The Professional Medical Journal
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ORIGINAL PROF-2702

PROSTATIC CARCINOMA;

ASSOCIATION BETWEEN SERUM PROSTATIC SPECIFIC ANTIGEN (PSA) AND GLEASON GRADE

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Article received on:
13/11/2014
Accepted for publication:
23/12/2014
Received after proof reading:
02/06/2015

ABSTRACT… Introduction: During the past many years the availability of serum PSA as a screening marker, has encouraged its use to diagnose both prostatic cancer and its recurrence. Patients with high S/PSA are at increased risk of advanced carcinoma prostate and screening at an earlier stage would help to manage it accordingly. The aim of this study was to determine association between serum prostatic specific antigen (PSA) levels and Gleason grade in prostatic carcinoma patients. **Study Design:** Descriptive, case series study. **Setting:** Department of Urology & Renal Transplantation in collaboration with Institutional laboratory of Bahawal Victoria Hospital, Bahawalpur. **Period:** June 2012 to June 2014. **Materials & Methods:** Total 160 patients of age 50-80 years with biopsy proven prostatic carcinoma were included. Patients with h/o radiotherapy for prostatic carcinoma and anti-androgen therapy were excluded. Histological slides of each patient were reviewed by using the Gleason grading system. Gleason grade of each patient was correlated with his serum prostatic specific antigen (PSA) report which was done before surgery or biopsy. **Results:** In our study, mean age was 66.89 ± 9.28 years. Mean serum PSA was 21.41 ± 13.67 ng/ml. Intermediate grade cancer was found in 38.75% patients followed by moderate to poorly differentiated cancer in 31.86% patients. Gleason score ≥7 was significantly higher in patients with serum PSA >20 ng/mL than those with serum PSA ≤ 20 ng/mL (p-value of 0.000). So, serum PSA was positively correlated with gleason grade (OR = 3.67, CI = 95%, P = 0.0001) **Conclusion:** This study concluded that there is statistically significant association between serum prostatic specific antigen (PSA) levels and Gleason grade in prostatic carcinoma patients and patients with high prostate specific antigen are at increased risk of advanced carcinoma prostate.

Key words: Advanced carcinoma, well differentiated, screening test, grading system, gleason score, correlation.

Article Citation: Rasool M, Iqbal SA, Pansota MS, Tabassum SA, Ahmad I. Prostatic carcinoma; association between serum prostatic specific antigen (PSA) and gleason grade. Professional Med J 2015;22(6):710-714.

INTRODUCTION

Prostate cancer is the most common cancer in males and the 2nd most common cause of cancer deaths in men, with an estimated 41,000 deaths and more than 125,000 new cases per year.[1,2] Although, the incidence of prostate cancer is low in Pakistan with a figure of 3.8% in our population but is the 2nd most common malignancy after lung cancer. The most reason for this incidence may be lower life expectancy and no screening for prostate cancer in Pakistan.[3] No clear causative factors have been identified for prostate cancer, although a familial predisposition has been demonstrated, and a strong association has been found with high fat diet and cigarette smoking.[4]

Nowadays, different protocols and screening tests are in practice for early detection of prostate cancer. Digital Rectal Examination, screening by serum Prostate Specific Antigen (PSA) and Transrectal Ultrasonography (TRUS) are the most commonly implied methods for its diagnosis.[5] Serum prostate specific antigen (PSA) has been used commonly for last many years as an acceptable screening marker for diagnosing both prostatic cancer and its recurrence. The serum prostate-specific antigen screening has shown a significant increase in the detection of prostate cancer.[6]

There is significantly a positive correlation has been found between serum PSA and Gleason grade. In a study, it was found that serum

PSA levels goes on increasing as the stage of disease progresses.[7] It is seen that the higher the Gleason score, the higher the possibility of tumor to invade into the surrounding tissues.[8] Therefore, the essential objective of screening for prostate cancer is detection of disease when it is localized and thus at curable stage before the cancer reaches to the bones where the success of treatment is only temporary.[9] Patients with high prostate specific antigen are at an increased risk of advanced carcinoma prostate and screening at an earlier stage would help to manage it accordingly, so morbidity and mortality of these patients could be reduced. The aim of this study was to determine association between serum prostatic specific antigen (PSA) levels and Gleason grade in prostatic carcinoma patients.

PATIENTS AND METHODS

After approval from the hospital ethical committee, this descriptive, case series study was done in the Department of Urology & Renal Transplantation in collaboration with Institutional laboratory of Bahawal Victoria Hospital, Bahawalpur from June 2012 to June 2014. Total 160 patients of age 50-80 years with biopsy proven prostatic carcinoma were included. Patients with h/o radiotherapy for prostatic carcinoma and anti-androgen therapy were excluded. Histological slides of each patient were reviewed by using the Gleason grading system. According to Gleason grading system growth patterns are described as: pattern 1 & 2: well circumscribed nodules of closely packed small acini, pattern 3: presented as single small infiltrating glands with wide stromal separation, pattern 4: displayed cribriform, fused small acinar or poorly formed glands and pattern 5: showed sheets, cords, single cells or comedocarcinoma.

The gleason score was calculated by summing up the predominant pattern and the second most common pattern and combined into four groups i.e. a score of 2-4 indicates a well differentiated cancer; a score of 5-6 indicates an intermediate grade cancer; a score of 7 indicates a moderate to poorly differentiated cancer; a score of 8-10 indicates a high grade cancer. This Gleason grade of each patient was correlated with his serum prostatic specific antigen (PSA) report which was done before surgery or biopsy. Collected data was analyzed through computer software SPSS 20.0. Mean and standard deviation were calculated for quantitative variables. Frequency and percentage was calculated for qualitative variables. Odds ratio was calculated to determine the association between serum PSA and Gleason grade. Odds Ratio >1 was considered as significant.

RESULTS

Mean age was 66.89 ± 9.28 years with majority (55.63%) of patients were within 60 to 70 years age. Mean serum PSA was 21.41 ± 13.67 ng/ml and %age of patients with different PSA ranges have shown in Table-I. Mean Gleason score was 6.33 ± 2.19. Majority of patients i.e. 62 (38.75%), had intermediate grade cancer followed by moderate to poorly differentiated cancer in 51 (31.86%) patients. Well differentiated cancer was found in only 17 (10.63%) patients while remaining 30 (18.75%) had shown high grade cancer. Gleason score ≥7 was significantly higher in patients with serum PSA >20 ng/mL than those with serum PSA ≤ 20 ng/mL with p-value of 0.000 which was statistically significant (Table-II). So, serum PSA was positively correlated with gleason grade (OR = 3.67, CI = 95%, P = 0.0001).

S/PSA (ng/ml)	No. of patients	%age
< 4.0	11	6.88
4-10	22	13.75
11-20	51	31.88
>20	76	47.5

Table-I. %age of patients with Serum PSA Levels.

Gleason Grade (score)	S/PSA Levels (ng/ml)			
	<4.0	4-10	11-20	>20
Grade 1: Well differentiated **(2-4)**	05	07	04	01
Grade 2: Intermediate grade **(5-6)**	04	09	25	24
Grade 3: Moderate to poorly differentiated **(7)**	02	05	14	30
Grade 4: High grade cancer **(8-10)**	00	01	08	21

Table-II. Relationship between Serum PSA levels and Gleason Grade

DISCUSSIONS

The main objective of early screening of prostate cancer is to diagnose it when it is confined to its limits and not spread to the bones where the treatment results are very poor.[10] Thus serum prostate specific antigen (PSA) has been accepted widely such a test for early detection of CaP with 70% sensitivity.[11] There has been considerable debate about the potential merits of a PSA-based screening programme, but there is little evidence at present to suggest that screening meets the World Health Organization (WHO) criteria for screening.[11] Over the last decade the use of Prostate Specific Antigen to test for carcinoma prostate has become common (normal values 0–4ng/ml). This study was conducted to see the association between S/PSA and gleason grade in prostatis carcinoma patients.

The mean age of patients in our study was 66.89 ± 9.28 years which was very much comparable to studies of Khan IA et al[12] and Rasool M et al[2] who had a mean age of 64 and 65 years respectively. On the other hand, Anwar F et al[13] had found mean age of 69 years in his study which is much larger compared to our study. Our study has also shown that majority of patients were between sixth decade. These results coincide with many previous publications in which also show high incidence of carcinoma prostate in sixth and seventh decade of life.[2,12-14]

Traditionally, prostate biopsy has been recommended when S/PSA value is >4.0 ng/ml. It was found in a study that cancer has spread beyond the surgical margins or extraprostatic tissue in almost 33% patients with S/PSA between 4 to 10 ng/mL and more than 50% with S/PSA >10 ng/mL.[15] In our study, we have found a positive association between serum PSA and gleason grade (OR = 3.67, CI = 95%, P = 0.0001). It was seen that Gleason score ≥7 was significantly higher in patients with serum PSA >20 ng/mL than those with serum PSA ≤ 20 ng/mL with p-value of 0.000 which was statistically significant. Similarly, Fang YQ et al[8] in his study has found the positive correlation between preoperative serum PSA and postoperative Gleason score (rs=0.279, P=0.015). He concluded that high serum PSA is associated with high gleason score.

In a study done by Freedl and SJ et al[16] also showed that high preoperative PSA level predicted high cancer grade and patients with high preoperative PSA level were more likely to have extraprostatic diseases. Gleason score increases as the prostatic carcinoma progresses because of disorganized gland growth, deformed glandular activity and reduction of matrix components. This results in serum PSA secretion from the cancer cells and leads to elevation of serum PSA levels.[8] It was also seen in previous studies that leakage of PSA into blood increases with increase microvessel density in prostatic carcinoma which is also a cause of positive correlation of serum PSA level with gleason grade.[17]

Okolo CA et al[18] had also found the statistically significant positive correlation between increasing serum PSA levels and gleason score and concluded that serum PSA is significantly higher in metastatic than in localized prostatic carcinoma. Partin AW et al[19] in a study on 703 men with localized prostatic carcinoma has studies their serum PSA levels and found that only 1% patients had serum PSA >50μg/l while 99% had <50μg/l. PSA improves detection of clinically important tumors without significantly increasing the detection of unimportant tumors, most PSA-detected tumors are curable, prostate cancer mortality is declining in regions where screening is done and curative treatments are available.[20] The routine use of PSA testing has had a profound effect on the management of the disease.[20,21] Furthermore, routine use of serum PSA on follow up can also help to detect recurrence of disease in these patients and take management accordingly to prolong their survival.

CONCLUSIONS

Our study concluded that there is statistically significant association between serum prostatic specific antigen (PSA) levels and Gleason grade in prostatic carcinoma patients and patients with high prostate specific antigen are at increased risk of advanced carcinoma prostate. So, we

recommend that serial monitoring of serum PSA should be done in patients with enlarged prostate for screening of carcinoma at an earlier stage and also on follow up for detection of recurrence which would help to manage it accordingly in order to reduce the morbidity and mortality of these patients.

REFERENCES

1. Jemal A, Center MM, DeSantis C, Ward EM. **Global patterns of cancer incidence and mortality rates and trends.** Cancer epidemiology, biomarkers & prevention. Am Assoc Cancer Res. 2010;19(8):1893-907.
2. Rasool M, Pansota MS, Tabassum SA, Saleem MS. **Frequency of carcinoma of prostate in clinically benign prostatic hyperplasia and role of different screening tests.** Pak Armed Forces Med J. 2012;62(3):431-34.
3. Aziz Z, Sana S, Saeed S, Akram M. **Institution based tumor registry from Punjab: five year data based analysis.** J Pak Med Assoc. 2003;53(8):350-3.
4. Schultz C, Meier M, Schmid HP. **Nutrition, dietary supplements and adenocarcinoma of the prostate.** Maturitas. 2011;70(4):339-42.
5. Adhyam M, Gupta AK. **A Review on the Clinical Utility of PSA in Cancer Prostate.** Indian J Surg Oncol. 2012;3(2):120-9.
6. Rosario DJ, Lane JA, Metcalfe C, Donovan JL, Doble A. **Short term outcomes of prostate biopsy in men tested for cancer by prostate specific antigen: prospective evaluation within ProtecT study.** *Br Med J.* 2012;344:d7894.
7. Anderson-Jackson L, McGrowder DA, Alexander-Lindo R. **Prostate specific antigen and Gleason score in men with prostate cancer at a private diagnostic radiology centre in Western Jamaica.** Asian Pac J Cancer Prevent. 2012;13(4):1453-6.
8. Fang YQ, Zhou XF, Qiu JG, Wen XQ, Wang DJ, Pang J, et al. **Serum psa level and gleason scores of needle biopsy specimens predict the postoperative pathologic grade of prostate cancer.** Acta Medica. 2013;29:279.
9. Walsh PC, De Weese TL, Eisenberger M A. **Localized Prostate Cancer.** New Engl J Med. 2007;357(26):2696–705.
10. Umbehr M, Kesseler TM, Sulser T, Prococ KG. **The prostate cancer outcomes cohort study.** BMC Urology. 2008;8(9):2490–9.
11. Macfarlane, Michael T: **Prostate Cancer.** Urology, 4th Edition: Lippincott William & Wilkins 2006; 22: 145-155.
12. Khan IA, Nasir M, Akbar M, Khattak ID, Khan AM, Jan A, et al. **Carcinoma of Prostate in Clinically Benign Enlarged Gland.** J Ayub Med Coll Abottabad. 2008:20(2):90-2.
13. Anwar F, Mohayuddin QN, Islam M, Aasim M, Riaz M, Khan A. **Cancer in Patients Undergoing Trans Urethral Resection of Prostate (TURP) for clinically benign Symptomatic Enlarged Prostate.** J Postgrad Med Inst. 2012;26(4):428-31.
14. Ries LAG, Eisner MP, Kosary CL. SEER Cancer Statistics Review, 1975-2001, Bethesda, Md: National Cancer Institute; 2008.
15. Leite KR, Srougi M, Dall'Oglio MF, Sanudo A, Camara-Lopes LH. **Histopathological findings in extended prostate biopsy with PSA < or = 4 ng/mL.** International Braz J Urol. 2008;34(3):283-90.
16. Freedland SJ, Mangold LA, Walsh PC, Partin AW. **The prostatic specific antigen era is alive and well: prostatic specific antigen and biochemical progression following radical prostatectomy.** J Urol. 2005;174:1276-81.
17. Gravdal K, Halvorsen OJ, Haukaas SA, Akslen LA. **Expression of bFGF/FGFR-1 and vascular proliferation related to clinicopathologic features and tumor progress in localized prostate cancer.** Virchows Arch. 2006;448:68-74.
18. Okolo CA, Akinosun OM, Shittu OB, Olapade-Olaopa EO, Okeke LI, Akan EEU, et al**. Cooreelation of serum PSA and gleason score in Nigerian men with prostate cancer.** Afr J Urol. 2008;14(1):15-22.
19. Partin AW, Yoo J, Carter HB, Pearson JD, Chan DW, Epstein JI, et al. **The use of prostate specific antigen, clinical stage and gleason score to predict pathological stage in men with localized prostate cancer.** J Urol. 1993;150(1):110-4.
20. Gelmann E P. **Complexities of Prostate _cancer risk.** New Engl J Med 2008; 358(9):96.
21. Walsh P C, De Weese TL, Eisenberger M A. **Localized Prostate Cancer.** New Engl J Med 2007; 357(26): 2696–705.
22. Efstathiou JA, Chen MH, Catalona WJ, Mcleod DG, Carroll PR, Moul JW, et al. **Prostate specific antigen based serial screening may decrease prostate cancer specific mortality.** Urol. 2006;68(2):342-7.

"An essential aspect of creativity is not being afraid to fail."

Edwin Land

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
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