

## Prostate Specific Antigen Level and Gleason Score in Indonesian Prostate Cancer Patients

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### Abstract

In Indonesia, the number of prostate cancer continues to increase and even becomes the most common malignancy in men in 2015. Delayed early detection of prostate cancer is a significant concern. Prostate-specific antigen (PSA) level is found to be elevated in various conditions of prostate tissue damage, including prostate cancer. The extent of tissue damage in prostate cancer, represented by the Gleason score, is suspected to be related to the increase in the PSA level in the bloodstream. To investigate the relationship between the PSA level and Gleason scores in prostate cancer patients, a cross-sectional observational study was conducted. The study population consisted of 83 prostate cancer patients treated in Dr. Hasan Sadikin General Hospital Bandung, Indonesia, from 2017 to 2021. Data collected were analyzed using Spearman correlation test was used with an alpha value of 5%. Results indicated that 37.3% patients had a PSA level above 200 ng/dL, and 25.3% had a PSA level between 10-50 ng/dL. The majority of patients (48.1%) had a Gleason score of 9-10 (ISUP 5), while 24.1% had a score of 8 (ISUP 4). Bivariate analysis showed no significant relationship between the PSA level and Gleason score ( $p$ -value=0.445). Further studies are needed to determine the sensitivity and specificity of PSA in diagnosing prostate cancer.

**Keywords:** Gleason grading, prostate cancer, prostate-specific antigen

### Introduction

Prostate cancer is the 4th most common cancer globally and the 2nd most common cancer in men.<sup>1</sup> As of 2018, it is estimated that there will be 164,690 new cases of prostate cancer, with 29,430 deaths.<sup>2</sup> Reports of prostate cancer have increased in the Asian region over the past ten years, with an incidence rate of 4.1 per 100,000. In Indonesia, based on histopathological data from the IAPI Cancer Registration Agency and the Indonesian Ministry of Health in 2015, prostate cancer was ranked first as the most common tumor in men.<sup>5</sup> According to data from the Indonesian Society of Urologic Oncology (ISUO) in 2011, in the period 2006-2010 there were 971 prostate cancer patients with an average age of 68.3 years.<sup>6</sup> At Dr. Hasan Sadikin General Hospital in Bandung, 318 cases were reported between 2004 and 2010, with 193 cases (60.7%)

being confined organs and 125 cases (39.3%) being metastatic.<sup>6</sup>

Prostate-specific antigen (PSA) is a serine protease enzyme produced by epithelial cells in the prostate gland. In prostate cancer, damage to the basal cell layer and basement cell membrane, along with increased angiogenesis, leads to PSA leakage into the bloodstream. PSA is organ-specific but not cancer-specific; an increase in PSA value can be caused by several conditions other than malignancy, such as urinary tract infections, prostatitis, BPH, or medical procedures such as the digital rectum and TURP.<sup>11</sup> In Indonesia, the PSA standard value used is 4 ng/ml.<sup>7</sup> When an increase of more than 4 ng/ml, serum PSA has a specificity of up to 91% in detecting prostate cancer.<sup>8</sup> At PSA levels > 4 ng/ml, prostate biopsy is highly recommended for the diagnosis and prognosis of prostate cancer.<sup>9</sup>

In determining the degree of malignancy of prostate cancer, the Gleason score is used as a parameter. Gleason's degree divides the pattern of histopathological findings of prostate cancer into 5 patterns.<sup>10</sup> Prostate cancer is known to have more than one Gleason pattern/degree; therefore, the Gleason Score is formed by

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adding up the most dominant and second most dominant Gleason degrees and grouping them into groups. The Gleason score is also used as one assessment for determining prostate cancer staging (according to AJCC). It is also used as a predictive determination of prostate cancer (Partin Table) and therapeutic modalities.

Amarneel et al.<sup>12</sup> stated that there was a significant correlation between serum PSA and Gleason Histological Grade in patients with prostate cancer. This is also in line with the study of Jayapradeep et al.,<sup>13</sup> which states that high serum PSA levels are associated with the Gleason Score. However, a study by Gurumurthy et al.<sup>14</sup> stated no relationship between increased PSA levels and increased Gleason degrees. Research on the relationship between PSA levels and Gleason scores in prostate cancer has not been conducted at Dr. Hasan Sadikin General Hospital in Bandung, a leading referral hospital for West Java Province. This gap in research has prompted the author to undertake this study. The findings are anticipated to provide valuable data on prostate cancer patients and offer insights into diagnosing and assessing the severity of prostate cancer.

## Methods

An observational cross-sectional study was conducted for this research. All men who had been diagnosed with prostate cancer and had prostate biopsies and histological tests between 2017 and 2021 made up the study population. Populations that matched the inclusion and exclusion criteria made up the whole sample for the research. Patients with prostate cancer who underwent PSA testing, histological analysis, and Gleason Score evaluation met the inclusion criteria. Patients with BPH, urinary tract infections, prostatitis, and insufficient medical record data were among those who were excluded. Eighty-three patients made up the study's final total sample.

PSA levels were categorized using an ordinal measurement scale based on intervals of 50 ng/dL. The Gleason score, determined by summing the Gleason grades and utilizing the International Society of Urological Pathology (ISUP) grouping system, was also assessed. Additionally, patient age and the number of years since treatment were considered in this study. Data were sourced from the medical records at Dr. Hasan Sadikin General Hospital in Bandung. The analysis employed the Spearman correlation test and

descriptive statistics, with a significance level set at 5% ( $p\text{-value} < 0.05$ ), using SPSS version 23. Ethical approval for the study was granted by the Health Research Ethics Committee of Dr. Hasan Sadikin General Hospital under reference number LB.02.01/X.6.5/246/2023.

## Results

Table 1 shows that the majority of patients were admitted in 2017 and 2018, accounting for 27.7% and 20.5% of the total cases, respectively. Regarding age, the predominant group consisted of patients older than 60 years. In terms of PSA levels, 37.3% of patients had levels exceeding 200 ng/dL, while 25.3% had PSA levels ranging from 10-50 ng/dL. Analysis of the Gleason scores revealed that most patients had scores in the 9-10 (ISUP 5) and 8 (ISUP 4) categories, representing 48.1% and 24.1% of the patient population, respectively.

The normality test of PSA serum level data and Gleason score in prostate cancer patients used the Komlogorov-Smirnov test, and it was found that the data distribution was not normal ( $p=0.000$ ). The bivariate analysis between serum PSA levels and the Gleason score (Table 2) showed a  $p\text{-value}$  of 0.445; at 5%  $\alpha$ , it can be concluded that there was no significant correlation between PSA levels and the Gleason score. In addition, an  $r$  correlation value of 0.085 was also obtained, which indicated a tendency for a weak correlation/no correlation between PSA serum levels and the Gleason score.

## Discussion

Out of the 83 data points collected, an analysis of the distribution of prostate cancer patients at Dr. Hasan Sadikin General Hospital in Bandung from 2017 to 2021 was performed. The year 2017 recorded the highest number of prostate cancer patients, with 23 patients (27.7%). This was followed by 2019 with 20 patients (24%) and 2018 with 17 patients (20.5%). In contrast, the number of prostate cancer patients in 2020 and 2021 was relatively lower, with 14 patients (16.9%) in 2020 and 9 patients (10.8%) in 2021. The decrease in patient numbers in 2020 and 2021 is suspected to be linked to the COVID-19 pandemic in Indonesia, which led to a higher volume of COVID-19 patients visiting health services. This observation is consistent with a survey conducted by the WHO across 155

**Table 1 Patient Characteristics**

Variable	n	
Year of admission	2017	23 (27.7)
	2018	17 (20.5)
	2019	20 (24)
	2020	14 (16.9)
	2021	9 (10.8)
Age group (years old)	45-50	3 (3.6)
	51-55	1 (1.2)
	56-60	9 (10.8)
	61-65	20 (24.1)
	66-70	20 (24.1)
	>70	30 (36.1)
PSA (ng/dl)	<10	10 (12)
	10-50	21 (25.3)
	51-100	14 (16.9)
	101-150	6 (7.2)
	151-200	1 (1.2)
	>200	31 (37.3)
Gleason score	≤ 6 (ISUP 1)	7 (8.4)
	7 (3+4) (ISUP 2)	3 (3.6)
	7 (4+3) (ISUP 3)	13 (15.7)
	8 (ISUP 4)	20 (24.1)
	9-10 ( ISUP 5)	40 (48.1)

\*\*PSA=prostate specific antigen; ISUP=International Society of Urological Pathology

countries, where 53% of respondents reported a decline in visits for non-communicable diseases, such as cardiovascular diseases, diabetes, and cancer, during the COVID-19 pandemic.<sup>15</sup>

The distribution of prostate cancer patients by age showed that the highest number was in the age group over 70 years with 30 patients (36.1%), followed by the age groups 61-65 years

**Table 2 Bivariate Analysis between PSA Serum with Gleason Score**

PSA serum (ng/mL)	Gleason Score										p-value	R Correlation
	≤6		7(3+4)		7(4+3)		8		9-10			
	n	%	n	%	n	%	n	%	n	%		
<10	3	3.6	0	0	1	1.2	3	3.6	3	3.6	0.445	0.085
10-50	2	2.4	0	0	3	3.6	6	7.2	10	12.0		
51-100	1	1.2	0	0	2	2.4	4	4.8	7	8.4		
101-150	1	1.2	0	0	2	2.4	1	1.2	2	2.4		
151-200	0	0	0	0	0	0	0	0	1	1.2		
>200	0	0	3	3.6	5	6.0	6	7.2	17	20.5		

Normality test result PSA: p-value 0.001; gleason score: p-value 0.001

and 66–70 years with 20 patients each (24.1%). This is in line with previous research conducted by Amarneel et al., which found that prostate cancer patients were more prevalent in patients over the age of 60, accounting 66.7% of total cases.<sup>12</sup> Similar results were also mentioned in a previous study conducted by Umbas, which indicated the incidence of prostate cancer would increase in the age group over 65 years and is very rare in those under 50 years of age.<sup>16</sup> The number of prostate cancer patients in the 56–60 age group was 9 patients (10.8%), 1 patient (1.2%) in the 51–55 year age group, and 3 patients (3.6%) in the 45–50 age group, with the youngest patient being 45 years old.

PSA is a serine protease produced by prostate epithelial cells, also known to be produced by prostate cancer cells. Some sources say that the ability of prostate cancer cells to secrete PSA is lower compared to normal prostate cells; however, PSA in prostate cancer cells penetrates the blood circulation more easily due to damage to the prostate basement membrane and its ability to avoid proteolysis in the circulation, thus increasing PSA serum levels in prostate cancer cases.<sup>17</sup>

This study found an overall increase in serum PSA levels among prostate cancer patients, with varying values. The largest proportion of patients had serum PSA levels exceeding 200 ng/ml, totaling 31 patients (37.3%). Conversely, the groups with lower PSA levels had fewer patients: 6 patients (7.2%) had PSA levels between 101–150 ng/mL, and only 1 patient (1.2%) was in the 151–200 ng/mL range. The second highest number of patients was in the PSA 10–50 ng/mL group, with 21 patients (25.3%). This was followed by the PSA 51–100 ng/mL group, which had 14 patients (16.9%), and the PSA <10 ng/mL group, which included 10 patients (12%).

In this study, it was found that the highest distribution of prostate cancer patients was at Gleason score 9–10 (ISUP degree 5) with 40 patients (48.1%), followed by the Gleason score group 8 (ISUP degree 4) with 20 patients (24.1%), 13 patients (15.7%) in the Gleason score group 7 (4+3) (ISUP Degree 3), while in the Gleason score group 6 (ISUP degree 1) there were 7 patients (8.4%), and the least was in the Gleason score group 7 (3+4) (ISUP degree 2) with 3 patients (3.6%). This is in line with the research conducted by Pai et al., which stated that many patients with adenocarcinoma had a higher histopathological degree of 77.77%.<sup>18</sup> Similar results were also mentioned in a study by Nina, which stated that a Gleason score

of 2–4 was typically found as a small tumor in the transitional zone, often discovered accidentally when examining a TURP specimen with suspected BPH. Most cancers found in needle biopsy preparations have a Gleason score between 5 and 7.

A normality test was carried out on the PSA serum level data and the Gleason score was used using the Komlogorov-Smirnov test. The results obtained were  $p=0.000$ , indicating that the data distribution was abnormal. Consequently, data transformation was performed, and the result was  $p=0.000$ , confirming the abnormal distribution of the data. Therefore, data analysis in this study was conducted using a non-parametric test, specifically the Spearman correlation test with a 95% confidence level. The results of the Spearman correlation test obtained  $p=0.445$  and  $r=0.085$ ; since the  $p$ -value was  $>0.05$ , so it can be concluded that there was no significant correlation between serum PSA levels and the Gleason score in this study. Similar findings were also reported in a previous study conducted in India, which found no relationship between serum PSA levels and the Gleason score in prostate cancer patients, it was stated that 17.5% of study subjects with a Gleason score of 8–10 had low serum PSA levels. Some studies mention that prostate cancer cells produce more PSA than normal cells, thus poorly differentiated cancer cells release greater amounts of PSA than well-differentiated ones. However, some studies also mention that the lack of correlation between Gleason score and PSA may be explained by a decrease in antigen production by higher-grade lesions due to loss of expression of the PSA encoding gene.<sup>14</sup> A few weaknesses of this study are acknowledged: the small sample size and the lack of comprehensive medical records, which resulted in many samples being excluded.

In conclusion, from 2017 to 2021, 37.3% of prostate cancer patients at Dr. Hasan Sadikin General Hospital in Bandung had blood PSA levels exceeding 200 ng/mL, while 48.1% had Gleason scores of 9–10 (ISUP 5). During this period, there was no significant link between PSA serum levels and Gleason scores among prostate cancer patients at the hospital.

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