# Adenocarcinoma of the Prostate: Correlation between Serum Prostate-Specific Antigen and Gleason Grade Group

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## Abstract

**Introduction:** Serum prostatic-specific antigen (PSA) concentration determination has established itself as the leading tool in screening for, as well as in estimating the prognosis of, adenocarcinoma of the prostate. This prognostication is usually done in conjunction with the Gleason score and other prognostic indices. The aim of this study was to determine the association between serum PSA concentration and the new (2016 modified) Gleason grade group of tumor among patients with adenocarcinoma of the prostate. **Study Design:** A retrospective, analytic study. **Study Setting:** Department of Pathology, Ahmadu Bello University Teaching Hospital, Zaria. **Study Period:** January 2006 to December 2013. **Materials and Methods:** A total of 211 patients with biopsy-based diagnosis of adenocarcinoma of the prostate were studied. Each of the cases was graded using the (2016 modified) Gleason grading system. Prebiopsy serum PSA concentration in each of the patients was retrieved from either the patient's case records in the Urology Unit of the hospital or from the values filled in by the requesting surgeon. Gleason grade groups of patients were correlated with serum PSA concentration. **Results:** Gleason grade group 1 was most common in our study with 68 (32.2%) of our patients falling within that category. The study revealed a statistically significant relationship between the serum PSA concentration and the Gleason grade group of cancer ($P = 0.00$). **Conclusion:** This study concluded that the serum PSA concentration has a statistically significant association with the Gleason grade group of the tumor in prostatic adenocarcinoma patients. Therefore, patients with high serum PSA concentrations are likely to have high tumor grade group.

**Keywords:** Adenocarcinoma, correlation, Gleason grade group, prostate-specific antigen

## INTRODUCTION

Prostate cancer (PCa) is an important cause of morbidity and mortality worldwide. It is the fifth most common cancer globally and second most common in men.[1]

In Nigeria, PCa is the most common cancer among males,[2] accounting for 6.1%–19.5% of all cancers and the incidence is increasing.[3] A peculiar finding in our setting is that most patients present with a high-grade tumor, resulting in high morbidity and mortality.[4]

In the United States of America, the National Cancer Institute Surveillance Epidemiology and End Results review estimated about 241,740 new cases of PCa to be diagnosed in 2012.[5] The estimated PCa attributable mortality for the same year was 28,170.

Determination of serum prostate-specific antigen (PSA) concentration and estimation of the degree of tumor differentiation (using Gleason grading system) are two important parameters that have found relevance over time in patients with PCa.[6]

Estimation of serum PSA concentration is being used both as a marker in screening for the disease and as a reasonably accurate correlate with other important parameters such as the grade and stage of cancer.[7,8]

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The most acceptable grading system for PCa is the one proposed by DF Gleason in 1966.[9] This system is based on tumor architectural patterns and is arrived at by assigning two grades to the two most common architectural patterns and reported as the Gleason score (GS).

However, the management of PCa has changed since the original system was proposed and pathologists felt a need for a modification of the original Gleason system to reflect modern practice.[10] This resulted in changes in the Gleason grading system by the International Society of Urological Pathology (ISUP) consensus conferences in 2005 and 2014.[11]

The new Gleason grade group system, which is a modification of the original Gleason scoring system, was first described in a 2013 paper in BJU International.[12] In 2014, the ISUP consensus conference endorsed the grade group system and proposed its adoption in a 2016 report published in the American Journal of Surgical Pathology.[13] Furthermore, the World Health Organization accepted it for inclusion in the 2016 edition of Pathology and Genetics: Tumours of the Urinary System and Male Genital Organs.

The system consists of five-grade groups that correspond to traditional GSs 6, 3 + 4, 4 + 3, 8, 9, and 10, with grade group 1 indicating the most favorable prognosis and grade group 5 the least favorable.[13]

The argument in favor of the 2016 modification is that it offers a more accurate prognostic categorization of patients with adenocarcinoma, therefore providing a more solid basis for clinical decision making in such patients.[13]

The aim of this study therefore is to investigate the correlation of serum PSA concentration (which is an established prognostic criterion) with the 2016 modification of the Gleason grading system (Gleason grade group system) among patients with adenocarcinoma of the prostate in Ahmadu Bello University Teaching Hospital (ABUTH), Zaria, Nigeria.

## MATERIALS AND METHODS

After obtaining clearance from the Ethical Committee, this retrospective study was conducted based on the analysis of hematoxylin and eosin-stained histological slides prepared from paraffin-embedded tissue specimen of prostate biopsies from January 2006 to December 2013 and the histology request cards were filled by the attending clinician. These were obtained from archives of the Pathology Department of the ABUTH, Shika, Zaria, Nigeria. Further, the clinical notes of the study patients were retrieved from the Urology Unit of the hospital from where values of the serum PSA concentration of the patients were extracted.

The tumors were then graded using the new (2016) Gleason grade group system. Cases in which core biopsies were followed by prostatectomy were assessed by the prostatectomy specimens to avoid duplication of cases.

**Table 1: Age distribution of patients (*n*=211)**

| Age group (years) | Frequency (%) |
|---|---|
| <40 | 2 (0.8) |
| 40-49 | 7 (3.3) |
| 50-59 | 38 (18.3) |
| 60-69 | 77 (36.5) |
| 70-79 | 61 (29.0) |
| 80-89 | 23 (10.5) |
| 90 and above | 3 (1.5) |

**Table 2: Percentage distribution of serum prostatic-specific antigen concentration among patients (*n*=211)**

| PSA value (ng/mL) | Frequency (%) |
|---|---|
| <4 | 0 |
| 4.0-9.9 | 16 (7.6) |
| 10.0-19.9 | 33 (15.6) |
| 20.0-29.9 | 37 (17.5) |
| 30.0-39.9 | 31 (14.7) |
| 40.0-49.9 | 15 (7.1) |
| 50.0-59.9 | 23 (10.9) |
| 60.0-69.9 | 16 (7.6) |
| 70.0-79.9 | 13 (6.2) |
| 80.0-89.9 | 6 (2.8) |
| 90.0-99.9 | 3 (1.4) |
| ≥100 | 18 (8.5) |

PSA: Prostatic-specific antigen

**Table 3: Distribution of (ungrouped) Gleason score among patients (*n*=211)**

| Gleason score | Frequency (%) |
|---|---|
| 2.00 | 2 (0.9) |
| 3.00 | 3 (1.4) |
| 4.00 | 5 (2.4) |
| 5.00 | 16 (7.6) |
| 6.00 | 42 (19.9) |
| 7.00 | 43 (20.4) |
| 8.00 | 62 (29.4) |
| 9.00 | 34 (16.1) |
| 10.00 | 4 (1.9) |

The Sextant Protocol was strictly followed in specimens gotten via trucut biopsies to ensure the grading is reflective of the tumor.

In the case of broken or missing slides, fresh sections were made from stored tissue blocks. Patients' clinical information including prebiopsy recorded serum PSA concentrations was retrieved from either the histology request cards filled by the attending clinician or the patient's clinical notes.

Analysis of the collected data was carried out using Microsoft Office Excel 2010 and Statistical Program for Social Sciences Version 20. Frequencies of variables were determined and

**Table 4: Distribution of Gleason grade groups among patients**

| Grade group | Frequency | Mean serum PSA |
|---|---|---|
| 1 | 68 | 36.62 |
| 2 | 13 | 4.70 |
| 3 | 29 | 49.24 |
| 4 | 63 | 54.84 |
| 5 | 38 | 59.05 |

PSA: Prostatic-specific antigen

**Table 5: One-way analysis of variance serum prostatic-specific antigen concentration versus Gleason grade group**

| | PSA values | | | | |
|---|---|---|---|---|---|
| | Sum of squares | df | Mean square | *F* | Significant |
| Between groups | 34,134.161 | 5 | 8533.540 | 67.398 | 0.000 |
| Within groups | 26,082.446 | 206 | 126.614 | | |
| Total | 60,216.607 | 211 | | | |

PSA: Prostatic-specific antigen



**Figure 1:** Scatter diagram representing the relationship between serum prostatic-specific antigen concentration and (ungrouped) Gleason score among patients

cross-tabulated. Continuous variables were summarized using means and standard deviations. Analysis of variance (ANOVA) was employed to compare means and determine statistical significance. Pearson's correlation coefficient was also employed to test the relationships between serum PSA and ungrouped GS. The level of statistical significance was set at $P \leq 0.05$.

Results were presented using figures and tables, and the findings were compared with similar studies done locally and internationally.
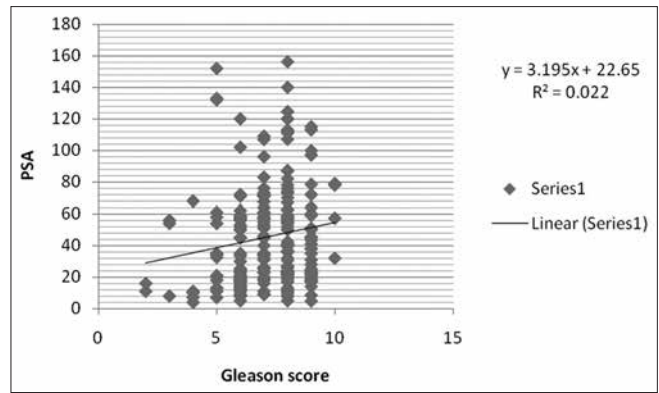
## RESULTS

The patients' ages ranged from 35 to 100 years, with a mean of $66.3 \pm 10.54$ years [Table 1]. The age range of 60–69 years (36.5%) was the largest among the patients in this series. Two (0.8%) of the patients were below the age of 40 years.

The mean serum PSA concentration was $45.48 \pm 32.39$ ng/mL (range 4.0–156.20 ng/mL) [Table 2]. None of the patients in our series had serum PSA concentration <4.0 ng/ml and only 16 (7.6%) had values <10 ng/mL. Eighteen patients (8.5%) had serum PSA values ≥100 ng/mL.

Gleason grade group 1 was most common in our study with 68 (32.2%) of our patients falling within that category [Table 3] while grade groups 2, 3, 4, and 5 had 13 (6.2%), 29 (14%), 63 (29.9%), and 38 (18%) patients, respectively.

The mean serum PSA concentration for patients falling within grade groups 1, 2, 3, 4, and 5 was 36.62, 44.7, 49.24, 54.84, and 59.05, respectively [Table 4].

ANOVA revealed a statistically significant relationship between the serum PSA concentration and the Gleason grade group of cancer ($P = 0.00$) [Table 5]. Equally, a statistically significant relationship was also found between the serum PSA concentration and the ungrouped GS of our patients (Pearson's correlation coefficient = 0.149, $P = 0.031$) [Figure 1].

## DISCUSSION

The patients' age range of 35–100 years found in our study is higher than reported by Oluwole *et al.*[14] (30–79 years) in a previous study from this center but in accordance with studies from Benin,[15] Port Harcourt,[16] and Côte d'Ivoire.[17]

The mean age of the patients in this series was 66.3 years and the age group of 60–69 years was the most common among our patients. A similar figure was found by Ahmed *et al.*[18] in a previous study from this center and by Okolo *et al.*[6] and Odubanjo *et al.*[19] from other centers in Nigeria. However, PCa occurred a decade earlier in our patients as compared to their White counterparts in Europe and America where it mainly presents in the eighth decade.[20] This probably reflects the profound effect genetic and environmental factors have on the natural history of PCa.[21]

Three (0.8%) of the patients are below the age of 40 years. Similar reports were made by Ekwere and Egbe.[22] in Southeastern Nigeria and by Sakr *et al.*[23] among American young men within the age group of 30–40 years. This may require further research for additional genetic, dietary, or environmental factors.

The mean serum PSA concentration was $45.48 \pm 32.39$ ng/mL (range 4.0–156.20 ng/mL). These are comparable to the values previously reported by Ahmed *et al.*[18] from our center and Odubanjo *et al.*[19] from Lagos but lower than the values reported by Okolo *et al.*[6] and Abbiyesuku *et al.*[24] among men with PCa from other parts of Nigeria. Significantly lower mean serum PSA concentration was reported by Rasool *et al.*[25] among Pakistani men with PCa and by Moul

*et al*.[26] among White men with PCa in the US. The variations among different ethnic groups may be attributable to genetic factors[21] while the variations among Blacks may be due to the fact that several other coexisting conditions other than PCa may lead to elevation of serum PSA. These include benign prostatic hyperplasia, prostatitis, urinary tract infection, and instrumentation.[6]

None of the patients in this series had serum PSA concentration <4.0 ng/mL. Some previous studies by Ekwere and Egbe[22] and Odubanjo *et al*.[19] also documented very small figures (2% and 3% respectively) and may be explained by the fact that most doctors only recommend prostate biopsy in patients with a serum PSA concentration of ≥4.0 ng/mL.

The mean (ungrouped) GS among the patients studied was 7.15 ± 1.51. GSs 8 and 7 were most common among the patients. This is in accordance with previous studies from Zaria[14] and with the works of Okolo *et al*.,[6] Ekwere and Egbe[22] and Odubanjo *et al*.[19] from other centers in Nigeria.

Gleason grade group 1 was the most common in our study with 68 (32.2%) of our patients falling within that category while grade groups 2, 3, 4, and 5 had 13 (6.2%), 29 (14%), 63 (29.9%), and 38 (18%) patients, respectively. This contrasted sharply with studies in many centres in Nigeria[6,19,22] and with studies among Black population in the US.[27] However, this may be explained by the fact that the other studies were all not based on the new (2016) Gleason grade group used in this study. The grade group system lumped up all hitherto GSs of 2–6 into grade group 1, therefore expanding the population of the group.[13]

Our study revealed a statistically positive correlation between the serum PSA value and the Gleason grade group of cancer. This is in keeping with previous works by Epstein *et al*.[28] and Spratt *et al*.[29] The above-cited works also demonstrated that serum PSA has a stronger correlation with the Gleason grade group than it does with the corresponding ungrouped GSs of cancer.

## Conclusion

This study concluded that in patients with prostatic adenocarcinoma, there is a statistically significant association between serum PSA levels and newly introduced (2016) Gleason grade group of prostatic carcinoma. It recommends for additional studies to be conducted to further investigate the clinical utility of the new grade group system in prospective clinical trials. Such studies should also examine the relationship between the new Gleason grade group and stage of cancer. This will further enhance prognostication and estimation of the risk of disease progression.

### Financial support and sponsorship
Nil.

### Conflicts of interest
There are no conflicts of interest.

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