# Correlation between Total PSA Level and the Histoprognostic Gleason Score

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## Abstract

Prostate cancer is a public health problem in Senegal. It is one of the most common cancers in men and can be detected early by PSA measurement and confirmed by the pathological study which specifies the histological type and evaluates the histoprognostic scores (Gleason and pTNM). We did not find any anatomopathological study highlighting a link between the PSA t rate and histoprognostic Gleason scores in Senegal. **Objective**: We carried out this work aimed at determining whether there is a correlation between the PSA t rate and the histoprognostic Gleason score, in our context. **Methodology**: This is a retrospective, descriptive and analytical study conducted from January 2013 to October 2021, based on histologically proven prostate cancer cases with a specified PSA level, diagnosed in the pathological anatomy and cytology laboratory of Aristide Le Dantec hospital. **Results**: We identified 654 cases of prostate cancer. The average age was 68.59 ± 5.8 years with extremes of 40 years to 92 years. More than half of our cohort presented a clinical stage T2c, *i.e.* 56.94%. The average prostate volume on ultrasound was 81.81 ± 66 cc. The median PSA t was 110.5 ng/ml, with extremes ranging from 2 ng/ml to 74,770 ng/ml. Prostatic adenocarcinoma was the only histological type found in our patients. There was a predominance of Gleason score 6 (PICU grade group 1) observed in 35.17% of patients. Well-differentiated cancers were predominant and represented 35.17%. There was a statistically significant positive correlation between PSA t level and Gleason score (Spearman's Rho = 0.305, p = 0.000). **Conclusion**: This study shows that in the Senegalese population, in patients with prostate cancer, the higher the PSA t level rises above normal, the higher the Gleason score tends to be.

## Keywords

Prostate Cancer, PSAt, Gleason, Dakar

## 1. Introduction

Prostate cancer corresponds to all malignant cell proliferations developed at the expense of prostate tissue. It can be suspected by an abnormal digital rectal examination and/or an elevated prostate specific antigen (PSA) level. Recommended individual screening consists of a prostate specific antigen (PSA) test coupled with a rectal exam every year in men aged 50 to 75 or from 45 years of age in the case of risk factors.

This condition is a public health problem. This condition corresponds to the second most common cancer and the fifth cause of cancer death among men worldwide in 2020 [1]. In Senegal, this malignant neoplasia is the most common in men, with an incidence rate of 21.8 per 100,000 men according to Globocan 2021 [2] and a frequency of 20% according to a study carried out on the state of the tumor registry in the same country between January 2010 and December 2015 [3]. The definitive diagnosis is based on anatomopathological examination, which makes it possible to assess tumor aggressiveness, its evolution and its prognosis [4]. We conducted a study aimed at studying the correlation between the total PSA level (PSA t) and the histoprognostic Gleason score cases of this pathology in Senegal.

## 2. Material and Method

- Type, period of study:

This is a retrospective, descriptive and analytical study over a period of eight years from January 2013 to October 2021. The study took place in the pathological anatomy and cytology laboratory (ACP) of the Aristide Le Dantec hospital (HALD) in Dakar.

- Study population:

The study population consisted of all the results, combining the report, the technical slides and the respective blocks (for each patient), archived at the HALD PCR laboratory, *i.e.* 64,856 patients' results archived with their respective reports, technical slides and paraffin blocks.

- Selection criteria:

The selection of patients was carried out based on the results and respective reports of anatomopathological examinations. We included all documented cases of patients with prostate cancer confirmed histologically on biopsy or surgical specimen, with a PSA level t at the time of the diagnosis.

- Methodology:

Firstly, we consulted the registers, then analyzed the archives of the results, reports and technical slides of anatomo-pathological examinations, taking into account the inclusion criteria. Exhaustive recruitment was carried out allowing us to collect 654 cases.

When the slides were not available or unusable, we used the relevant paraffin blocks, and proceeded again with the histopathological technique until new technical slides were obtained.

Secondly, we reread the technical slides:

- The determination of the Gleason score followed the new recommendations of the prognostic grade groups adopted by the 2016 WHO classification of prostate carcinomas [5] [6].
- The ISUP (International Society of Urological Pathology) group was determined according to the recommendations of the International Society of Urological Pathology [5] [6]. The ISUP grades were divided into 4 categories according to their degree of differentiation [5] [6]. The tumor was considered well differentiated when the ISUP score was 1, moderately differentiated for an ISUP score 2, moderately to poorly differentiated for an ISUP score 3 and poorly differentiated for an ISUP score of 4 and 5.

Data were collected identically on all histological examination reports from an Excel file. The study parameters were: age, digital rectal examination, PSA t level, prostate volume, type of sample, histological type, Gleason score, and ISUP group. The information was collected in the same way using a collection sheet developed for this purpose.

Data entry and analysis were carried out with Epi Info French version software and IBM SPSS Statistic 26 software for the descriptive analysis. The qualitative variables were described by frequency tables. The quantitative variables were described by their position (average, median) and dispersion (standard deviation, extremes) parameters. The analytical part consisted of bivariate analysis to look for associations between variables using appropriate statistical tests. The alpha error risk was set at 5%.

The correlation between the Gleason score and the PSA t level was made using the Spearman test.

The Spearman test makes it possible to specify the existence of a link between 2 quantitative variables and its intensity. The Spearman correlation coefficient (Rs) varies from −1 to +1:

- A value of $p < 0.05$ was considered significant, therefore concluding the existence of a correlation.
  - A positive correlation ($p < 0.05$ and positive Rs) means that when one variable increases, the other variable also tends to increase.
  - A negative correlation ($p < 0.05$ and negative Rs) means that when one variable increases, the other tends to decrease.
- A p value $\geq 0.05$ was considered non-significant and therefore showed that there was no correlation.

## 3. Results

Over a period of 8 years from January 2013 to October 2021, we collected 654 cases of prostate cancer (**Figure 1**).

The average age was 68.59 years ± 8.29, the median 70 years with extremes of 40 and 92 years. The age group (61 - 70) was the most represented (42.64%) (**Figure 2**).
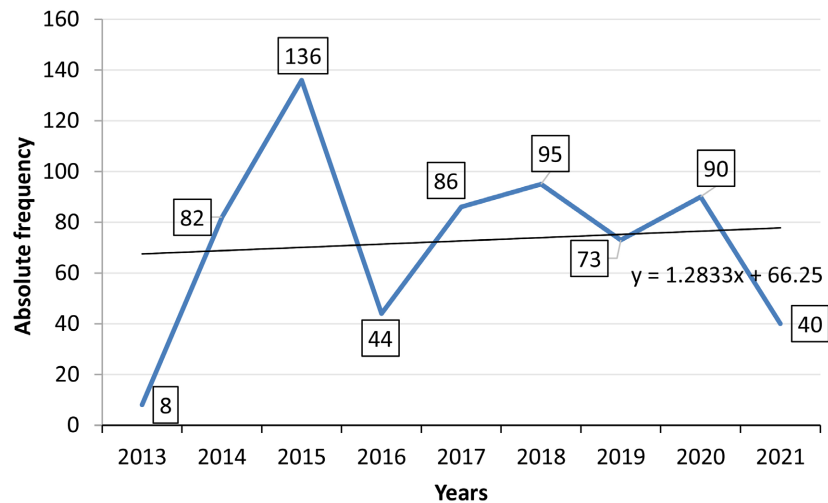
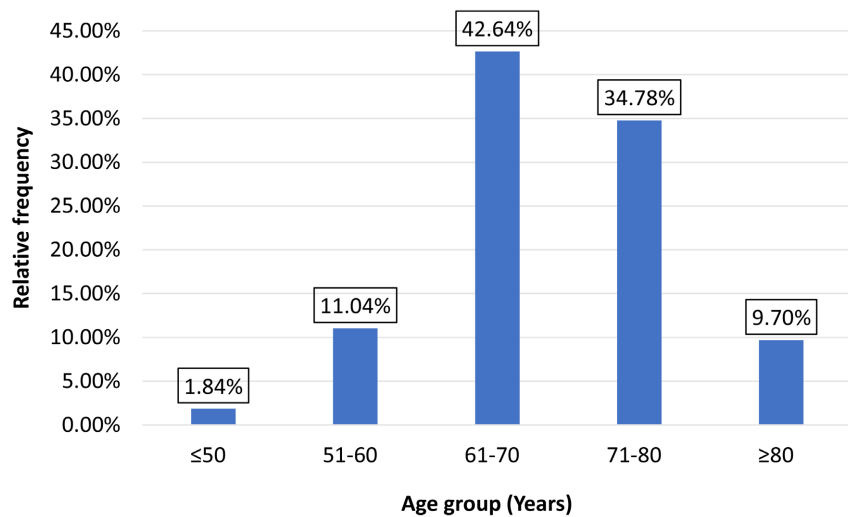**Figure 1.** Distribution of cases according to year (N = 654).



**Figure 2.** Distribution of patients according to age groups (N = 598).

Clinical stage T2 was the most common (87%), divided into stage T2c (56.94%), followed by stage T2b (20.37%), then stage T4 (18.51%) (**Figure 3**).

The prostate volume was recorded in 50 patients (*i.e.* 7.65%). The average prostate volume was 81.81 cm$^3$ ± 66.7. The median was 54 with extremes of 19.50 and 323 cm$^3$. The average PSA t level was 867.12 ng/ml ± 3489.32. The median was 110.5 ng/ml with extremes of 2 and 74,770 ng/ml. Patients with a PSA t level greater than 50 ng/ml were the most represented, *i.e.* in 70.03% (458 cases) (**Figure 4**).

Biopsy was the main type of sample found (91.6%) followed by surgical specimens (8.4%). The only histological type highlighted was prostatic adenocarcinoma. The Gleason score (3 + 3) = 6 was the most represented, *i.e.* 35.17% (230 cases), followed by the score (4 + 3) = 7 representing 30.89% and the Gleason score 8 (4 + 4) or 22.18% (145 cases). Gleason score 5 + 5 = 10 was the least representing 0.15% (1 case) (**Figure 5**).
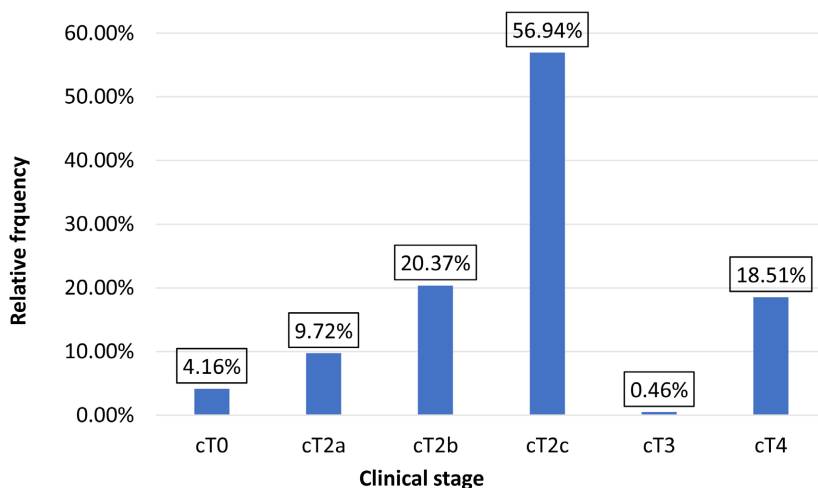
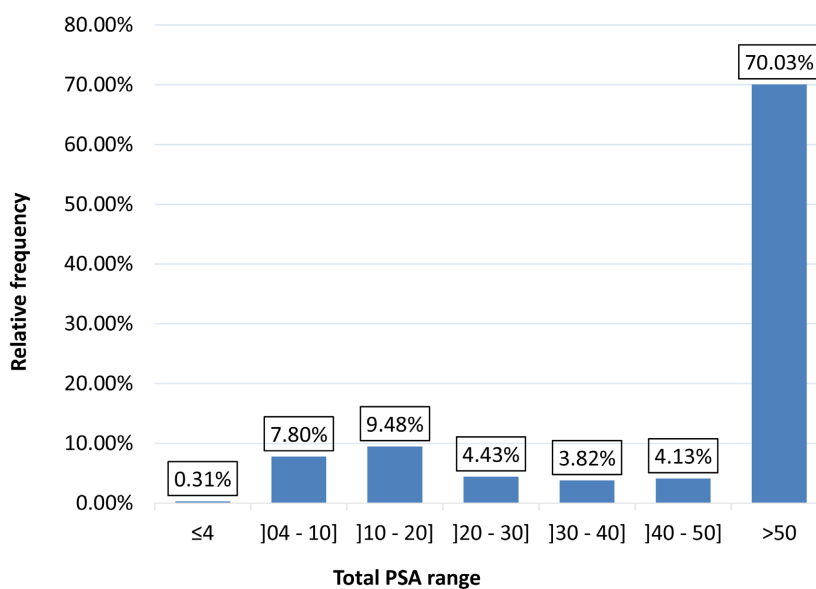**Figure 3.** Distribution of patients according to clinical stage (N = 216).



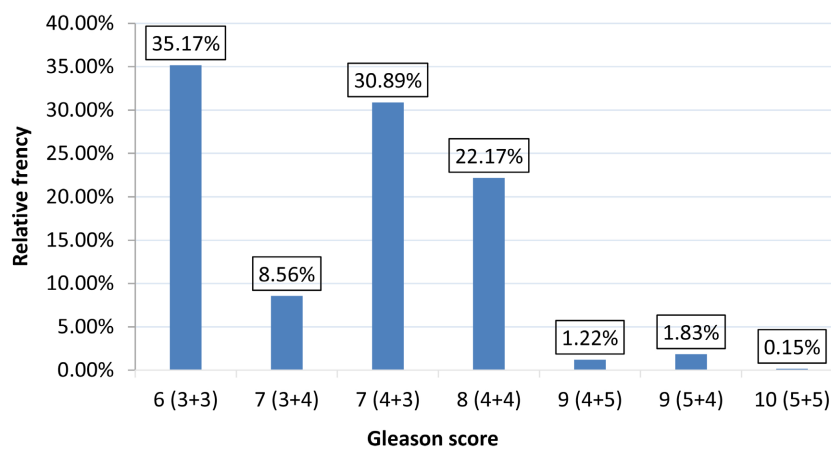**Figure 4.** Distribution of patients according to PSA t levels (N = 654).



**Figure 5.** Distribution of patients according to Gleason score (N = 654).

Group ISUP 1 was the most common (35.17%), followed by ISUP 3 (31.04%) then ISUP 5 (3.21%) (Figure 6).

The different correlations were studied using the Spearman correlation coefficient (Spearman's Rho). The study finds a monotonic positive correlation between the PSA t level and respectively the Gleason score ($Rs = 0.305$; $n = 654$; $p < 0.001$), the ISUP grade group ($Rs = 0.303$ $n = 654$, $p < 0.001$) and the degree of differentiation ($Rs = 0.306$; $n = 654$; $p < 0.001$) (Table 1).

The comparison of the averages and medians of the PSA level according to the degree of differentiation, supports the results of the correlation and shows that the PSA t tends to increase when the tumor becomes less differentiated (Figure 7).

No correlation was found ($p$ value $> 0.05$) between age and, respectively, Gleason score, PSA t level and rectal examination (Table 2).
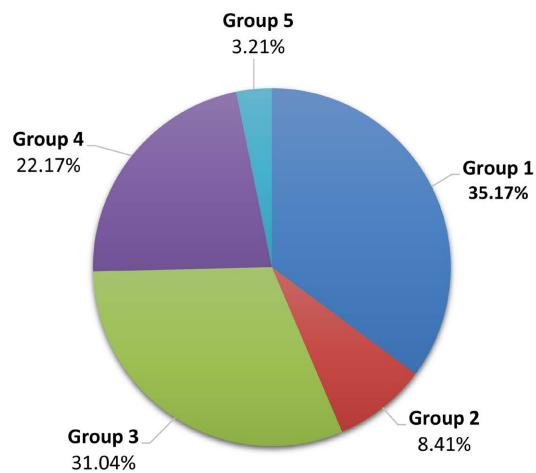


**Figure 6.** Distribution of patients according to their ISUP grade.
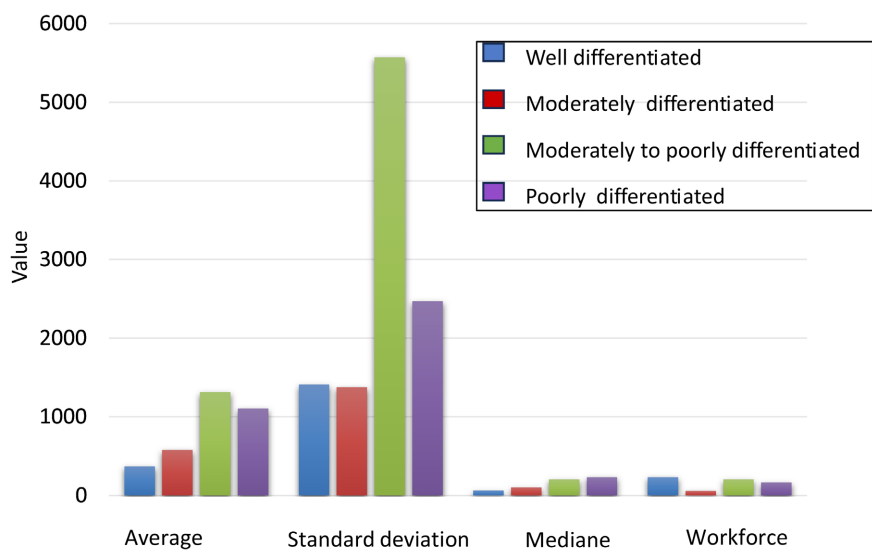


**Figure 7.** Comparison of averages, standard deviations, medians of PSA t according to the degree of differentiation.

Table 1. Comparative table of the results of the Spearman correlation between the PSA t level and the Gleason score, the ISUP grade group and the degree of differentiation.

|  | PSA t and Gleason score | PSA t and ISUP group level | PSA t et differen-tiation |
|---|---|---|---|
| Rho by Spearman (Rs) | 0.305 | 0.303 | 0.306 |
| p value | 0.000 | 0.000 | 0.000 |
| Workforce (n) | 654 | 654 | 654 |

Table 2. Comparative table of the results of the Spearman correlation between age and PSA t level, TR results and Gleason score.

|  | Age and PSA t level | Age and TR result | Age and Gleason score |
|---|---|---|---|
| Rho by Spearman (Rs) | 0.070 | 0.056 | 0.022 |
| p value | 0.087 | 0.407 | 0.595 |

## 4. Discussion

In Senegal, according to Globocan 2020, prostate cancer is the most common cancer in men. This condition generally affects men in the sixth decade, in Black Africa and particularly in Senegal, as evidenced by the average age in our study and several series in Nigeria, Togo and Senegal (Table 3).

However, the proportion of prostate cancers in subjects under 50 years of age may be worrying. Several studies show an increase in this proportion with the wider use of PSA testing, going from 1% according to studies carried out by Alexander *et al.* in 1987 [11] and Aprikian *et al.* in 1994 [12] to 4.5% according to the study by Parker *et al.* in 2011 [13]. The PSA assay being relatively used in Senegal and Africa, this would explain the rates of 1.84% and 1.7% of patients aged less than 50 years, found respectively in our cohort and that of Mohammed *et al.* [8] in Nigeria. In our context, a little more than 12% of patients are part of the active population (<65 years). A significant proportion (3.78%) had a benign prostate on rectal examination, associating an isolated increase in the PSA t level and thus allowing the indication for a prostate biopsy. According to Catalona *et al.* [14] 23% to 45% of cancers would be unrecognized if the indications for biopsies were based solely on digital rectal examination because several prostate cancers do not cause palpable changes.

Prostate cancer in black Africa is frequently associated with a significant elevation in PSA t, often greater than 10 times normal, as corroborated by our work as well as several West African studies [7] [15] [16] [17]. This observation confirms the diagnostic delay (a long evolution of the disease before diagnosis), especially since the PSA level is correlated with the clinical stage [18], it increases with the extension of the disease (Table 4).

The indication for prostate biopsy based on the PSA level has been known since the work of Stamey in 1989; for this, the threshold value most used in the

Table 3. Comparison of the average age and extremes of CaP cases from various series.

|  | Average age | Extreme |
|---|---|---|
| Niang *et al.* [7] | 65 years | (43 - 96 years) |
| Mohammed *et al.* [8] | 68 years | (47 - 96 years) |
| Ndiaye *et al.* [9] | 68.6 years | (43 - 93 years) |
| Amegbor *et al.* [10] | 70 years | (45 - 95 years) |
| **Our study** | **68.59 years** | **(40 - 92 years)** |

Table 4. Comparison of the average PSA t of various series.

| Authors | Period | Number of cases | Average of PSA t (ng/ml) |
|---|---|---|---|
| Jalloh *et al.* [15] | 2015-2016 | 67 | 94.07 |
| Loko *et al.* [17] | 2008 | 250 | 241.7 |
| Kabore *et al.* [16] | 2009-2010 | 166 | 537 |
| Niang *et al.* [7] | 2004-2010 | 164 | 1447.57 |
| Our study | 2013-2021 | 654 | 867 |

literature is 4 ng/ml. Only in our series, two patients (0.31%) had a PSA t level below 4 ng/ml, but showed abnormalities on digital rectal examination (cT2), indicating prostate biopsy. This same type of observation was also noted by Gurumurthy *et al.* [19], Mohammed *et al.* [9]. Thus it appears necessary to couple the PSA t level to the clinical examination and more particularly to the rectal examination for efficient screening. Although the PSA level has good sensitivity for this condi-tion, when it is greater than 4 ng/ml, the probability of finding prostate cancer below the threshold of 2 ng/mL and a PSA level between 2.5 and 4 ng/mL is 2% and 18% respectively [20]. Some experts have therefore proposed lowering the threshold value from which the biopsy must be performed to 2.5 ng/mL in order to improve early detection of cancer [21].

Our cohort, as well as several series, found a large predominance of the cT2c class at more than 50%, such as the study of Ndiaye [22] (51%) and Niang *et al.* [7] (61.1%). A significant proportion of our patients presented with advanced cancer (18.5%). This trend is found in the studies of Ndiaye *et al.* [9], Gueye *et al.* [18] and Amegbor *et al.* [10]. The cause would be the late diagnosis of pros-tate cancer secondary to [9]:

- The absence of organized systematic screening for prostate cancer;
- The absence of individual screening in patients with a family past history of prostate cancer;
- Accessibility to health structures, cost of examinations;
- Delay in patient consultation in African populations.

Prostatic adenocarcinoma is the most common histological type of prostate cancer. Several studies confirm this [15] [23]. This predominance can be ex-

plained by the fact that the prostate is composed mainly of glandular tissue. According to McNeal [24] prostate cancers develop preferentially (68%) in the peripheral zone which is made up of 70% glandular tissue. There are other rarer histological types such as sarcoma, including a case reported by Niang *et al.* [7].

Gleason 6 (3 + 3) is often the most common, as shown by our work and the studies of Okolo *et al.* [25], Čamdžić *et al.* [26], while Niang *et al.* [7] observed a preponderance of Gleason score 7 (3 + 4) (ISUP group 2).

Data from the literature frequently shows that there is a statistically significant correlation between the elevation of the PSA t level and the elevation of the Gleason score as demonstrated in our study (Table 5).

Our data show that more PSA t rated, the more the ISUP group was raised and the more cancer was dedifferentiated. Some authors such as Blackwell *et al.* [29], explain these findings with a theory, "although individually the cells of a poorly differentiated prostatic adenocarcinoma produce less PSA than those of a well and moderately differentiated adenocarcinoma, they are generally presenting such large numbers, that the PSA t level is higher".

The study by Partin *et al.* [30], on the other hand, found a negative correlation between the PSA t rate and the Gleason score.

This work could present limitations which we were able to identify as follows:

- This is a monocentric retrospective study, although the HALD laboratory is one of the two public laboratories receiving the most prostate histological samples in Senegal, and these samples come from all regions.
- We did not carry out a control group to compare PSA levels and Gleason scores in men without prostate cancer.
- Genetic, environmental and comorbidity factors were not considered in the study.
- The study did not include a longitudinal follow-up of prostate cancer patients in relation to initial PSA levels and Gleason scores, because several patients died or were lost to follow-up.

This study may have some limitations, which we have identified as follows:

- This is a retrospective monocentric study, although the HALD laboratory is one of the two public laboratories receiving the most prostate histological samples in Senegal, and these samples come from all regions.

**Table 5.** Comparison of the p value of the correlation between the elevation of the PSA t level and the elevation of the Gleason score of various series.

|  | Period | Number of cases | Countries | p value |
|---|---|---|---|---|
| Yarney *et al.* [27] | 2004-2013 | 669 | Ghana | 0.000 |
| Okolo *et al.* [25] | 1998-2000 | 67 | Nigéria | 0.000 |
| Lovely *et al.* [28] | 2015-2017 | 620 | Inde | 0.035 |
| Čamdžić *et al.* [26] | 2015-2019 | 615 | Bosnie-Herzégovine | 0.003 |
| Our study | 2013-2021 | 654 | Sénégal | 0.000 |

- We did not use a control group to compare PSA levels and Gleason scores in men without prostate cancer.
- Genetic, environmental and comorbidity factors were not taken into account in the study.
- The study did not include long-term follow-up of prostate cancer patients in relation to baseline PSA levels and Gleason scores, as many patients died or were lost to follow-up.

## 5. Conclusions

Prostate cancer in Senegal occurs preferentially in men in their sixth decade with a high PSA t level. Our study shows that there is a statistically significant correlation between elevated PSA t and elevated Gleason score.

The PSA t level should be considered in our context as a useful tool for both detecting and suggesting the aggressiveness of prostate cancer.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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