 27 were BPH and one case were Prostatitis.

In our study 49 cases (51.58%) of BPH shows PSA levels <4 ng/ml, 41 cases (43.16%) of BPH shows PSA levels of 4-10ng/ml and 5 cases (5.26%) of BPH shows PSA levels of >10ng/ml. 14 cases (82.35%) of prostatic adenocarcinoma shows PSA levels of >10ng/ml, One case (5.88%) of prostatic adenocarcinoma shows PSA levels of <4 ng/ml and 2cases (11.76%) of prostatic adenocarcinoma shows PSA levels of 4-10 ng/ml . 5 cases (71.43%) of prostatitis shows PSA levels of 4-10ng/ml and 2 cases of prostatitis shows PSA levels of <4 ng/ml. PSA levels are higher in prostatic adenocarcinoma when compared to BPH and prostatitis and this difference is statistically significant (p=0.000) (Table1).

PSA levels in prostatic carcinoma were compared with Gleason’s histopathological grade of the tumors. Maximum number of prostatic adenocarcinoma were in grade 2 [12 cases (70.59%)]. Maximum cases of grade 2 and grade 3 prostatic adenocarcinomas had PSA range of 20-49.49 ng/ml. One case (5.88%) of grade 2 adenocarcinoma had PSA range of 0-3.98 ng/ml . One case (5.88%) of grade 1 and one case (5.88%) of grade 2 adenocarcinoma had PSA range of 4-9.99 ng/ml. 4 Cases (23.53%) of grade 2 prostatic adenocarcinoma had PSA range of 50- 99.99 ng/ml. In our study there is a difference in PSA levels across the grades which is statistically significant (p=0.043) (Table 2).

Table 1: Histopathology diagnosis related with range of Prostate Specific antigen level:

PSA	Adenocarcinoma	BPH	Prostatitis
0-4.0ng/ml	1(5.88%)	49(51.58%)	2(28.57%)
4-10.0ng/ml	2(11.76%)	41(43.16%)	5(71.43%)
10-20ng/ml	4(23.53%)	5(5.26%)	0
>20ng/ml	10(58.82%)	0	0
Total	17(100%)	95(100%)	7(100%)

P=0.000 significant PSA level are higher in prostate adeno carcinoma when compared to BPH & prostatitis and this difference is statistically significant (P=0.000).

Table 2: Correlation between serum PSA levels and Gleason grade of prostatic adeno carcinoma

PSA Range(ng/ml)	Grade1	Grade 2	Grade3
0-3.99	0	1(5.88%)	0
4-9.99	1(5.88%)	1(5.88%)	0
10-19.99	0	3(17.65%)	1(5.88%)
20-49.99	0	3(17.65%)	3(17.65%)
50-99.99	0	4(23.53%)	0
Total (no=17)	1(5.88%)	12(70.59%)	4(23.53%)

There is a difference in PSA levels across the grades and this is statistically significant (P=0.043).

Table 3: Comparison between different types of lesion with other studies

S. No	Histopathological Diagnosis	Kshitij et al ^[10]	Azmi .A Haroun et al ^[11]	Jevan et al ^[12]	Arunchitale et al ^[13]	Janardan et al ^[13]	Present study
1	BPH	85.8%	64.48%	83%	89%	93.9%	95(79.83%)
2	Prostatic adenocarcinoma	8.35%	27.1%	17%	11%	6.06%	17(14.28%)
3.	Prostatitis	0.64%	8.4%	-	-	-	7(5.88%)

Table 4: Benign and malignant prostatic lesion: Comparison between Prostate Specific Antigen level with other studies

PSA range (ng/ml)	BPH			Malignant prostatic lesion			
	Kshitij et al ^[10]	Ishtiaq Ali Khan et al ^[14]	Present study	Kshitij et al ^[10]	H.A Mwalyoma et al ^[9]	Sladana Zivkovic et al ^[15]	Present study
0-4.0	71.6%	-	51.58%	10.5%	-	2.50%	5.88%
4-10.0	22.6%	85%	43.16%	26.3%	5.3%	27.50%	11.76%
>10	3%	15%	5.26%	63.15%	94.7%	70.0%	82.35%

Table 5: Comparison between our study and other studies in relation to PSA levels and Prostatic adenocarcinoma

PSA levels (ng/ml)	SladanaZivkovic et al (2004) ^[15]	Shanthi.V etal(2012-2015) ^[16]	Our study(2015)
0-3.99	1(2.5%)	0	1(5.88%)
4-9.99	11(27.5%)	2(4.76%)	2(11.76%)
10-19.99	7(17.5%)	6(14.29%)	4(23.53%)
>20	21(52.25%)	34(80.95%)	10(58.82%)

Table: 6 Comparison between our study and Shanthi v et al^[16]study in relation to serum PSA levels and Gleason grade of prostatic adeno carcinoma.

PSA levels (ng/ml)	Grade 1		Grade 2		Grade 3	
	Shanthi V etal ^[16]	Our study	Shanthi V etal ^[16]	Our study	Shanthi V etal ^[16]	Our study
0-3.99	0	0	0	1(5.88%)	0	0
4-9.99	2(4.76%)	1(5.88%)	0	1(5.88%)	0	0
10-19.99	0	0	5(11.9%)	3(17.65%)	0	1(5.88%)
20-49.99	0	0	7(16.67%)	3(17.65%)	0	3(17.65%)
50-99.99	0	0	10(23.8%)	4(23.53%)	4(9.52%)	0
100-149.99	0	0	7(16.67%)	0	2(4.76%)	0
150-199.99	0	0	0	0	0	0
>200	0	0	5(11.9%)	0	0	0
Total	2(4.76%)	1(5.88%)	34(80.95%)	12(70.59%)	6(14.29%)	4(23.53%)

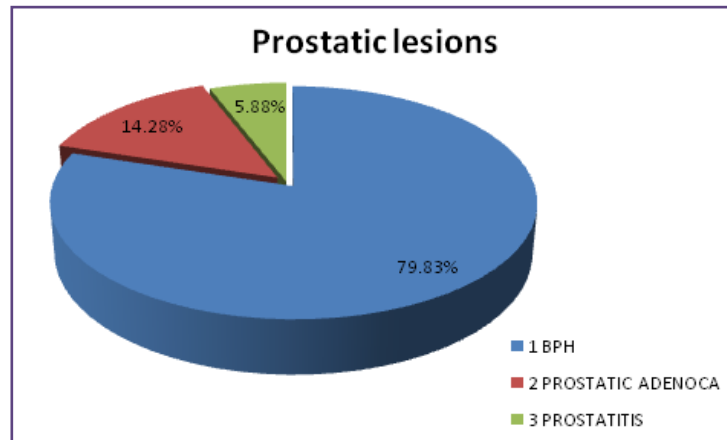


Fig. 1: Pie chart showing percentage of BPH, Prostatic Adenocarcinoma and Prostatitis

Discussion

The prostate is a pear-shaped glandular organ that weighs up to 20g in the normal adult male and it has been divided into anterior, middle, posterior and two lateral lobes by drawing divergent lines from the centrally located urethra. The prostate can be divided into four biological and anatomical zones, peripheral zone, central zone, transitional zone and periurethral gland regions. The transitional zone and periurethral regions are the exclusive sites of origin of nodular hyperplasia, whereas the peripheral zone is the one most susceptible to prostatitis and carcinoma. The glandular component of the organ is composed of acini and ducts, the latter subdivided into large (primary, major, excretory) and peripheral (secretory, minor). Both acini and ducts contain secretory cells, basal cells and scattered neuroendocrine cells. The secretory cells which are located in the luminal side of the gland, contribute a wide variety of products of the seminal fluid. They produce prostatic acid phosphate (PAP) and prostate specific antigen (PSA). PSA is glycoprotein that has been identified as a kallikrein like protease. In the present study most common lesion is BPH with mean age 63.67 ± 11.29 and BPH is more common between 51-80 years of age. Prostatic adenocarcinoma (Figure 2) is second most common lesion in our study. Prostatic adenocarcinoma mean age is 68.88 ± 6.49 and more common between 61 to 80 years of age in this study. In our study prostatic adenocarcinoma mean age figure are comparable with finding from other studies which report the mean age of 69 years by Thompson IM et al,^[7] mean age of 65 years by Lyn et al,^[8] and mean age of 68 years by H A Mwakyoma et al.^[9] In the present study BPH cases are 79.83% which is nearby comparable with Kshitij et al,^[10] Jevan et al,^[12] Arunchitale et al^[13] and Janardan et al studies.^[13] In our study prostatic adenocarcinoma incidence was 14.28% which is nearby comparable with Jevan et al^[12] and Arun Chitale et al studies.^[13] (Table 3). In our study

BPH cases are most commonly present between PSA level 0-4.0ng/ml (51.58%) which is compared with study of Kshitij et al,^[10] and prostatic adenocarcinoma cases are more commonly present with PSA level >10.0ng/ml (82.35%) and it is nearly compared with Walyomaet al^[9] Kshitij et al^[10] and Sladana Zivkovic et al studies.^[15] (Table 4).

In the present study we evaluated the prognostic importance of serum PSA levels with grades of adenocarcinoma prostate. In our study maximum number of malignancies (58.82%) has serum PSA value of more than 20 ng/ml which coincided with study done by Sladana Zivkovic et al study (52.25%)^[15] and lower than Shanthi V et al study (80.95%).^[16] 2 cases (11.76%) of prostatic adenocarcinoma was detected with PSA values in the range of 4-9.99 ng/ml which is higher than the Shanthi V et al study (4.76%)^[16] and lower than the Sladana Zivkovic et al study (27.5%).^[15] 4 cases of (23.53%) prostatic adeno carcinoma was detected with PSA values in the range of 10-19.99 ng/ml which is higher than the Sladana Zivkovic et al study (17.5%)^[15] and Shanthi V et al study (14.29%).^[16] (Table 5).

In the present study, one case (5.88%) of grade 2 prostatic adenocarcinoma was noted with serum PSA range of 0-3.99 ng/ml. One case (5.88%) of grade 1 prostatic adenocarcinoma are noted with serum PSA range of 4-9.99 ng/ml which is slightly higher than Shanthi V et al study (4.76%).^[16] One case (5.88%) of grade 2 prostatic adeno carcinoma. 3 cases (17.65%) of grade 2 prostatic adenocarcinoma were noted with serum PSA range of 10-19.99 ng/ml which is higher than the Shanthi V et al study (11.9%).^[16] One case (5.88%) of grade 3 prostatic adeno carcinoma, 3 cases (17.65%) of grade 2 prostatic adeno carcinomas were noted with serum PSA range of 20-49.99 ng/ml which is slightly higher than Shanthi V et al study (16.67%).^[16] 3 cases (17.65%) of grade 3 prostatic adeno carcinoma, 4 cases of (23.53%) grade 2 prostatic adeno carcinoma were

noted with serum PSA range of 50-99.99 ng/ml which is similar to Shanthi V et al study (23.8%).^[16] In our study histopathological grade 2 prostatic adeno carcinoma were restricted to PSA levels of 10ng/ml and above ,but grade 1 prostatic adeno carcinomas was restricted to PSA levels of < 10 ng/ml and grade 3 carcinomas were not having any correlation with specific PSA levels (Table 6).

In studies done by Shanthi V et al (2012-2015)^[16] and Lennox Anderson Jackson et al (2012),^[15] histopathological grade 3 adeno carcinomas had a PSA range of 50-149.99ng/ml and 76-190 ng/ml respectively . Our study coincided with the conclusion drawn from the studies of Shanthi V et al (2012-2015)^[16] and Lennox Anderson Jackson et al (2012)^[17] that histological higher grades of prostatic carcinomas are associated with higher PSA levels.

Conclusion

Benign prostatic hyperplasia was the most frequent lesion encountered followed by adenocarcinoma prostate . Prostatic adenocarcinomas were associated with raised prostate specific antigen more than 10ng/ml. In our study, there was a positive relation between higher levels of serum PSA and Gleason's histopathological grade of prostatic adenocarcinoma. But poorly differentiated prostatic adenocarcinomas (higher grade) did not show correlation with serum PSA levels indicating that as the tumor becomes poorly differentiated, tumor cell production of PSA is reduced.

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*Corresponding author:

Dr. N. Mohan Rao, Associate Professor, Department of Pathology Narayana Medical College, Nellore Andhra Pradesh, India, Pincode:524003

Phone: +91 919849229201

Email: nmr2020kmc@gmail.com

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