

RELATIONSHIP BETWEEN AGE AND PROSTATE-SPECIFIC ANTIGEN IN AFRICAN MEN SEEKING UROLOGICAL SERVICES AT A REFFERAL HOSPITAL IN KISUMU, KENYA.

ABSTRACT

Background:As men age increases, they become prone to prostate lesions such as benign prostatic hypertrophy and prostate cancer. Cells of a prostate gland with benign prostate hypertrophy (BPH) or prostate cancer (Pca) secrete prostate specific antigen (PSA) in large amounts above the normal levels of 0-4ng/ml and thus elevated PSA is biological marker for the diagnosisof prostate cancer therefore early diagnosis using PSA facilitates disease detection; the higher the level of PSA the higher the chance to have prostate cancer (Negahdary et al., 2020; Zhang & Sun, 2018).

Methods:The main aim was to correlate the patient age and PSA level at the time of prostate specimen collection at Jaramogi Oginga Odinga Teaching and referral Hospital (JOOTRH).The study was a cross-sectional retrospective study. The target specimens in this study consisted of reported prostate specimens that had a prostate specific antigen level that were analyzed and reported between 2017 and 2022.

Comment [C.G.1]: Move to background.

Comment [C.G.2]: The study population is not clear.

Results:Majority 55 (65%) of patients who presented with high PSA levels (>4 ng/ml) were aged between 60 and 79 years old, followed by >80 years at 15 (18.75%) and 50 to 59 years at 10 (10%). Age group 40–49 did not have any patients with elevated PSA. The study sought to establish the correlation between age and PSA level. The mean age at which patients presented with elevated PSA was (60–79) years. The Pearson correlation between age and PSA levels was found to have a statistically significant positive correlation ($r = 0.236$, $p = 0.035$, 95% CI).

Conclusions:The findings of this study suggest that age and PSA have a weak positive correlation ($r = 0.283$) and higher PSA levels are likely to be observed in males aged 60 years and older who may have prostate cancer or benign prostate hyperplasia in order of occurrence.

KEY WORDS: Prostate specific antigen, prostate specimens, prostate cancer

Comment [C.G.3]: What is prostate specimen?

Introduction

Prostate cancer and benign prostate hypertrophy are common problems among aging male population that necessitate seeking for urological services. Prostate cancer is the second common cancer diagnosis made in men behind skin cancer. Globally, prostate cancer is the fifth leading cause of death and may be asymptomatic at the early stage with an indolent course (Rawla, 2019). Diagnosis of prostate malignancy is made on the underpinning of urinary tract symptoms and elevated PSA levels (>10ng/mL) which then prompts the need for biopsy to confirm the diagnosis through histological characterization. Prostate gland is regarded to be at risk of old age-related conditions such as benign prostatic hyperplasia (BPH) and carcinoma. The prostate consists of glands and stroma both of which are tightly packed within the prostate capsule. (Henry et al., 2018). The prostate has unique histological features. Histologically the prostate consists of three tissues: fibrous, muscular and glandular (Ittmann, 2018). The prostate can also be described regionally divided into four histological zones: central zone, transition zone, peripheral zone and anterior fibromuscular stroma (Bhavsar & Verma, 2014). Prostate consists of three main glandular regions that are histologically and biologically distinct; the peripheral-central zone being the transition zone. Each region of the prostate exhibits distinct histological characteristics associated with susceptibility to various prostate pathologies (McNeal, 1988). The central region is rather resistant to prostate carcinoma and other prostatic lesions so that the transition region is largely affected by benign prostatic hyperplasia. In cross section, the prostate is divided into two areas. The external and internal compartments are separated by an internal fibrous capsule (surgical capsule) (Humphrey, 2017). Carcinoma affects the peripheral zone and benign prostatic hypertrophy (BPH) affects the central region of the prostate (Gilbert et al., 2015). The main aim was to correlate the patient's age and PSA level at the time of prostate specimen collection at JOOTRH

[Add a note on PSA.](#)

METHODS

Study design

The current study was a descriptive cross-sectional retrospective study design that utilized prostate specimen histology reported in a pathology laboratory as reported between 2018 and 2022. Random sampling was used to get the specimen as reported. A sampling frame consisted of pathology register of the histopathological reports of the prostate specimens analyzed in the laboratory. Each name in the register was assigned serial numbers.

Comment [C.G.4]: Clarify the statement

Comment [C.G.5]: The methodology is not clear. The data collected is for what category of patients, BPH, CaP or Prostatitis? These pathologies increase PSA, how did the author adjust for these? Randomization is not applicable to retrospective study.

All the numbers were fed in a computer program (randomizer application) to randomly sample (determined by Yamano Taro formula) 80 names out of those so that each had an equal chance of getting selected.

Data collection

The study was conducted between December 2022 and March 2023. The researcher collected the data from hospital pathology laboratory with the help of two research assistants who were laboratory technicians working in the pathology laboratory and conversant with retrieving soft copy data from the storage site. The data from each prostate pathology report was then transferred into each data extraction form for each patient profile: the age, clinical and PSA levels.

Data analysis

Descriptive and inferential statistics were done with SPSS version 29 for Windows. Pearson correlation was used to correlate the age and prostate specific levels. A p value less than 0.05 was considered statistically significant.

Ethical consideration

This study was licensed by national commission for science, innovation and technology vide license number NACOSTI/P/23/22845. Maseno University Board of post graduate approved this study vide approval letter reference number: MSC/SM/00009/020. This study was approved by ethics committee at Jaramogi Oginga Odinga Teaching and referral hospital ethics committee vide reference number ISERC/JOOTRH/659/22. Consent to collect access data was obtained from hospital chief executive officer before prostate histology reports were retrieved from January 2017 to December 2022. All records were anonymized before print out and therefore no patient identifiers were collected during and after the study.

RESULTS

Comment [C.G.6]: Give the sample size.

Majority 55 (65%) of patients who presented with high PSA levels (>4 ng/ml) were aged between 60 and 79 years old, followed by >80 years at 15 (18.75%) and 50 to 59 years at 10 (10%) (Figure 1). Age group 40–49 did not have any patients with elevated PSA. The study sought to establish the correlation between age and PSA level. The mean age at which patients presented with elevated PSA was 62.25 (60–79) years.

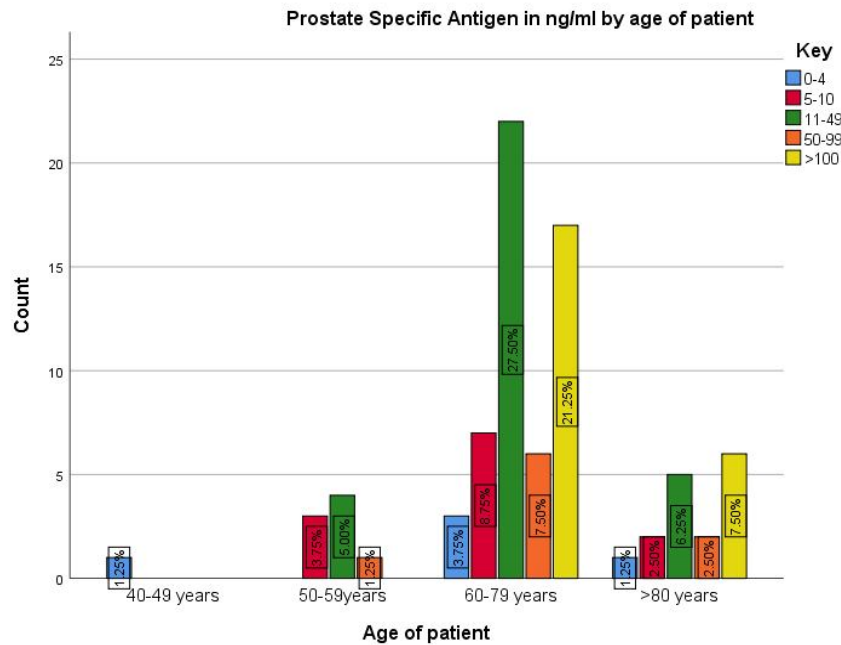


Figure 1: Prostate Specific Antigen levels by age

Comment [C.G.7]: Simplify Figure 1. it is difficult to understand.

The Pearson correlation between age and PSA levels was found to have a statistically significant positive correlation ($r = 0.236$, $p = 0.035$, 95% CI) (Table 1). Hence, H1 was supported. This shows that an increase in age would lead to an increase in PSA levels, and a high PSA level is likely to be observed in men older than 60 who may test positive for prostate cancer on a prostate biopsy.

Table 1: Patient Age and PSA Pearson correlation

		Correlations	
		PSA (ng/ml)	Age of patient
PSA (ng/ml)	Pearson Correlation	1	.236*
	Sig. (2-tailed)		.035
	N	80	80
Age of patient	Pearson Correlation	.236*	1
	Sig. (2-tailed)	.035	
	N	80	80

*. Correlation is significant at the 0.05 level (2-tailed).

DISCUSSIONS

The results of the current study indicate that PSA levels rise with age, and males aged 60 and older were likely to have higher PSA levels ranging from 11 ng/ml to greater than 100 ng/ml. The current study findings agree with Liu et al. (2020; Maciel et al. (2018), whose studies found that the PSA levels start to rise at 58 years, compared to Cihan et al. (2019), who found that the median age at which PSA levels start increasing is 63 years. The findings in the current study agree with (Cinislioglu et al., 2022; Gilbert et al., 2015b) that 30% (compared to the current 25%) of patients with high PSA test positive for cancer of prostate. The age differences in different studies (Cihan et al., 2019; Liu et al., 2020; Maciel et al., 2018) at the time PSA started rising may be an indication that race plays an important role in the PSA levels among males in relation to prostate pathology.

Although the findings of the current study agree with those of Cihan et al. (2019); Cinislioglu et al. (2022); and Gilbert et al. (2015b), it is important to note that Cihan et al. (2019) carried out a prospective descriptive study in which a decision to undergo prostate biopsy was made due to complaints of decreased urinary tract symptoms and elevated PSA between July 2019 and December 2019. These findings, however are in contrast with those of Wang et al. (2019), who found that some of the patients with low PSA levels (0–4 ng/dL) tested positive for prostate cancer. These findings could be interpreted to mean that patients with advanced prostate disease can present with low PSA levels when the function of the prostate is diminished.

The current study findings indicate that 25% of those who presented with high PSA tested positive for prostate cancer. These findings agree with Zhang and Sun (2018), and perhaps this would suggest that an increase in age would lead to an increase in PSA levels, and a high PSA level is likely to be observed in men older than 60 years who may test positive for prostate cancer on a prostate biopsy. The findings of the current study agree with Maciel et al. (2018) who found that age groups 60–69 and 70–80 show a significant association between free PSA and total PSA ($p = 0.008$). The current study findings are in agreement with other studies (Maciel et al., 2018; Matti et al., 2022; Zhang & Sun, 2018), implying that perhaps PSA is indeed an important variable that changes positively as age advances. Another explanation could be that other studies also employed retrospective cross-sectional studies similar to the current study except for variations in the study population.

Overall, the study findings suggest that age and PSA have a positive correlation ($r = 0.283$) and higher PSA levels are likely to be observed in males aged 60 years and older who may

Comment [C.G.8]: ?

Comment [C.G.9]: Incorrect statement. Do a proper literature search and give an appropriate answer.

Comment [C.G.10]: The study is on age and PSA not Prostate cancer.

have prostate cancer or benign prostate hyperplasia in order of occurrence. The current study findings, alongside other research findings (Cinislioglu et al., 2022; Kim et al., 2021; Matti et al., 2022; Negahdary et al., 2020; Zhang & Sun, 2018), point to the potential value of routine prostate evaluation in males older than 60 years who present with urinary symptoms so as to detect prostate lesions early enough. It should be kept in mind that the current study was a retrospective study that reviewed only prostate reports as opposed to prospective studies such as those by Cinislioglu et al. (2022). Further research is therefore needed to determine the extent of prostate lesions in patients who present with an elevated PSA level.

CONCLUSIONS

The findings of this study suggest that age and PSA have a weak positive correlation ($r = 0.283$) and higher PSA levels are likely to be observed in males aged 60 years and older who may have prostate cancer or benign prostate hyperplasia in order of occurrence. The research also points to the potential value of routine prostate evaluation in males aged 50-59 years who present with urinary symptoms so as to detect prostate lesions early enough. It should be kept in mind that this study was a retrospective study that reviewed only prostate reports. Further research is therefore needed to determine the extent of prostate lesions in patients who present with an elevated PSA level. Based on these conclusions, the following recommendations are made

REFERENCES

- Bhavsar, A., & Verma, S. (2014). Anatomic Imaging of the Prostate. In *BioMed Research International* (Vol. 2014). Hindawi Publishing Corporation.
<https://doi.org/10.1155/2014/728539>
- Cinislioglu, A. E., Demirdogen, S. O., Cinislioglu, N., Altay, M. S., Sam, E., Akkas, F., Tor, I. H., Aydin, H. R., Karabulut, I., & Ozbey, I. (2022). Variation of Serum PSA Levels in COVID-19 Infected Male Patients with Benign Prostatic Hyperplasia (BPH): A Prospective Cohort Studys. *Urology*, *159*, 16–21.
<https://doi.org/10.1016/J.UROLOGY.2021.09.016>
- Gilbert, R., Martin, R. M., Evans, D. M., Tilling, K., Smith, G. D., Kemp, J. P., Athene Lane, J., Hamdy, F. C., Neal, D. E., Donovan, J. L., & Metcalfe, C. (2015a). Incorporating known genetic variants does not improve the accuracy of PSA testing to identify high risk prostate cancer on biopsy. *PLoS ONE*, *10*(10).
<https://doi.org/10.1371/journal.pone.0136735>
- Gilbert, R., Martin, R. M., Evans, D. M., Tilling, K., Smith, G. D., Kemp, J. P., Athene Lane, J., Hamdy, F. C., Neal, D. E., Donovan, J. L., & Metcalfe, C. (2015b). Incorporating known genetic variants does not improve the accuracy of PSA testing to identify high risk prostate cancer on biopsy. *PLoS ONE*, *10*(10).
<https://doi.org/10.1371/journal.pone.0136735>
- Henry, G. H., Malewska, A., Joseph, D. B., Malladi, V. S., Lee, J., Torrealba, J., Mauck, R. J., Gahan, J. C., Raj, G. v., Roehrborn, C. G., Hon, G. C., MacConmara, M. P., Reese, J. C., Hutchinson, R. C., Vezina, C. M., & Strand, D. W. (2018). A Cellular Anatomy of the Normal Adult Human Prostate and Prostatic Urethra. *Cell Reports*, *25*(12), 3530-3542.e5. <https://doi.org/10.1016/j.celrep.2018.11.086>
- Humphrey, P. A. (2017). Histopathology of prostate cancer. *Cold Spring Harbor Perspectives in Medicine*, *7*(10). <https://doi.org/10.1101/cshperspect.a030411>
- Ittmann, M. (2018). Anatomy and histology of the human and murine prostate. *Cold Spring Harbor Perspectives in Medicine*, *8*(5).
<https://doi.org/10.1101/cshperspect.a030346>
- McNeal, J. (1988). *Normal Histology of the Prostate : The American Journal of Surgical Pathology*. American Journal of Surgical Pathology.
https://journals.lww.com/ajsp/Abstract/1988/08000/Normal_Histology_of_the_Prostate.3.aspx
- Negahdary, M., Sattarahmady, N., & Heli, H. (2020). Advances in prostate specific antigen biosensors-impact of nanotechnology. *Clinica Chimica Acta; International Journal of Clinical Chemistry*, *504*, 43–55.
<https://doi.org/10.1016/J.CCA.2020.01.028>
- Rawla, P. (2019). Epidemiology of Prostate Cancer. *World Journal of Oncology*, *10*(2), 63–89. <https://doi.org/10.14740/wjon1191>

Zhang, S.-J., & Sun, Z.-Y. (2018). [Correlation of prostate-specific antigen with the progression and metastasis of human prostate cancer]. *Zhonghua Nan Ke Xue = National Journal of Andrology*, 24(5), 457–461.
<https://pubmed.ncbi.nlm.nih.gov/30171764/>

UNDER PEER REVIEW