



Original Research Article

Correlation between Gleason score of adenocarcinoma prostate and serum PSA levels in the western Himalayan region of India

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ABSTRACT

Background: The diseases of the prostate gland are the major cause of morbidity and mortality among adult males worldwide. Prostate cancer is the most common malignant tumour in men over the age of 65 years. The present study was done to evaluate the histomorphological spectrum of malignant lesion of prostate and to establish the correlation between S.PSA (Serum Prostate-Specific Antigen) levels and Gleason's grade in the Western Himalayan region of India.

Materials and Methods: Histopathological examination of 100 prostatic tissue was done. Serum PSA assessed and its values were correlated with Gleason's grading of prostate cancer.

Result: Malignancy was found in 29 per cent of cases. Conventional adenocarcinoma encountered in 96.6 per cent cases. Undifferentiated carcinoma was reported in 3.4 per cent cases. Serum prostate-specific antigens level was increased in 93.1% of malignant cases. More than 10ng/ml was seen in 68.9 per cent cases. Mean S.PSA level in malignancy was 122.9ng/ml. The Commonest Gleason's score being seven (37.9 percent).

Conclusion: This prospective study concluded that there is a higher percentage of prostatic carcinoma in the Western Himalayan region of India. PSA is found to be a sensitive marker for the diagnosis of prostate cancer. With a cut off value 4ng/ml sensitivity was found to be 93.75% and specificity was 46.15%, and there is a positive correlation between Serum PSA level and Gleason's grading. Mean serum PSA level of moderately and poorly differentiated carcinoma was 32.15ng/ml and 325.3ng/ml respectively.

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1. Introduction

Adenocarcinoma of the prostate is one of the most common form of cancer in men, accounting for 29% of cancer in the United States in 2007.¹ Incidence of carcinoma prostate increases proportionally after 50 years of age. It is the second important cause of cancer-related death in men after lung cancer.² It is estimated that incidence rates for prostate cancer in India ranged from 5.0 to 9.1 per 100, 000/year.³ Serum PSA, a glycoprotein identified by Wang et al (1979), is produced exclusively by the

epithelial cells of benign and malignant prostatic tissue with normal levels of 0-4ng/ml.⁴ Increased PSA levels are seen in all prostatic diseases but markedly elevated levels are indicative of carcinoma prostate. Interpretation of prostatic biopsies have been a continuous problem to the practicing pathologists. Histological type, grade & stage of prostate carcinoma is vital in planning treatment strategies & predicting survival rate. For prognostic correlation, various histological grading systems have been introduced. The Gleason s grading system being the most popular one, based on the architectural pattern of growth.⁵ Gleason score of less than 6 are generally low grade cancers and are not

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aggressive. Advanced carcinomas with regional invasion and metastasis, generally belong to scores 8 and beyond. In contrast to many other carcinomas, prostate cancer can be completely cured if detected in the early stage. The combination of the digital rectal examination (DRE), trans rectal ultrasonography (TRUS), and serum Prostate Specific Antigen (S.PSA) represents a powerful diagnostic triad for the detection of early prostatic carcinoma.

2. Materials and Methods

1-year Prospective Study was done on 100 patients at Department of Pathology, Indira Gandhi Medical College, Shimla H.P. Paraffin-embedded hematoxylin and eosin stain sections studied. The PSA levels were estimated using automated Chemiluminescence method on Beckman Coulter Access –II System. A value of 4ng/ml was taken as cut off point for Serum PSA. Its values were correlated with Gleason's grading of prostate cancer.

3. Result

The present study was conducted on 100 patients over a period of one year (1st June 2014 to 31st May 2015). On microscopic examination, out of a total 100 patients, 29 showed features of malignancy constituted 29 per cent.

The most common presenting complaint in this study was dribbling of urine, increases in the frequency and retention of urine constituting 97.3 per cent patients. Associated hematuria was seen in 7 of these patients.

Based on DRE (Digital Rectal Examination), serum PSA (Prostate-Specific Antigen) and USG (Ultrasonography) 35 clinically suspected cases of malignant lesions were subjected to biopsy. On microscopic examination 25 were confirmed as adenocarcinoma. Out of 65 clinically benign cases 4 were turned out as malignancy on histopathological examination. Most common surgical Procedure was TRUS (Trans rectal Ultrasound) guided biopsy followed by TURP (Transurethral Resection of the Prostate).

Malignancy was common in the 8th decade with mean age 70.58 years. The youngest patient was 50 years of age.

On microscopy examination of prostatic biopsy out of 29 malignant cases, 28 cases of adenocarcinoma with Gleason grade 3,4,5 (Figures 1, 2 and 3) & one case of undifferentiated carcinoma (Figure 4) was observed. Eleven of 29 cases of carcinoma showed perineal invasion (Figure 2). It is defined as the presence of prostate cancer tracking along or around a nerve within the perineural space and signals an increased likelihood of an extra prostatic extension of cancer or, ultimately, of cancer recurrence. All the cases of adenocarcinoma prostate were graded according to Gleason's grading system. A primary and secondary grade was assigned and the final Gleason's score was given by adding the two grades. The Gleason's score in the present study ranged from 5 to 10. Majority of the cases (n=11) were

given score seven, followed by score six seen in 7 cases. Eight and nine scores were seen in 4 cases each. One patient each with Gleason's score ten and score five were found.

Up to 4ng/ml of serum PSA level was considered normal in the present study. Twenty-seven of twenty-nine showed increased S.PSA levels. Mean S.PSA level was 122.8ng/ml. Ten of Twenty-seven (37.03 per cent) had very high S.PSA levels (>50 ng/ml) which also included one case of undifferentiated carcinoma (59 ng/ml) (Table 1).

Another 10 cases (37.03 per cent) had S.PSA levels more than 10 ng/ml and less than 50ng/ml. Seven cases of adenocarcinoma including one case with Gleason's score 10 had relatively lower levels of S.PSA ranging from more than 4 ng/ml to 10 ng/ml. All the cases of Gleason's score 8 and 9 had high levels of S.PSA (>10 ng/ml). Six out of eleven cases with Gleason's score 7 had a serum PSA level more than 10ng/ml.

Only 2 cases had S.PSA levels within normal limits both were found to have adenocarcinoma with Gleason's score 5 and 6 (Table 2).

S.PSA level is correlated with the histopathological findings. The accuracy of increased serum PSA in malignant cases was evaluated taking histopathology as the gold standard test.

The result was interrelated as follows

True positive (TP)-High level of S.PSA correctly interpreting malignant. (n=27)

True negative (TN)-Normal levels of S.PSA correctly interpreting nonmalignant condition. (n=35)

False-positive (FP)-Increase level of S.PSA wrongly interpreting nonmalignant condition. (n=36)

False-negative (FN)-Normal level of S.PSA wrongly interpreting malignant condition. (n=2)

The sensitivity of the test was 93.10%. It is a likelihood that the patient with the disease has positive test results.

The test is 49.29% specificity. It is a likelihood that the patient without disease has negative test results.

The positive predictive value is 42.85%. It is the probability that subjects with a positive screening test truly have the disease.

The negative predictive value is 94.59%. It is the probability that subjects with a negative screening test truly don't have the disease.

4. Discussion

Carcinoma prostate constituted the second commonest group next to BPH (Benign Prostatic Hyperplasia) and its incidence varied from 15 to 32.2 per cent as reported by different authors.

In the present study 97.3 percent of the patients, the presenting complaint was LUTS (lower urinary tract symptoms) with or without hematuria. This increased frequency of urine, urgency, hesitancy and nocturia were related to compression of the prostatic urethra due to

Table 1: Serum PSA level in malignant lesion (n=29)

S. PSA (ng/ml)	Total No. of cases	Adenocarcinoma		Undifferentiated Carcinoma	
		No. of Patients	Percentage	No. of Patients	Percentage
0-4	02	02	6.9	-	-
>4-10	07	07	24.14	-	-
>10-20	04	04	13.8	-	-
>20-50	06	06	20.68	-	-
>50	10	9	34.48	1	100
Total	29	28	100	1	100

Highest level of S.PSA was 1684ng/ml with Gleason's score-8

Table 2: Distribution of serum PSA level according to Gleason score (n=28)*

S. PSA (ng/ml)	Gleason's Score						Total
	5	6	7	8	9	10	
0-4	01	01	-	-	-	-	02
>4-10	-	01	05	-	-	01	07
>10-20	-	02	01	01	-	-	04
>20-50	-	01	03	-	02	-	06
>50	-	02	02	03	02	-	9
Total	01	07	11	04	04	01	28

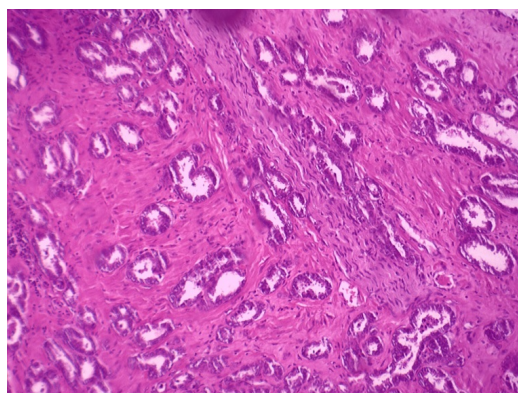
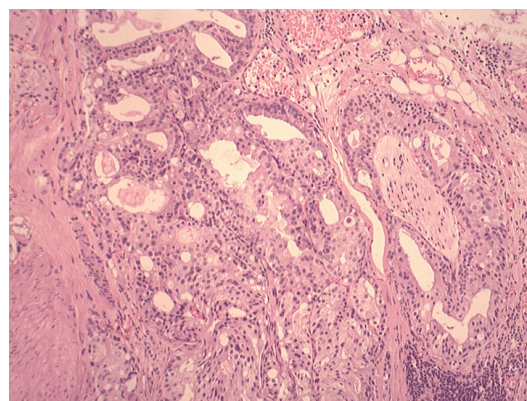
Table 3: Comparison of distribution of serum PSA level in malignancy

Studies	Year	Upto4ng/ml	4-10ng/ml	>10ng/ml
Xess et al	2001	-	16%	74%
Zivkovic S et al	2004	2.5%	27.50%	70%
Wadgaonkar et al	2013	-	08%	92%
Present study	2015	6.2%	31.25%	68.75

Table 4: Comparison of correlation of serum PSA level and differentiation of carcinoma

Author	Year	No. of Cases	Well Differentiated		Moderate differentiated		Poor Differentiated	
			Percentage of Total Cases	Mean S.PSA ng/ml	Percentage of Total cases	Mean S.PSA ng/ml	Percentage of total cases	Mean S.PSA ng/ml
Zivkovic S et al	2004	40	17.5	7.9	52.5	22	30	41.5
Albashri A.et al	2014	65	5.6	100	41	210	36.6	588
Present study n=28*	2015	29	-	-	67.85	30.15	32.14	325.3

*one case of undifferentiated carcinoma was not taken into account.

**Fig. 1:** Adenocarcinoma prostate, Gleason's grade 3 with perineural invasion (100x, H&E)**Fig. 2:** Adenocarcinoma prostate, Gleason's grade 4, with perineural invasion (100x, H&E)

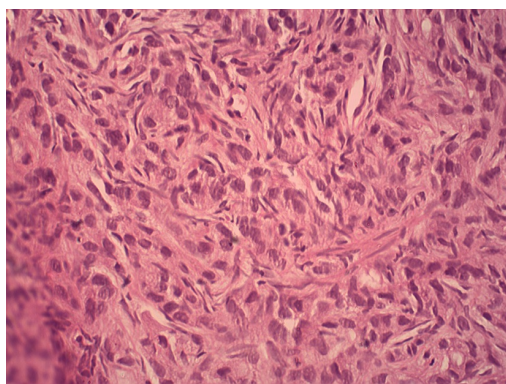


Fig. 3: Adenocarcinoma prostate, Gleason's grade 5 (200x, H&E)

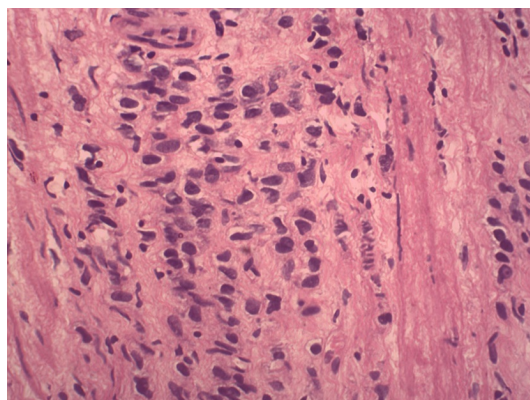


Fig. 4: Undifferentiated carcinoma (200x, H&E)

increased prostatic size. Aslam et al (2013)⁶ and Raza et al (2015)⁷ also found LUTS as the most common presenting symptom. So our study is comparable to both.

The peak age incidence of malignancy in our study was in 7th and 8th decades with a mean of 70.58 years similar to the other previous studies. Albashari A et al⁸ studied 417 cases and observed 74 of malignancy with a maximum number of patients falling in 70 -89 years of age group with a mean age of 71.2 years, comparable to our study.

Malignancy of prostate was seen in 29 (29percent) patients in the present study. Histomorphological spectrum of prostatic malignancy revealed Adenocarcinoma as the commonest histological type of malignancy in our study accounting for 96.9% of cases. Jishani et al,⁹ Mosli H et al¹⁰ and Wadgaonkar et al¹¹ also had a similar observation.

As compared to other studies, our study showed a higher percentage of carcinoma. Tyagi B et al¹² (2010) in their study observed that the incidence rate is higher in North India and it is rapidly increasing. Smoking and alcohol consumption has been being attributed as the main culprit.

Histological grading of adenocarcinomas is a good prognostic index and so has been done in every biopsy report. D.F Gleason published his proposed grading system for carcinoma of the prostate in the seventies, which is now

universally accepted.

In the present study, Gleason's score ranged from 5 to 10 with a predominance of score six and seven (62.5 per cent) as also studied by Mosli et al (2009) and Shiris et al¹³ (2013) with 57.7 per cent and 70.5 per cent cases respectively.

A major disparity was observed in AZ Mohammad et al study¹⁴ (n=493) who observed maximum cases with Gleason's score 4 whereas in the present study there was no case of score 4. This difference could be due to small sample size and predominance of TRUS guided biopsy in the present study where grade 1 and 2 is not assigned due to the limited amount of available tissue.

S.PSA is a tumour marker for the carcinoma prostate. Increased PSA levels are seen in all prostatic diseases but markedly elevated levels are indicative of carcinoma prostate. It is considered as a most sensitive marker for detection of Carcinoma prostate. However acute urinary retention, digital rectal examination, cystoscopy examination, drug and prostate biopsy can cause spurious elevation of serum PSA concentration.

In this study, the S.PSA levels were increased in 93.8 per cent cases of adenocarcinoma. Two cases of carcinoma (6.2 per cent) had S.PSA levels within normal limits. Which could be due to, biochemical and technical error.

A study carried by Zivkovic S et al¹⁵ (2004) showed 70 per cent of their patients with adenocarcinoma had S.PSA values more than 10ng/ml. They also found 2.5 per cent of patients had serum levels within normal limits. Similarly, another study by Xess et al¹⁶ in 2001 with 51 cases of adenocarcinoma shows the majority of patients (74 per cent) having S.PSA levels more than 10.

Our study is comparable to these studies (Table 3).

The results of the present study show that S.PSA values in patients with prostate carcinoma were distributed widely ranging from normal (0-4ng/ml) to intermediate (>4-10ng/ml) to high levels (>10ng/ml). Approximately one-third of adenocarcinoma cases had serum PSA levels in the interval of intermediary values. It was necessary to distinguish these cases as benign or malignant. The biopsy was the only possible way to confirm the diagnosis. This is one of the examples of limited use of the SPSA test.

To correlate between serum PSA level with Gleason's score the patients were divided into three groups according to the value of Gleason's score: group I (Gleason's score 2-4), group II (Gleason's score 5-7), and group III (Gleason's score 8-10). The various Gleason grades were lumped together in a three grade system - Well, moderately and poorly differentiated carcinoma which corresponds to the group I, II& III respectively.¹⁷

There was no case of well-differentiated carcinoma in the present study as most of our carcinoma patients had undergone TRUS guided biopsy. Moderately and poorly differentiated carcinoma accounted for 67.85 per cent and

32.14 per cent respectively, Mean serum PSA level of moderately and poorly differentiated carcinoma was 30.15 ng/dl and 325.3ng/dl respectively.

The mean value of S.PSA of moderately differentiated carcinoma in our study was similar to that of Zevkovic's study. In Albashari et al study mean S.PSA level of well and moderately differentiated carcinoma was 100ng/ml and 210ng/ml respectively. The mean S.PSA levels of poorly differentiated carcinoma were 588ng/ml in comparison to 325.3ng/ml in the present study (Table 4).

The Sensitivity and specificity of S.PSA in the diagnosis of malignancy of prostate were found to be 93.75 and 46.15 when the cut off for S.PSA is up to 4 ng/ml. This study is comparable to Lakhey et al¹⁸ (2010) and Shalini Agnihotri et al¹⁹ (2012). They found 100% and 79% sensitivity respectively. Lakhey M et al found 49% sensitivity whereas Agnihotri et al observed 59% specificity.

5. Conclusion

The serum PSA levels are a good indicator for the glandular proliferation of the prostate and can be used as a marker to check for the progression of prostate cancer. It is a highly sensitive tumor marker with a low specificity as many benign and iatrogenic conditions also increases its level. It has a high negative predictive value which is important in ruling out the suspicion of malignancy. In combination with DRE and USG serum PSA can give a better result in detection of early prostate cancer.

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None.

8. Conflict of Interest

None.

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