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Study of Serum Prostate Specific Antigen Level in Prostate Biopsy Specimens

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Abstract:
Background: Prostatic adenocarcinoma is one of the most common cancer occurring in the men above 50 years of age. Prostate specific antigen (PSA) is an important serum marker which helps in the diagnosis of prostatic adenocarcinoma and also aids in estimating the tumor grade. Objective: To evaluate the correlation between serum PSA levels and Gleason's histological grade of prostatic adenocarcinoma.
Methods: A retrospective study analysis was done for 64 patients whose transrectal ultrasonography (TRUS) guided prostate biopsy were studied in our hospital. The serum PSA levels were noted and compared with different Gleason histological grading in adenocarcinoma patients.
Results: Our study included 64 cases, out of which 43 cases were benign and 21 cases were malignant. Maximum numbers of benign and malignant lesions were in the age group of 60 – 69 years. Most of the malignant cases (85.71%) had PSA level above 20ng/ml. Histological grade III carcinomas were restricted to PSA levels of 50ng/ml and above, while grade I was restricted to PSA level of less than 10ng/ml and grade II carcinomas did not have any correlation with specific PSA levels.
Conclusion: Our study showed that there was significant correlation between serum PSA value and Gleasons histological grade of prostatic adenocarcinoma.

Keywords: *Prostate Specific Antigen, Gleason Histological Grade, Adenocarcinoma*

1. Introduction

Prostate specific antigen (PSA) is a glycoprotein enzyme secreted by epithelial cells of the prostate. PSA is a member of the kallikrein related peptidase family, which is an important tumor marker in the diagnosis of prostatic adenocarcinoma. PSA is present in serum of men, with normal prostate, but the levels are elevated in pathological conditions like prostatitis, hyperplasia and prostatic carcinoma[i]. PSA is produced by normal epithelial cells lining the prostatic glands, hyperplastic epithelial cells and pleomorphic epithelial cells in the prostatic adenocarcinoma. In conditions like inflammation, hyperplasia and malignancy, there is destruction of cell integrity which leads to release of PSA into circulation. This produces increase in serum PSA level[ii].

In prostatic adenocarcinoma, the malignant cells produce less PSA then healthy epithelial cells. But as there is great increase in number of cells in carcinoma, the PSA produced is more and serum levels are raised. The malignant cells in most of the prostatic carcinoma are immunopositive for PSA and have been used for identifying the metastatic deposits.

In protatic carcinomas, serum PSA value depends upon the differentiation of the tumor cells. The poorly differentiated prostatic tumors will have low serum PSA levels when compared to well differentiated tumors.

A pretreatment serum PSA level not only predicts the grade of prostatic adenocarcinoma but also acts as an independent predictor of response to therapy [iii].

2. Material and Methods

This is retrospective study performed at Government Medical college and Sir Takhtsinhji hospital, Bhavnagar during the period of Dec 2012 to Dec 2014. This study included 64 patients, in whom transrectal ultrasonography (TRUS) guided prostatic biopsy were taken and sent for histopathological examination. Biopsy was performed under ultrasound guidance using 18- gauge, Tru cut core biopsy needle which is 20 cm long. The specimen was sent in formalin to pathology department where they were examined for the presence of carcinoma. Preoperative serum PSA levels are noted in these cases. PSA levels in these cases were compared with the Gleasons grade of these tumors.

3. Results

Prostatic biopsy specimens obtained from 64 patients who attended surgical department in Sir Takhtsinhji hospital, Bhavnagar during the period of Dec 2012 to Dec. Out of 64 prostatic biopsy specimens 43 were diagnosed as benign and 21 were diagnosed as malignancy. These cases were studied in relation to age and serum PSA levels. In malignant cases serum PSA levels were compared with grades of carcinoma.

Prostatic biopsies in relation to age were studied by dividing them into 7 groups (Table 1).

Age group	Total number of cases	Benign cases	Malignant cases
30-39 yrs	1(1.56%)	0	1(4.76%)
40-49 yrs	2(3.13%)	2(4.65%)	0
50-59 yrs	14(21.87%)	8(18.6%)	6(28.57%)
60-69 yrs	26(40.62%)	19(44.18%)	7(33.33%)
70-79 yrs	18(28.12%)	14(32.56%)	4(19.04%)
80-89 yrs	2(3.12%)	0	2(9.52%)
90-99 yrs	1(1.56%)	0	1(4.76%)
Total	64	43	21

Table 1: Prostatic lesions in relation to different age groups

Maximum numbers of benign and malignant cases were in the group of 60 -69 years.

PSA range (ng/ml)	Total number of cases	Benign cases	Malignant cases
0.01 – 3.99	0	0	0
4.00 – 9.99	11(8.59%)	10(23.25%)	01(4.76%)
10.0 – 19.99	20(15.62%)	18(41.86%)	02(9.52%)
20.0 – 49.99	14(10.93%)	11(25.58%)	03(14.28%)
50.0 – 99.99	10(7.81%)	03(6.97%)	07(33.33%)
100.0 – 149.99	06(4.68%)	01(2.32%)	05(23.80%)
150.0 – 199.99	0	0	0
>200	03(2.34%)	0	03(14.28%)
Total	64	43	21

Table 2: Correlation of PSA levels with Prostate biopsy.

PSA levels in all the cases were studied (Table 2). In our study no case was found to have PSA levels less than 4ng/ml. 11 cases had PSA levels in the range of 4.0 – 9.99 ng/ml. Out of these 10 cases were benign and 1 case was malignant. In the PSA range of 10 – 19.99 ng/ml, 20 cases were noted, out of which 18 were benign and 2 were malignant. 14 cases had PSA values in the range of 20 – 49.99 ng/ml, out of which 11 were benign and 3 cases were malignant. In the range of 50 – 99.99 ng/ml, 10 cases were noted, out of which 3 cases were benign and 7 cases were malignant. 6 cases had PSA values in the range of 100-149.99 ng/ml, out of which 1 case was benign and 5 cases were malignant. There were 3 cases which had PSA values of more than 200 and all were malignant.

PSA range (ng/ml)	Grade 1	Grade 2	Grade 3
4 – 9.99	1	0	0
10.0 – 19.99	0	2	0
20 – 49.99	0	3	0
50 – 99.99	0	5	2
100 – 149.99	0	4	1
150 – 199.99	0	0	0
≥200	0	3	0
TOTAL	1(4.76%)	17(80.95%)	3(14.28%)

Table 3: Correlation between serum PSA levels and Gleason grade of prostatic adenocarcinoma

PSA levels in prostatic carcinomas were compared with Gleason's grade of the tumor (Table 3). Maximum numbers of prostatic adenocarcinomas were in grade 2 [17 cases (80.95%)]. Maximum cases in grade 2 and grade 3 had PSA range of 50 – 99.99 ng/ml. 1 case of grade 3 adenocarcinoma were in the PSA range of 100 – 149.99 ng/ml and 1 case of grade 1 adenocarcinoma had PSA range of 4 – 9.99 ng/ml.

In our study there was a good correlation of rising PSA with grade upto PSA level of 50. Beyond that PSA level, there was no significant correlation in between the PSA level and Gleasons grade.

4. Discussion

Prostatic carcinoma is the most common malignancy among men and is responsible for 10% of cancer deaths[iv]. Prostatic carcinoma is second to lung cancer as a leading cause of cancer related deaths in men. Hormonal factors play a role in the development of prostatic carcinoma. Incidence of prostatic carcinoma is low in patients with hyperestrogenism resulting from liver cirrhosis and does not occur in eunuchs castrated before puberty. Occupational exposure, smoking, venereal diseases, sexual habits and diet do not show any demonstrable correlation with prostatic carcinoma[v].

Almost 75% of the men diagnosed with prostatic cancer are age 65 or older and the frequency increases with age. Clinical stage, Gleason's score and serum PSA are independent prognostic factors in prostatic carcinoma and help to choose a definitive treatment in carcinoma [vi]. The U.S. Food and Drug Administration [FDA] in the United States has approved that the annual screening of the prostatic cancer in men of age 50 and older is by assessing serum PSA levels. If the PSA levels are between 4 to 10 ng/ml, then it is considered to be suspicious and a repeat PSA test is performed. Finally prostate biopsy should be taken for histopathological analysis, if indicated[vii]. PSA also known as Seminin, Kallikrein III, Semenogelase, P-30 antigen and γ – Semino protein is a serine protease enzyme, which has its gene located on the 19th chromosome. It is a 34KD glycoprotein produced by epithelial cells of prostate[viii].

Papsidero in 1980 first quantitatively measured PSA in blood and its clinical use as marker of prostatic cancer was studied by Stamey[ix]. In the blood normally PSA is present at very low levels of less than 4ng/ml. Increase in the serum PSA levels indicate prostatic cancer. PSA levels can also be increased in benign prostatic hyperplasia, prostatitis, irritation, and recent ejaculation[x,xi]. PSA levels can also be raised on digital rectal examination[xii]. In the blood only a small amount of PSA is available freely and large amount of it is bound to the serum proteins. The ratio of free PSA to total PSA will be reduced in Prostatic carcinoma. If the ratio is less than 25% the risk of prostatic cancer increases. In men whose PSA levels are between 4 to 10 ng/ml, the ratio of free to total PSA levels helps in avoiding unnecessary biopsies[xiii].

Along with measuring the free to total PSA, the measurement of proteolytic activity of the enzyme can improve the diagnostic value of the test. The proteolytically active PSA has anti-angiogenic effect and the presence of inactive proenzyme forms of PSA indicates presence of disease[xiv].

PSA levels (ng/ml)	Our study (2012-2014)	Sladana Zivkovic (2004)
0.01 – 3.99	0	1(2.5%)
4 – 9.99	1(4.76%)	11(27.5%)
10 – 99.99	6(9.52%)	7(17.5%)
>20	18(85.71%)	21(52.25%)

Table 4: Correlation between our study and other study in relation to PSA levels and malignancy

In the present study, we evaluated the prognostic importance of preoperative total serum PSA levels with grades of adenocarcinoma of prostate. In our study maximum number of malignancies has serum PSA value of more than 20ng/ml which coincided with study done by Sladana Zivkovic (2004) who got 21 cases (52.5%) having PSA values above 20 ng/ml[xv] (Table -4).

In our study no maliganancy was detected with PSA values in the range of 0 – 3.99 ng/ml. In our study histological grade III carcinomas were restricted to PSA levels of 50 and above, while grade I was restricted to PSA level of less than 10ng/ml and grade II carcinomas did not have any correlation with specific PSA levels. In studies done by Lennox Anderson Jackson et al. (2012), histological grade III adenocarcinoma had a PSA range of 76 to 190 ng/ml, while grade II carcinomas had PSA range of 20-100 ng/ml . Our study coincided with the conclusion drawn from the studies of Lennox Anderson Jackson et al. (2012) that histologically higher grades of prostatic carcinomas are associated with higher PSA levels[xvi].

5. Conclusion

With increasing PSA levels the possibility of malignancy is more, although malignancies were seen at low PSA levels also. Moreover, positive relation was seen between higher levels of PSA and Gleasons grade. But as the tumor becomes more poorly differentiated it may not correlate with PSA levels because the tumor cells may not produce PSA as they have lost differentiation.

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