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PROSTATIC CARCINOMA: CORRELATION OF GLEASON'S SCORE WITH SERUM PSA LEVELS

Rubeena Naz Mohroo*[1] and Swami Ravi[2]

Bharati Vidyapeeth Medical College, Pune 411043, Maharashtra, India.

***Corresponding Author: Rubeena Naz Mohroo**
Bharati Vidyapeeth Medical College, Pune 411043, Maharashtra, India.

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ABSTRACT

Background: Prostate carcinoma is the sixth most common cancer in men and is second leading cause of cancer related death in men. Gleason's grading system is recommended by World Health Organisation (WHO), is a unique histopathological method for grading prostate cancer based solely on tumour architecture. Prostate specific antigen (PSA) is a protein secreted by both normal and abnormal prostate cells. **Objective:** The objective of the study was to determine the histopathological features and Gleason grading in Prostatic Carcinoma and to correlate with pre-treatment PSA levels with the Gleason score. **Results**: Twenty seven cases of prostatic carcinoma were studied. Most of the patients were in age group of 61-70. Median for serum PSA levels were 49.8 ng /ml and P – value < 0.001. Majority cases of cases had Gleason score of 5 – 7 (74.07%). The patients with Gleason Score of 5 – 7 had serum PSA levels >40 ng/ml. **Conclusion**: It was observed that the levels of serum PSA increased with increasing Gleason grade and score of the tumour.

KEYWORD: Prostate carcinoma, Gleason score, serum PSA.

INTRODUCTION

Prostate carcinoma is the sixth most common cancer in men and is a second leading cause of cancer related death in men.[1] It is predominantly a disease of elderly men over 50 years. United States death rate for cancer of prostate is high as compared to the other countries. Prostate cancer incidence is increasing in India.

Gleason's scoring system is recommended by World Health Organisation (WHO), is a unique histopathological method for grading prostate cancer based solely on tumour architecture.[2][3] Majority of urologist and radiotherapist base their therapeutic/management decisions on this scoring system. It correlates well with extra prostatic extension, seminal vesicle invasion and regional lymph node metastasis.[4],[5] Gleason's score of 7 or more behave worse than tumours with Gleason's score of 6 or less.[4] Gleason designed this system to accommodate the fact that carcinoma of the prostate has different patterns of growth, that each range from well differentiated to poorly differentiated, and that usually more than one pattern coexists in any prostate gland.[5] Grading is of particular importance in prostatic cancer, because grade and stage are the best prognostic predictors.[6]

Currently, prostate specific antigen is most commonly used biomarker for the diagnosis as well as for prediction of prognosis of prostate cancer. However, PSA is not a cancer specific marker, as it is present in both benign and malignant prostatic epithelial cells. Serum PSA levels are frequently elevated in benign conditions such as Benign Prostatic Hyperplasia (BPH) and prostatitis in addition to prostate cancer. Consequently patients with elevated serum PSA must undergo a biopsy to confirm or exclude the presence of prostate cancer.

MATERIAL AND METHODS

This prospective observational study was carried out in the department of pathology at Bharati Vidyapeeth Medical College, Pune after prior approval by Institutional Ethics Committee. 27 cases were studied over two years period 2014 and 2015.

Initially a detailed history of every patient with particular reference to age, family history, history regarding complaints of hesitancy, dysuria, frequency, urgency, dribbling of urine after completing urination, incomplete empting sensation was recorded.

General physical examination, abdominal examination including digital rectal examination (DRE), and genitourinary examination were done in urology OPD and were noted. The pre-treatment estimation of serum PSA levels was done by chemilluminescence method.

All transurethral resection of Prostate (TURP) and transrectal USG Guided biopsy (TRUS Bx) were sent for histopathological study. The Specimen were kept in 10% buffered formalin for 24 hours for fixation. Tissue processing and Hematoxylin and Eosin staining was done. On histopathological examination, prostatic adenocarcinomas were diagnosed and scoring was done using Gleason Microscopic Score. The collected data were entered in the MS Excel spread sheet, coded appropriately and later cleaned for any possible errors. Analysis was carried out using SPSS (Statistical Package for Social Studies).

RESULTS

The age distribution in patients with adenocarcinoma were in age group of 61-70 (40.74%), followed by age group of 71-80 (37.04%) with mean age of 71.41 years.

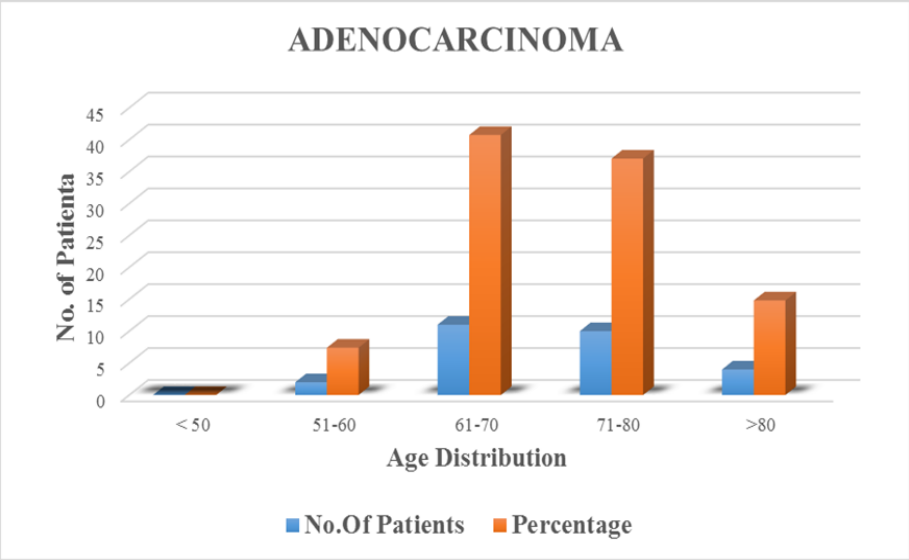

Figure 1: Age Distribution of Patients with Adenocarcinoma (N=27).

The patients with adenocarcinoma, 24 (88.89%) had serum PSA levels > 20 ng/ml. Eight patients had serum PSA levels > 100 ng/ml. The median for serum PSA levels were 49.8 ng/ml & P – value < 0.001.

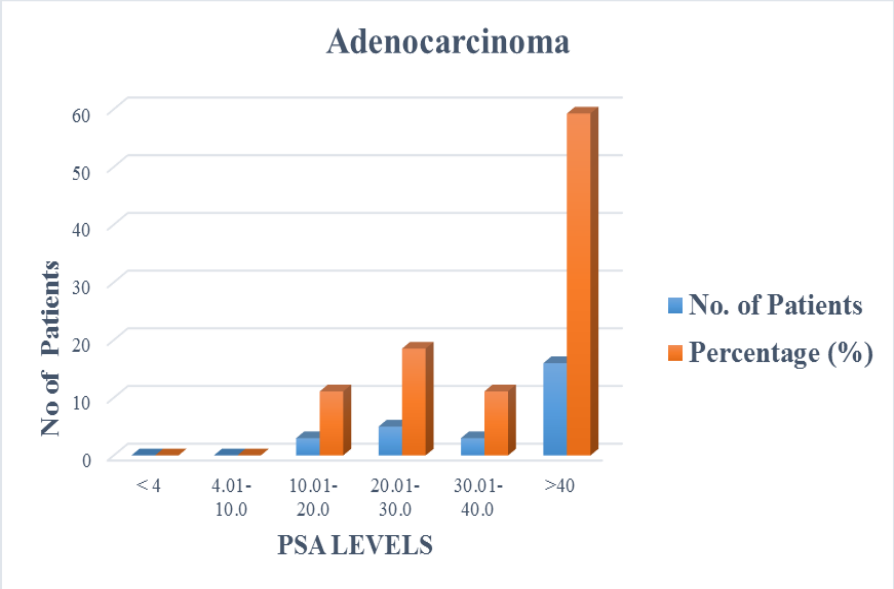

Figure 2: PSA Levels in Patients with Adenocarcinoma (N=27).

Almost all malignant the cases were of Acinar Adenocarcinoma (Ordinary type). The different microscopic patterns seen were glands, cords, cribriform, sheets, hypernephroid and comedonecrosis. The most common was glandular pattern (40.74%) followed by hypernephroid pattern (22.22%).

Table 1: Different Microscopic Patterns seen patients with adenocarcinoma.

Architectural Pattern	No. of cases N=27	Percentage %
Glands	11	40.74
Cribriform	5	18.52
Sheets	4	14.81
Hypernephroid	6	22.22
Comedonecrosis	1	3.71

In our study, out of 27 patients of adenocarcinoma majority had Gleason Grade of 5 – 7 (74.07%) followed by 8 -10(14.82%).

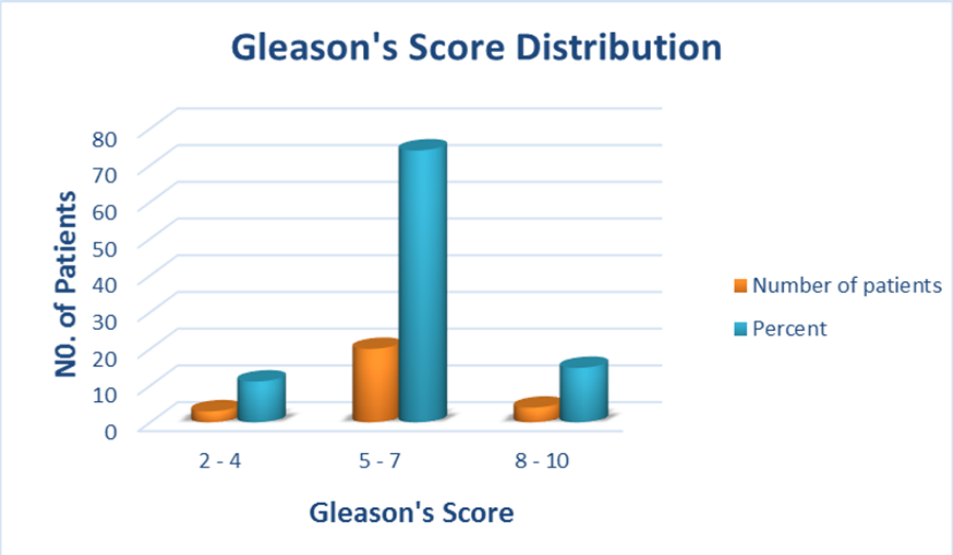

Figure 3: Gleason's Score in Patients of Adenocarcinoma (N=27).

Correlation of Gleason Score with serum PSA levels was done. Most of patients with Gleason Score of 5 – 7 had serum PSA levels >40 ng/ml.

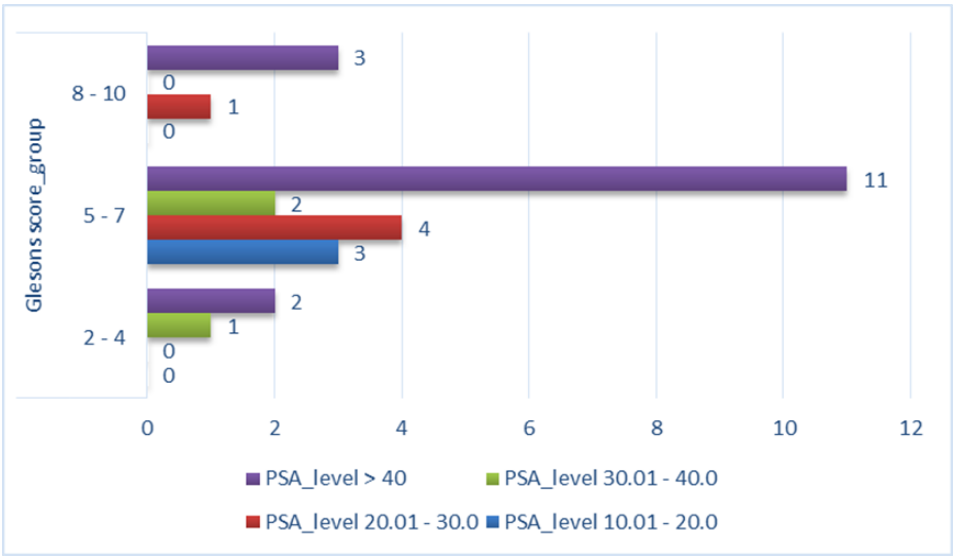

Figure 4: Correlation of Gleason score with serum PSA.

The sensitivity and specificity was calculated after taking the cut off value of serum PSA 4 and 10 ng/ml respectively.

Table 2

Serum PSA Reference Range ng/ml	Sensitivity %	Specificity %	Positive Predictive Value	Negative Predictive Value
≥4	100	53.47	30.93	98.72
≥10	96.77	82.64	54.55	99.17

By taking cut off reference value of '4', the sensitivity was 100% but specificity was only 53.47%. However, with cut off reference value of '10', the sensitivity fell to 96.77% but specificity and positive predictive value rose to 82.64% and 54.55 respectively.

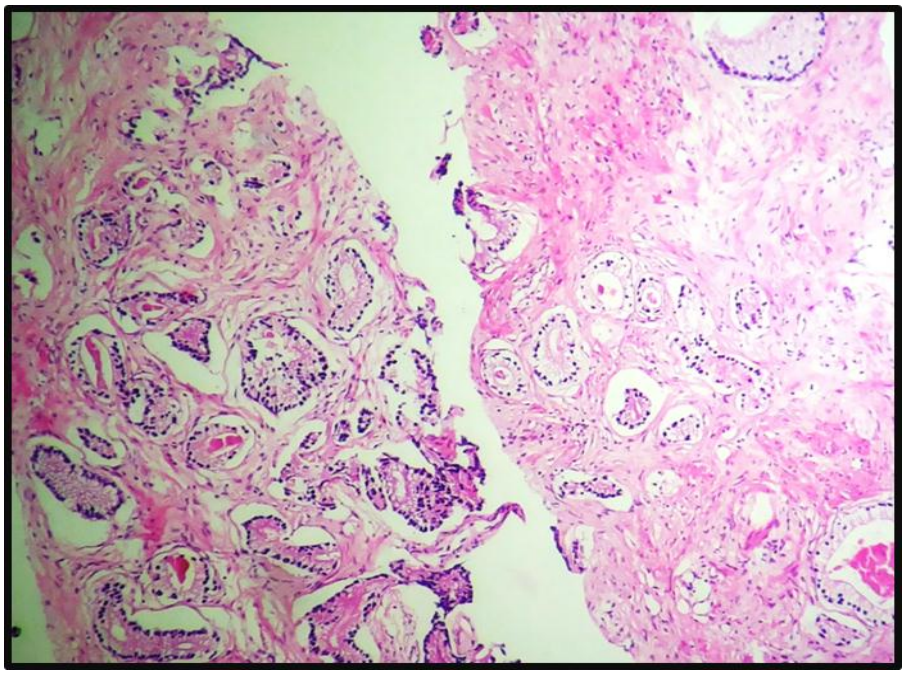

Figure 5: Photomicrograph of showing moderately differentiating adenocarcinoma of prostate. Gleason's score 3+3=6(H&E x100).

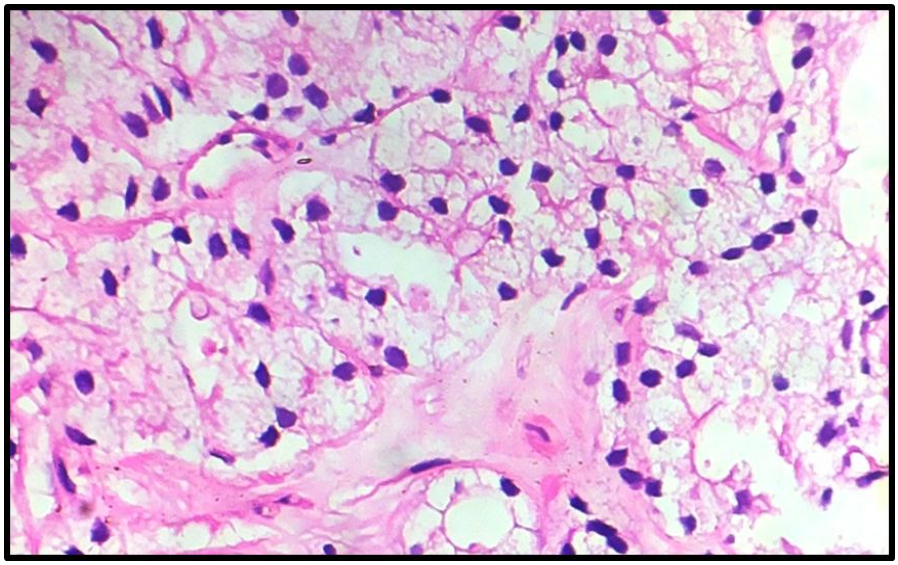

Figure 6: Photomicrograph of showing moderate to poorly differentiating adenocarcinoma of prostate. Gleason's score 4+3=7(H&E x100).

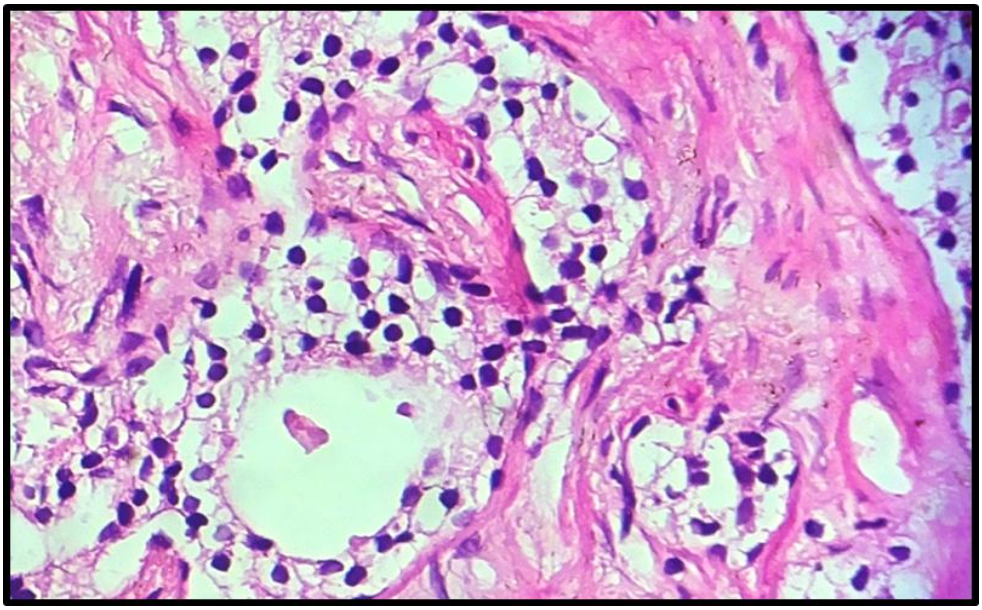

Figure 7: Photomicrograph of showing poorly differentiating adenocarcinoma of prostate. Gleason's score 4+4=8(H&E x400).

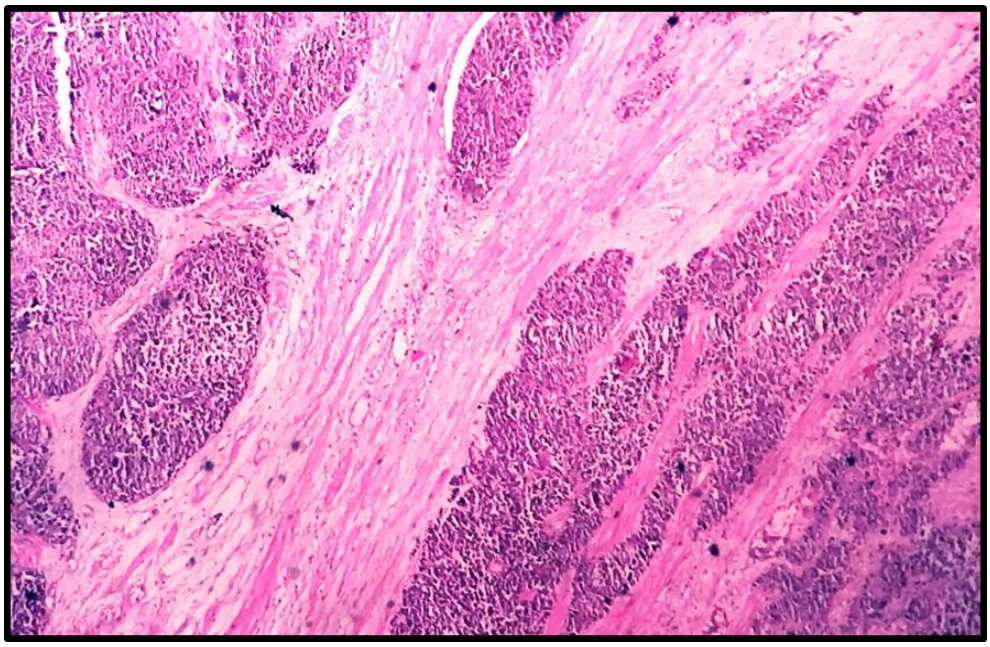

Figure 8: Photomicrograph of showing poorly differentiating adenocarcinoma of prostate. Gleason's score 5+4=9 (H&E x100).

DISCUSSION

The prostatic carcinoma is the most common cancer among elderly men. By the fifth decade of life, 14% of the male population suffer from carcinoma of the prostate, the incidence rises with increasing age.

The patients with prostatic carcinoma were in age group of 61-70 (40.74%), followed by age group of 71-80 (37.04%) with mean age of 71.41 years. The results were compared to the study done by William et al,[7] were majority of carcinoma cases were in the age group of 70-79 years, and study done by Ronimel et al,[8] 39% malignant lesions were between 75-79 years. The finding of both the studies were consistent with our study.

Out of 27 patients of adenocarcinoma, majority 20(74.07%) were having a Gleason's score of 5 – 7. Our results were comparable with the studies conducted by Chiusa L et al[9] (67.7%), Petrescu A et al,[10] (56.6%) and Jackson LA et al 114(69.68%) who have reported majority of cases with Gleason's score of 5 – 7. On the contrary, Madani SH et al[11] (51%), Shirley SE et al[12] (60%) who have reported majority with Gleason's score of 8 – 10.

Serum prostate specific antigen (PSA) is currently the most popular marker of prostatic disease and pathological states.

Normal levels of PSA are usually <4ng/ml but they vary according to the age of the patient. PSA is elevated by any change that destroys the normal architecture of the prostate which allows its diffusion into the microvascular circulation.[13] Thus elevated serum PSA levels are observed in conditions such as prostatitis, prostatic infarcts and benign prostatic hyperplasia though the most clinically important elevations are seen in adenocarcinoma of the prostate.

In our study, all patients with adenocarcinoma had serum PSA levels more than 10ng/ml. 88.89% of the patient had serum PSA levels > 20 ng/ml, 8 patients had serum PSA levels > 100 ng/ml. Median for serum PSA levels were 49.9 ng /ml & P – value < 0.001. It revealed a statistically significant correlation between serum PSA and adenocarcinoma. These findings were consistent with the study conducted by Berman JJ et al.[14]

In our study out of 27 patients of adenocarcinoma, 8(30%) had PSA >100 ng/ml, had increased Gleason score. Anunobi et al,[15] reported PSA levels above 50 ng/ml were only present in malignant cases which was also seen in our study. Anderson-Jackson et al,[16] study 423 patient and diagnosed 191 with adenocarcinoma. They observed comparative increased PSA levels with increased Gleason score.

Tayib et al,[17] observed that when PSA was elevated to 4-10 ng/ ml TRUS guided biopsy detected cancer in 21.4%, while elevation of PSA to 10-20 ng/ml lead to cancer detection in 40% of the patients, and when PSA was above 20 ng/ ml all cases were positive for cancer. In our study, patients diagnosed with cancer none had PSA less than 10 ng/ml, while 11.11% had PSA in range of 10-20 ng/ml and rest all of the patients had PSA above 20ng/ml.

In our study for detection of adenocarcinoma, sensitivity and specificity of this assay was determined by using reference values of 4 and 10 ng/ml. With reference value of '4' ng/ml, sensitivity of 100% was achieved but specificity was only 53.47%. However, with reference value of 10 ng/ml, the sensitivity of 96.77% was achieved and specificity and positive predictive value rose to 82.64% and 54.55 respectively.

CONCLUSION

For detection of prostatic malignancy by serum PSA, the specificity and positive predictive value increases by raising the cut off level from 4 ng/ml to 10 ng/ml. It was observed that the levels of serum PSA increased with increasing Gleason grade and score of the tumour.

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