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RESEARCH ARTICLE

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# Relationship of Prostate-Specific Antigen (PSA), Age and Urine Examination in Healthy Adult Men at Community Service Activities

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**Abstract:**

Prostate-specific antigen (PSA) is a glycoprotein molecule that is produced by all epithelial cells of the prostate gland. PSA levels are also produced by the neoplastic prostate gland. Getting older is one factor that can cause an increase in PSA values. PSA values increase with age and increase from 0.7 to 1.5 ng/mL per year. A urinalysis is a routine urine examination that is frequently used because it is relatively easy, inexpensive, and noninvasive. This study aims to determine the relationship between age, PSA value, and urine examination results of healthy adult men in community service activities. The design used in this study was observational analytic with cross-sectional design. The sample was taken by total sampling, namely, all respondents who came to the November 2023 Community Service activity. Data analysis in this study was conducted using the Chi-square test. Fisher's exact test is used if it does not meet the requirements of the Chi-square test. The results of the study showed that 19 respondents (50%) aged 50–59 years had normal PSA and 6 (15.8%) aged 50–59 years had abnormal PSA increased. Eight respondents (21%) aged ≥60 years obtained PSA scores with normal values, while 5 (13.2%) had abnormal/increased values. The data was conducted using the Chi-square test; however, if it did not meet the requirements of the Chi-square test, then Fisher's exact test was conducted to obtain a P-value of 0.457. There was no significant difference between age and PSA values of healthy adult men at the community service activities in November 2023. The urinalysis results, namely, urine protein, urinary leukocytes, urinary erythrocytes, and urinary osmolality with the Chi-square test and Fisher's exact test did not differ from the PSA value of healthy adult men at the November 2023 Community Service activity. There was no significant difference between PSA values, age, and urinalysis.

**Keywords:** Prostate-specific antigen (PSA); Age; Urinalysis

## Introduction

Prostate-specific antigen (PSA) is a glycoprotein molecule that is produced by all epithelial cells of the prostate gland.[1] PSA levels as a glycoprotein biomarker can be produced by either a normal or neoplastic prostate gland.[2] PSA levels have the same structure and function as the kallikrein gland, so the PSA gene is encoded as KLK3 (kallikrein-related peptidase 3), and the location of the gene on the long arm of chromosome 19 (19q13.2-q13.4).[1, 3] PSA levels are produced by the epithelium ducts of the prostate gland and are excreted along with large amounts of semen. PSA levels maintain the viscosity of cement liquid through the process of semenogelin hydrolysis so that the cement liquid becomes liquid. PSA levels were first detected in seminal vesicle fluid by Hara et al. in 1971 and successfully isolated from prostate tissue by Wang et al. in 1979.[3]

PSA levels are organ-specific but not specific for carcinoma or prostate malignancy, as levels can also be elevated in benign prostate hypertrophy (BPH), acute prostatitis, and urinary retention accompanied by infection, after digital rectal examination (DRE) procedures and after sexual activity.[1, 4] Some of the condition that can also create elevated PSA levels include advancing age, urinary tract infections, sexual activity such as ejaculation, prostate gland cancer, sports such as cycling that can increase the risk of prostate gland trauma, prostate biopsy, and medications.[3, 5] PSA levels are a strong predictor of prostate growth compared to prostate volume.[5] Normal PSA levels are <4 ng/mL, and PSA levels increase with age and increase from 0.7 to 1.5 ng/mL per year. Oesterling et al. found an increase in PSA levels of about 0.04 ng/mL annually in men aged 60 years.[6]

Okafor et al.'s (2023) study reported that there is a significant relationship between age and PSA level values ($p < 0.0001$).[1] This is also in line with Birinci and Ulgu's (2023) study that there is a significant relationship between age and increased PSA levels.[2] Moreover, Antony et al.'s (2019) study showed a significant relationship between age and PSA levels ($p = 0.008$), where there was an increase in PSA levels with increasing age.[7] Bo et al.'s (2003) study reported that there is no correlation between PSA values and age ($r = 0.947$), and it is recommended to evaluate normal limits based on specific ages for the elderly.[8] Chang et al.'s study reported that age was not significantly correlated with PSA levels and prostate volume ($p > 0.05$).[9]

A urinalysis is a routine urine examination that is frequently used because it is relatively easy, inexpensive, and noninvasive. It includes macroscopic, chemical, and microscopic examination of urine.[10] It can be done manually or automatically by examining dipstick or urine sediment, where substances contained in urine such as erythrocytes, leukocytes, and proteins will be obtained.[11, 12]

Based on the description above, researchers are interested in knowing the relationship between PSA, age, and urinalysis results with data obtained from respondents during community service activities.

## Research Method

The design used in this study was observational analytic with a cross-sectional design. The sample was taken by total sampling, namely, all respondents who came to the November 2023 Community Service activity. Data analysis in this study was conducted using the Chi-square test; however, if it does not meet the requirements of the Chi-square test, Fisher's exact test is used. This research will be carried out in November 2023 at community service activities.

## Results

Based on the study conducted by taking data from community service activities in November 2023, it obtained that there were 25 respondents (65.8%) aged 50–59 years and 13 (34.2) aged ≥60 years. Researchers grouped the ages of respondents based on Oesterling et al.'s study. which found that there was an increase in PSA levels of about 0.04 ng/mL each year in men aged 60 years. Okafor et al.'s study found that there was a progressive increase in PSA values with age in each age group from 50–59, 60–69, and 70–79 years.[1] The average normal PSA values are <2.5, <3.5, <4.5, and <6.5 ng/ml for ages 40–49, 50–59, 60–69, and 70–79 years, respectively.[3]

**Table 1.** PSA value characteristics

| PSA Value Characteristics | Total | % |
|---|---|---|
| Normal (<4 ng/ml) | 27 | 71% |
| Abnormal (>4 ng/ml) | 11 | 29% |

Table 1 shows that 27 respondents (71%) had normal PSA values (<4 ng/ml) and 11 (29%) had abnormal PSA values (>4 ng/ml). PSA levels may increase after prostate manipulation (prostate biopsy, instrumentation), urinary retention with infection, and advancing age. The current standard value of PSA in Indonesia is 4 ng/ml.[5]

**Table 2.** Characteristics of Urinalysis Results of Respondents

| Urinalysis | Usual | Abnormal |
|---|---|---|
| Color | 36 (94.7%) | 2 (5.3%) |
| Ph | 38 (100%) | 0 (0%) |
| Leukocytes (urine chemistry) | 36 (94.7%) | 2 (5.3%) |
| Protein | 26 (68.4%) | 12 (31.6%) |
| Nitrite | 38 (100%) | 0 (0%) |
| Bilirubin | 38 (100%) | 0 (0%) |
| Urobilinogen | 38 (100%) | 0 (0%) |
| Glucose | 30 (79%) | 8 (21%) |
| Ketone | 38 (100%) | 0 (0%) |
| Leukocytes (microscopic) | 37 (97.3%) | 1 (2.7%) |
| Erythrocytes (microscopic) | 37 (97.3%) | 1 (2.7%) |
| Epithelium | 38 (100%) | 0 (0%) |
| Osmolality | 16 (42.1%) | 22 (57.9%) |

**Table 3.** Age and PSA Relationship

| Age | PSA | | |
|---|---|---|---|
| | Normal (<4 ng/ml) | Abnormal/increased (>4 ng/ml) | Fisher's exact test |
| 50–59 years | 19 (50%) | 6 (15.8%) | p = 0.457 |
| ≥60 years | 8 (21%) | 5 (13.2%) | |

Table 2 shows that the relationship between age and PSA value was obtained by 19 respondents (50%) aged 50–59 years with normal PSA and 6 (15.8%) aged 50–59 years with abnormal/increased PSA and by 8 respondents (21%) aged ≥60 years with normal PSA and 5 (13.2%) aged ≥60 years with abnormal/increased PSA. The data was conducted using Fisher's exact test because it did not meet the requirements for the Chi-square test. A P-value of 0.457 was obtained. There was no significant difference between

the age and PSA values of healthy adult men in respondents obtained during the November 2023 Community Service activity.

Bo et al.'s (2003) study reported that there is no correlation/relationship between PSA values and age (r = 0.947).[8] Moreover, Chang et al.'s study found that there was no significant relationship between age and PSA scores and values (p > 0.05).[9] This study reported that there was also no relationship between age and PSA scores. PSA levels are serine-kallikrein proteases that are almost entirely produced by prostate epithelial cells. In practice, PSA levels are organ-specific but not cancer-specific. Therefore, increased PSA levels are also found in BPH, prostatitis, malignant, and nonmalignant conditions and with age. Until now, there has been no agreement on the value of the standard internationally. The current standard value of PSA in Indonesia is 4 ng/ml.[13]

Although PSA values have relatively high tissue specificity, many factors affect PSA values without being related to prostate disease itself, namely, age, race, ethnicity, lifestyle, geographic region, and smoking. The upper limit of normal PSA values (4 ng/ml) is not appropriate for all ages; therefore it is recommended that there is a standard value for a specific range of normal values based on age, because age-specific PSA values are more useful for screening. Age is one of the key risk factors for prostate disease.[14]

**Table 4.** Urine Protein with PSA values

| Urine protein | PSA | | |
|---|---|---|---|
| | Normal (<4 ng/ml) | Abnormal/increased (>4 ng/ml) | Fisher's exact test |
| 0 (normal) | 18 | 8 | p = 1,000 |
| Trace s.d +4 (increased) | 9 | 3 | |

Table 6 shows that Fisher's exact test value of 1,000 is obtained, which means that there is no significant relationship between urine protein and PSA values. The causes of proteinuria can be grouped into two: physiological and pathological proteinuria. Physiological proteinuria occurs due to increased blood flow to the glomerular or increased glomerular permeability in the absence of kidney abnormalities such as prolonged standing (orthostatic, postural proteinuria), physical exercise, emotional stress, pregnancy, use of vasoconstrictor drugs, and fever. Pathological proteinuria is a protein caused by kidney abnormalities, usually occurring due to impaired glomerular filtration due to various causes.[10] BPH can also cause damage to the kidneys such as chronic kidney disease, one of the complications of BPH. High intravesical pressure in BPH patients can cause backflow from the bulbs to the ureters or vesicoureteral reflux occurs. If this situation continues, it will cause hydronephrosis leading to kidney failure.[20]

**Table 5.** Urinary Leukocytes with PSA values

| Leukosit Urin | PSA | | |
|---|---|---|---|
| | Normal (<4 ng/ml) | Abnormal/increased (>4 ng/ml) | Fisher's exact test |
| 0–20 (normal) | 27 | 10 | p = 0.289 |
| >20 (increased) | 0 | 1 | |

Table 5 shows that Fisher's exact test value of 0.289 was obtained, which shows that there is no significant relationship between urinary leukocytes and PSA values. In this study, one respondent was found with urinary leukocytes 148.4 and his PSA value increased by 10.9. Urinary leukocytes may be elevated due to infection (pyelonephritis, cystitis, urethritis) or noninfection (glomerulonephritis, dehydration, fever, SLE).[10] Leukocytes can also be elevated in BPH, due to obstruction in the bladder and urethra that causes urinary retention. This urinary retention is very risky for urinary tract infections so an increase in urinary leukocytes will be found.[16] Fujita et al.'s (2016) study found that the number of leukocytes was associated with the degree of prostate enlargement and lower urinary tract symptoms with a P-value of 0.027.[17] This is also in line with Jamil et al.'s (2018) study that there was an increase in leukocytes in patients with BPH with a value of 67.86% of benign prostate enlargement patients experiencing leukocyturia.[18] PSA may be elevated in BPH, acute prostatitis, and urinary retention accompanied by infection, after DRE procedures and after sexual activity.[1, 4] Aulia et al.'s (2018) study showed that there is a moderately significant relationship between PSA levels and the number of urinary leukocytes in BPH patients (r = 0.041).[19] Respondents of this study with PSA values of 10.9 and urinary leukocytes of 148.4 had no history and further examination of symptoms of BPH or urinary tract infection.

**Table 6.** Urinary Erythrocytes with PSA values

| Urine Erythrocytes | PSA | | |
|---|---|---|---|
| | Normal (<4 ng/ml) | Abnormal/increased (>4 ng/ml) | Fisher's exact test |
| 0–25 (normal) | 26 | 11 | p = 1,000 |
| >25 (increased) | 1 | 0 | |

Table 4 shows that Fisher's exact test value of 1,000 was obtained, which shows that there was no significant relationship between urinary erythrocytes and PSA values. In this study, one respondent was found with urine erythrocyte of 33.2 and the PSA value was normal, which was 2. Hematuria is when there are intact red blood cells in the urine. Hematuria can be caused by hemorrhages in the uropoetic tract due to kidney disease, pyelonephritis, infections, tumors, jejas or stones, abnormalities of the blood clotting process, and the use of anticoagulant drugs.[10] Hematuria can also occur due to complications from benign prostate enlargement that is usually caused by the hypervascular state of prostate enlargement that causes the surface of prostate blood vessels to become brittle and easily disturbed by physical activity.[15]

**Table 7.** Urinary Osmolality with PSA values

| Urine Osmolality | PSA | | |
|---|---|---|---|
| | Normal (<4 ng/ml) | Abnormal/increased (>4 ng/ml) | Chi-square test |
| <500 (downgrade) | 13 | 8 | p = 0.355 |
| 500–850 (normal) | 13 | 3 | |
| >850 (increased) | 1 | 0 | |

Table 7 shows that the Chi-square test value of 0.355 is obtained, which shows that there is no significant relationship between urine osmolality and PSA value. In this study, 13

respondents had decreased osmolality with normal PSA values and 8 had increased PSA values and 13 respondents also had normal osmolality with normal PSA values and 3 had increased PSA values. Only 1 respondent had increased osmolality with normal PSA values. Urine osmolality may increase in states of dehydration, syndrome of improper secretion of antidiuretic hormone, adrenal insufficiency, glycosuria, hypernatremia, and a high-protein diet. Urine osmolality may decrease in diabetes insipidus, excessive fluid intake, acute renal insufficiency, and glomerulonephritis.[21]

## Discussion

In urinalysis, namely, urine protein, urinary leukocytes, urinary erythrocytes, and urinary osmolality, there was no significant difference with the PSA value of healthy adult men at the November 2023 Community Service activity. One respondent of this study had a PSA value of 10.9 and urinary leukocytes of 148.4 has not been anamnesis and further examination of symptoms of BPH or urinary tract infection. Fujita et al.'s (2016) study found that the number of leukocytes was associated with the degree of prostate enlargement and lower urinary tract symptoms (p = 0.027). This is also in line with Jamil et al.'s (2018) study that there is an increase in leukocytes in patients with BPH. Aulia DR et al.'s (2018) study showed that there is a moderately significant relationship between PSA levels and the number of urinary leukocytes in BPH patients (r = 0.041).

## Conclusions

There was no significant difference between the age and PSA scores of healthy adult men at the November 2023 Community Service activity. Increase in PSA values was influenced by many factors such as BPH, urinary retention with infection, prostatitis, prostate cancer, prostate manipulation (prostate biopsy, instrumentation), and getting older. Further research on various factors that affect PSA values is needed to determine the relationship between age, PSA values, and urinalysis.

The limitation of this study is the small number of respondents and the need for an anamnesis of respondents' clinical complaints so that they can also associate clinical complaints with the results of PSA and urinalysis examinations.

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