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Research Article

Relationship between Serum Prostate Specific Antigen (PSA) and Gleason Score in Patients Diagnosed with Prostate Cancer. A Hospital Based Study

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Abstract: Adenocarcinoma of the prostate has been known as a disease of the aging males. It is commonly diagnosed in the industrialized countries and becoming an increasing burden in the developing countries because of increasing health awareness and life expectancy. Diagnosis is made by digital rectal examination (DRE) of the prostate for malignant features beside an elevated prostate specific antigen (PSA) and positive prostate biopsy results on histology. Gleason score derived by adding the two (2) predominant histologic patterns helps in prognostication of individual patients. In this study, we retrospectively studied the relationship (correlation) between serum PSA and Gleason Score (GS) in Prostate Cancer (PCa) Patients. One hundred and ten (110) patients diagnosed with Pca between January 2016 and December 2017 were studied. Their case notes from the health records department were retrieved and data collected together with their histopathology reports of prostate biopsy from the pathology records department. Pre-biopsy PSA were correlated with Gleason score. Results showed that majority of the men presented with a serum PSA >50ng/ml with a corresponding high Gleason Score (Gs of 9). PSA also correlated positively with Gleason Score. Therefore patients with high PSA may likely harbor tumours with high Gleason scores indicating poor prognosis.

Keywords: Prostate specific antigen, Gleason Score, Prostate cancer.

INTRODUCTION

The prostate gland can be a site for both benign and malignant lesions. Adenocarcinoma of the prostate is a malignant tumor most commonly diagnosed in the industrialized countries[1] and becoming an increasing burden in the developing countries due to increasing health awareness and life expectancy.[2] Risk factors considered non-modifiable include race, family history and age[3,4] while lifestyle such as physical inactivity, eating habit; for instance increased intake of dietary fat are modifiable risk factors involved in the pathogenesis of prostate cancer.[5] It is said to be a silent disease until quite advanced in its evolution. DRE of the prostate may suggest Pca and in conjunction with elevated serum PSA assay will give a stronger suspicion. Prostate biopsy and histological examination of the cells will ultimately confirm the diagnosis based on cellular architectural disturbances. The level of cellular differentiation is normally graded according to the Gleason system using the primary and secondary patterns to form the Score ranging from 2 to 10. Grading of Pca is further classified as well differentiated when the score is between 2 and 4, moderately differentiated with scores of between 5 and 7 and poorly differentiated when the score is $\geq$ 8. Prognostically, Gleason Scores of 2 to 6 are considered favourable while Gleason scores of 7 to 10 are considered non-favourable associated with high mortality rate.[6]

PSA has been noted, as the best circulating tumor marker in oncology,[7] which has been widely used for screening, diagnosis, staging and monitoring of Pca. It is secreted by the ductal epithelial cells of the prostate and serum levels beyond 4.0ng/ml has been noted by many authors to represent abnormal values.[8] However, it is noteworthy that other benign lesions and procedures can also raise PSA above this level, notably benign prostatic hyperplasia, acute and chronic prostatitis, urinary tract infection, Urethral instrumentation, prostate biopsy and ejaculation.[9] Some authors had noted that higher grade tumors produce less PSA per cell than lower grade tumours, however, the high PSA levels in the former compared to the latter group of cancers are due to large size and more advanced tumour stage.[10] Studies have also shown a direct relationship between serum PSA and Gleason

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Score in Pca patients.[10,11] In this study, we also set out to investigate such relationship in our cohort of patients. This can enhance prediction of tumour pathologic grade and stage using serum PSA assay.

MATERIALS AND METHOD

This was a retrospective study of 110 men who were diagnosed of prostate cancer. The study period was between January, 2016 and December, 2017. A search was made in the medical records department for all case notes of these patients. The inclusion criteria were as follows: All patients with histologically confirmed prostate cancer on biopsy with well documented Gleason grades and scores, also a pre-biopsy PSA. Patients without these information were excluded from the study. Data obtained were entered into Microsoft office excel and analyzed using statistical package for Social Sciences (SPSS) Version 20.0 software. Frequencies were determined for categorized variables, continuous variables were summarized using means and standard deviations. Cross tabulation of variables were also generated. Pearson correlation coefficient was employed to test the relationship between PSA and Gleason Score. The level of statistical Significance was set at $\leq$0.05. Results were presented using tables and figures. The findings were compared with similar studies done locally and internationally.

RESULTS

Table 1 illustrates Descriptive Statistics for the variables. The mean age was 68.22$\pm$ 9.18 years ranging from 48 to 93years. Figure 1 shows that most of the patients presented in their eighth (8^{th}) decade of life. Majority of them (46.4%) had a PSA of >50ng/ml (Table 2). 60% of the patients presented with poorly differentiated tumour (GS 8-10), followed by a GS of between 5-7 (38.2%) and few patients (1.8%) had well differentiated tumours (GS 2-4) (Table 3). In fig 2, Modal GS was 9 (32.7%) followed by 7 (25.5%). Table 4 shows cross-tabulation between PSA and Gleason Score. PSA increases as Gleason Score increases. There was a statistically significant positive correlation between serum PSA and Gleason Score (r=.246, P<.05), PSA and P_1 (r=.240, P<.05), PSA and Gleason Score severity (r= 207, P<.05) and no correlation between PSA and P_2 (r=.081, P<.398).

DISCUSSION

Adenocarcinoma of the prostate is a disease of the middle aged and elderly males being rare below the age of 50 years.[12] In Nigeria, it is the most common cancer in males and the trend is increasing because of increasing life expectancy and health awareness.[13,14] PSA had been recognized as the best circulating tumour marker in oncology, widely used for the diagnosis, staging, monitoring treatment outcomes and as a general prognostic factor for PCa patient.[7] With generally reported low specificity, it has a high sensitivity for clinical use.[9] Serum PSA measurement is rapid, cheap and minimally invasive. It was first indentified and purified by Wang et al[15] in 1979. Seamonds B. et al[16] reported its superiority over Prostatic acid phosphatase in prostate cancer detection and in monitoring response to therapy. In most population studies, PSA correlates fairly well with tumour volume.[17] DF Gleason[9] in 1966 proposed the grading system of prostate cancer histology and has been the most acceptable means of prognosticating Pca patients. This system is based on cellular architectural pattern of the tumour. The Gleason Score is arrived by adding the two most predominant grades. Higher scores are associated with higher mortality rates.[6] Gleason score in combination with local extent of the disease by DRE together with serum PSA can be used to accurately stage prostate cancer. Clinically, staging tools are the American Joint Committee on Cancer (AJCC) and the Whitmore –Jewett Clinical staging systems.

In this study, the mean age of the patients was 68.22 $\pm$ 9.18 years. Similar mean age has been reported in Nigerian[10,11] and Jamaican[19] men treated for prostate cancer. In the two Nigerian Studies,[10,11] majority of their men were in their 7^{th} decade of life and in agreement with previous studies done in this centre.[20,21] We reviewed men who were mostly in their 8^{th} decade of life, this was also documented in the Jamaican Study.[19] A shift to the next decade of life in the present study is difficult to explain but could be due to retrieval or selection bias being a retrospective study coupled with an increasing life expectancy. No patient was seen below the age of 40years in this study, contrary to other studies in Nigerian men. Abubakar M. et al[11] in Zaria reported 0.8%, same small but significant values in this age group were documented by Ekwere PD et al[22] and Sakr et al[23] respectively in South Eastern Nigeria and Young American men. We think that this population of patients may have adhered strictly to screening programmes for younger men leading to early detection of Pca. In our locality, the programme is ongoing but ignorance and superstition are in the background significantly stalling commendable outcome.

We documented a mean serum PSA of 55.31 $\pm$38.56ng/ml (Table 1). In another study in Northern Nigerian (Sokoto) men with Pca and similar mean age group, the mean serum PSA was 45.48$\pm$ 32.39 ng/ml. There are comparable values from other centers in Nigeria who also evaluated Pca patients; Ahmed et al[24] in Northern part of the country (Zaira), Odubanjo et al[25] in the West (Lagos). A study of Pakistani men by Rasool et al[26] and Moul et al[27] among the whites in USA revealed significantly lower mean PSA values. This reveals a sharp contrast among mean of different races, ethnic and geographical location as these factors are known to influence the growth, development and progression of Pca[28]. However, across board, several co-existing factors can also elevate PSA different from

malignant conditions.[10] Our study being retrospective, we could not effectively eliminate sub-clinical prostatitis and even coexisting BPH. No patient was seen with a PSA <4ng/ml, similar to another work in Northern part of the country.[11] In two other Nigerian studies, 2% and 3% of the population had PSA <4ng/ml respectively of Ekwere PD et al [22] and Odubanjo et al.[25] Possible explanation is that, most urologists do not subject their patients to prostate biopsy with PSA results below this value unless strongly indicated by DRE and trans-rectal ultrasound scan findings.

Majority of our patients (46.4%) had serum PSA of > 50ng/ml (Table 2). In a similar work by Abubakar M et al,[11] 37.4% of their men had similar results. Inferred from this level of PSA, our patients were likely harboring poorly differentiated tumors. High PSA had been reported in high grade Pca by reason of size and advanced stage.[29] PSA of $\geq$ 50ng/ml was also associated with a Gleason Score of 9 (Table 5) which also supports poorly differentiated tumours with associated higher mortality rate.

We recorded a men Gleason score of 7.85 $\pm$1.19 (Table 1) and a modal Gleason score of 9. This shows that the distribution was skewed towards higher Gleason scores and hence poorly differentiated tumours. In other Nigerian studies, [10,11,22,25] Gleason score of 8 was the commonest which still reflects poorly differentiated condition with worse prognosis. Two (2) Jamaican studies, [19,30] documented majority of their men with Gleason score of 6 representing well differentiated tumours and better prognosis. This underscores the influence of environmental factors as they affect prostate cancer development and differentiation as majority of these patients were of African descent.

Correlation between PSA and Gleason score was positive and statistically significant (r=.246, P<.05). Comparable report was documented by Abubakar M et al[11] (r=.149, P =.031). It follows that PSA as a strong variable in Pca evaluation and in combination with Gleason score can effectively define patient's clinical outcome.

Limitations: This study being retrospective, we could not completely role out co-existence of other conditions that could have falsely raised serum PSA. Again, being a hospital based study, we may have been dealing with merely advanced tumours with comparatively larger sizes hence the higher PSA values. However, this study is very informative and critical to patients management in our locality where majority of them may likely present with poorly differentiated tumours necessitating aggressive protocol of care.

CONCLUSION

Prostate cancer evaluation demands the use of DRE, PSA and Gleason Score by biopsy. PSA correlated with Gleason score in this study. Majority of the patients had serum PSA in excess of 50ng/ml with a corresponding high Gleason grade and Score reflecting poorly differentiated tumours. The level of differentiation of Pca is critical in determining prognostic status of the patient and the poorly differentiated a tumour is the worse the prognosis. From this study, we gather that majority of our men diagnosed of Pca may harbor poorly differentiated tumours and so a high index of suspicion is expected when new cases with symptoms and signs of Pca are evaluated to attract aggressive management protocols especially in early or localized disease.

Table1: Descriptive Statistics

Variables	Mean	Median	Mode	Min.	Max.
Age	68.22 $\pm$9.18	68.50	65	48	93
PSA	55.31 $\pm$38.56	47.80	8.43	6.90	185.70
GS	7.85$\pm$1.19	8.00	9	5	10
P_1	4.04$\pm$.97	4.00	5	1	5
P_2	3.82$\pm$.73	4.00	4	3	5

Table 2: PSA Categories

PSA (ng/ml)	Frequency(n)	Valid Percent	Cumulative percent
4-10	5	4.5	4.5
>10-20	20	18.2	22.7
>20-30	10	9.1	31.8
>30-40	9	8.2	40.0
>40-50	15	13.6	53.6
>50	51	46.4	100.0
Total	110	100.0	

Table 3: Gleason Score: Levels Of Differentiation

Gleason Score	Frequency(n)	Valid Percent	Cumulative percent
2-4 (well differentiated)	2	1.8	1.8
5-7 (moderately differentiated)	42	38.2	40.0
8-10 (poorly differentiated)	66	60.0	100.0
Total	110	100.0	

Table 4: Cross-Tabulation between PSA Categories and Gleason Scores:

PSA Categories		Gleason scores						
		5	**6**	**7**	**8**	**9**	**10**	**Total**
4-10		0	2	1	1	1	0	5
>10-20	1	3	6	7	2	1	20	
>20-30	0	1	3	3	3	0	10	
>30-40	0	1	3	1	3	1	9	
>40-50	0	5	5	1	3	1	15	
>50		1	2	10	12	24	2	51
Total		2	14	28	25	36	5	110

Table 5: Correlations:

	Pearson Correlation Coefficients	**P Values**
PSA/Gleason Score (GS)	.246	.010*
PSA/GS severity	.207	.030*
PSA/P_1	.240	.011*
PSA/P_2	.081	.398

*Correlation is significant at P<.05 (2-tailed).

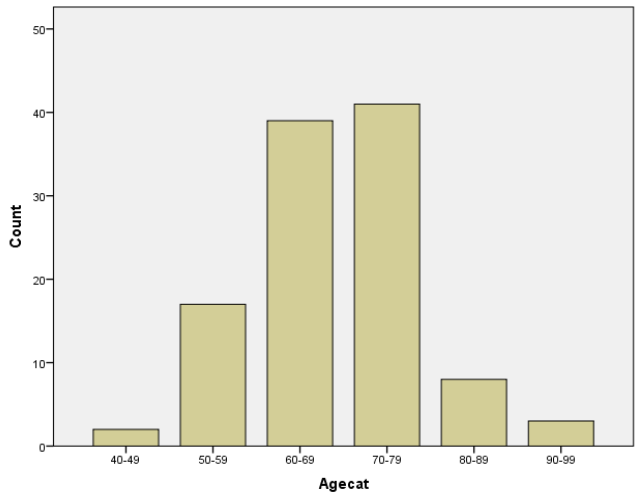

Fig. 1: Age of Patients in Decades

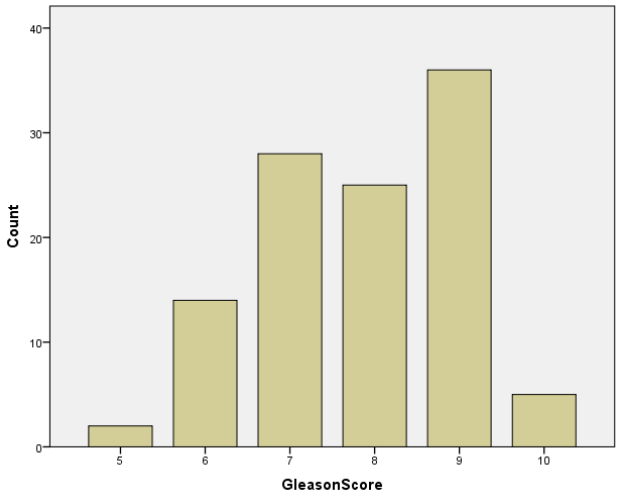

Fig.2 : Frequency of Gleason Score

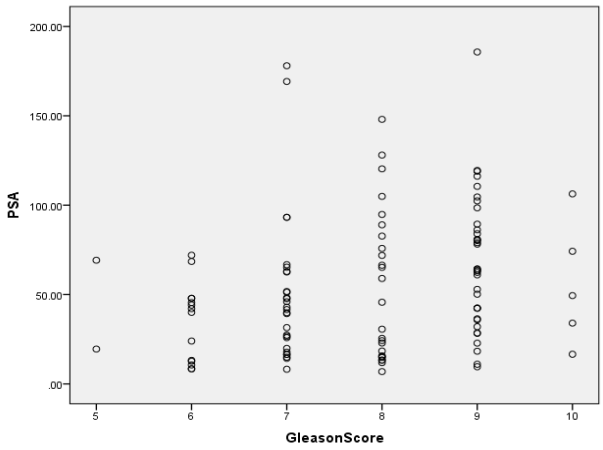

Fig. 3: Scatter Plot between PSA and Gleason Score

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