Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/27569s89

LINK BETWEEN PROSTATE CANCER PROGNOSTICATION AND PROSTATE-SPECIFIC ANTIGEN DENSITY AMONG PAKISTANI PEOPLE'S

Muhammad Wasif Saleem[1*], Shomaila Ameer Alam[1], Taqia Fouzia[2], Afshan Iftikhar[3], Syed Inayat Ali[4], Shazia Hashmat[5] and Syeda Zehra Ahmed[6]

[1*]Assistant Professor, Department of Pathology, Mekran Medical College, Turbat, Pakistan.
[2]Assistant Professor, Department of Pathology, SMBBMU lyari, Pakistan.
[3]Associate Professor, Department of Physiology, Rehman Medical College, Peshawar, Pakistan.
[4]Professor, Department of Anatomy, Baqai Medical College, karachi, Pakistan.
[5]Associate Professor, Department of Physiology, Ziauddin Medical College, Karachi, Pakistan.
[6]Assistant Professor, Department of Pathology, Ziauddin Medical College, Karachi, Pakistan.

[*]**Corresponding Author:** Muhammad Wasif Saleem
[*]Department of Pathology, Turbat, Pakistan, drwasifsaleem@outlook.com

ABSTRACT

Background: Prostate specific antigen density has been displayed as an important gizmo for prostate cancer diagnostics and prognostication.

Materials and Methods: The research was a logical cross-sectional study including 470 patients at Mekran Medical College/ Teaching Hospital with prostate specific antigen levels of > 4.0 ng/ml and typical or abnormal rectal examination findings. Prostate Specific Antigen Density was figured and transrectal ultrasound guided prostate biopsies were performed. Statistical examination was performed utilizing a SPSS version 20. Suitable test measurements including mean, standard deviation, Chi-square, t-test, Fischer's careful test, Pearson's r-test) with p-value < 0.05 considered as significant.

Results: The mean age for the patients was 55.7 + long term while the mean ages of 52.9 + 3.3 years and 65.1 + 11.3 years were for patients with non-cancer and malignant prostate lesion separately. 26.2 % were adenocarcinomas. The mean and median of Prostate Specific Antigen Density for prostate cancer were 0.31 + 0.23 and 0.31 ng/mL/cm individually. Prostate Specific Antigen Density had positive prognosticating relationship with prostate cancer risk (p=0.004) utilizing univariate logistic regression. The Area Under the Curve (AUC) and optimal cutoff point for the density was 0.9 (95% CI: 0.83-0.97) and 0.052 separately, showing solid diagnostic execution for prognosticating prostate cancer. Prostate Specific Antigen Density showed statistical significant in cancer detection (p < 0.001) with a sensitivity and false positive rate of 90.0 %, 85.0 % and 8.0 % separately.

Conclusion: A Prostate Specific Antigen Density of 0.052 ng/ml/cm can be used as a cut-off value to prognosticating prostate cancer when evaluating patients with raised Prostate Specific Antigen in Pakistani population.

Key Words: Prostate specific antigen density, Gleason score, Digital rectal examination, cancer.

INTRODUCTION

Prostate cancer stays the most well-known malignant growth among men regardless tested with late show in certain nations.[1,2] Digital rectal examinations is as yet a significant method in the determination of prostate malignant growth and shows developed nodular, hard to jagged prostate with decimated middle notch and sulci as well as fixed rectal mucosa reminiscent of dubious for prostate cancer.[3] Serum prostate-specific antigen assessment has been utilized to anticipate men who in danger of prostate cancer and decide the decision of clinical treatment in harmless prostatic hyperplasia.[4,5] In any case, convenience of prostate specific antigen is restricted by possible gamble of misleading energy or pessimism might be related with over-conclusion, under-determination, and overtreatment of prostate cancer as well as other prostatic lesions like urinary tract diseases, benign prostatic hyperplasia (BPE), intense and constant urinary maintenance, and prostatic injury from a trucut biopsy or energetic digital rectal examination might deliver raised serum prostate-specific antigen.[6,7] It is likewise relevant to feature the job of transrectal ultrasonography of prostate in expanding the discovery pace of prostate cancer among other emulating prostatic lesions close by other free symptomatic devices including transrectal ultrasound directed prostate biopsy, prostate specific antigen and digital rectal examination.[8,9]

It has been reported that prostate specific antigen density is a preferable indicator of prostate cancer over prostate specific antigen however its pertinence is in many cases moved by rare usage in everyday clinical practice throughout the long term.[10,11] Besides, prostate specific antigen density could illuminate biopsy choices, and extra a few men from the morbidity related with a prostate biopsy and finding of low grade prostate cancer as well as being utilized as a significant dynamic observation device for generally safe prostate cancer requiring revolutionary treatment at a long haul follow-up.[12.13] A document in 2020 featured the job of Prostate Specific Antigen Density in distinctive benign and malignant prostatic lesions particularly in patients with ill-defined situation of 4.0-10.0 ng/ml as prostate specific antigen wherein just 25.0 % of the cases are analyzed to have cancer, while staying 75% go through superfluous biopsies, subsequently forestalling pointless biopsies. They likewise showed that Prostate Specific Antigen Density is genuinely huge in cancer location ($p < 0.001$) with a recognition rate, sensitivity and specificity of 51.5%, 89.5% and 69.8% separately as well as a higher sensitivity (95%) at a cut-off of 0.12, demonstrating the handiness of Prostate Specific Antigen Density in prostate disease discovery among men with prostate specific antigen 4-10 ng/ml. This research is intended to discover the utility of Prostate Specific Antigen Density in anticipating prostate cancer in patients with typical or unusual Digital Rectal Examination findings and Prostate Specific Antigen > 4.0 ng/ml as well as to assess how viable these factors are in prognosticating seriousness of prostate cancer as far as Gleason score and grade group.

MATERIALS AND METHODS

A cross-sectional study which is hospital based for diagnostic test assessment of male members aged 40 years or more regardless of side effects reminiscent of obstructive uropathy, typical or strange Digital Rectal Examination and raised serum Prostate Specific Antigen (> 4.0 ng/ml). The study span was for a time of 10 months from February to December 2024. The members were seen at the different Urologic Clinics in different hospitals of Pakistan and those prepared to go through completely suggested periods of the clinical, lab and radiological evaluation were the objective populace. Informed consent was gotten from all qualified patients. Every segment datum and findings of clinical and physical assessments were reported. Five milliliters of blood tests for prostate specific antigen were gotten somewhere in the range of 08.00 and 10.00 hours in a plain bottle from the members, centrifuged at 5000 Cycles each moment and frozen at −20°C in no less than 2 hours of assortment preceding examining in the lab. Measures for prostate specific antigen were led in three groups for every one of the examples utilizing an ELISA pack (C-profiles Perfemed Inc, California, USA). The outcome was perused utilizing a microtitre-well peruser. Immunoassay quality control sera (Biorad, Hercules, CA, USA) were utilized to screen the accuracy of the outcomes. Digital rectal examination and transrectal ultrasonography of prostate organ were led on the patients and their findings archived in the proforma intended for the study.

Prostate specific antigen density was registered by isolating prostate specific antigen levels with prostatic volume acquired from transrectal ultrasonography of prostate organ. Biopsy was performed with satisfactory 12-center prostate biopsies (from right and left sidelong both ways paramedian locales in base, mid zone and apical region of prostate) on out-patient premise. The 12-center biopsy example was sent for histopathological evaluation. The histopathologic report was arranged as benign and malignant. Malignant (adenocarcinoma) was subcategorized as grade groups (Grade group 1 to grade group 5) in view of Gleason score. This was utilized to survey severity of cancer and figure out any relationship with Prostate Specific Antigen Density.

The sample size was estimated using the formula $N = Z^2 pq/d^2$ where p is derived from the study done in Lagos which is 1.046.[14,15] Hence, the sample size is 500. All statistical procedures were performed using SPSS version 20. All quantitative variables were expressed in mean and standard deviation while qualitative variables were expressed in percentages. Inferential statistics (Chi-square, t-test, Fisher's exact test, and Pearson's r-test) were utilized for exploring the association between two or more variables. Cl of 95 % was used while $p< 0.05$ was considered statistically significant. Univariate logistics analyses were performed for each independent variable and outcome. A multivariate logistic regression analyses was used to estimate adjusted odds of outcome after controlling for demographic characteristics, comorbidities, hospital teaching status, and potential confounders. Receiver operating characteristic (ROC) curves were plotted as sensitivity versus 1- specificity for Prostate Specific Antigen Density outcome. A receiver operator characteristic (ROC) curve analysis was used to evaluate the properties of the Prostate Specific Antigen Density as a predictor of prostate cancer risk and identify an optimal cutoff point for the test in this particular study population.

Inclusion criteria:

- Participants who are aged 40 years and above with or without symptomatic obstructive uropathy.
- Normal or abnormal Digital Rectal Examination and elevated serum Prostate Specific Antigen (> 4.0 ng/ml)
- Who were willing to participate in the study and signed the informed consent form.

Exclusion criteria:

- Patients on medications known to lower Prostate Specific Antigen (fiuasteride or dutasteride), receiving anticoagulant therapy a symptomatic or asymptomatic urinary tract infection, bleeding disorders, acute prostatitis before prostate biopsy and previous prostatic biopsy or prostate surgery.
- Those with contraindications to transrectal ultrasonography such as peri-anal infections and hemorrhoid's.

RESULTS

A total of 500 successive men were included in a study, of which 470 (94%) with ages going from 40 to 89 years were screened. The mean age for every one of the members was 56.5 + 3 years. 316 (67.2%) members were >50 years old, with the 50-59 years old gathering having the most elevated recurrence (32.9%). The mean, and middle ages as well as 95% Certainty stretch for members analyzed of prostate malignant growth were 65.1 + 3 years. The mean, and middle ages as well as 95% Certainty span for patients analyzed of non-cancer prostate were 52.9 + 3 years. **(Table no.1)**

TABLE NO.1: Age distribution and Type of Prostate disease among the participants

AGE GROUP	NON-CANCER PROSTATE	PROSTATE CANCER	PERCENTAGE %
40-49	140	04	144 **(30.6%)**
50-59	120	35	155 **(32.9%)**
60-69	55	45	100 **(21.2%)**
70-79	40	10	50 **(10.6%)**
80-89	15	06	21 **(4.4%)**
TOTAL	370	100	470 **(100%)**

A sum of 470 prostate tissue tests was biopsied. Of this number, 370 (78.7%) were non-cancer, while 100 (21.2 %) were carcinomas giving a carcinoma recurrence of 21.2 %. All the prostate disease cases were adenocarcinoma. Of the men with adenocarcinoma, 95% had clinically huge prostate malignant growth, the Global Society for Urological Pathologists/World Health Organization (ISUP/WHO) grade group ≥ 2 (Gleason score ≥ 7) while the leftover 5% of members had clinically irrelevant prostate disease including poor quality adenocarcinoma described by ISUP/WHO grade group 1 and Gleason score of <6. Larger part of patients with adenocarcinoma gave an exceptionally high-grade growth demonstrated by ISUP/WHO grade group 5 and summated Gleason score of 9 (n=47, 47.0 %), ISUP/WHO grade group 4 and summated Gleason score of 8 (n=17, 17.0 %) and ISUP/WHO grade bunch 5 and summated Gleason score of 10 (n=7, 7.0%). A few members gave transitional grade cancer including ISUP/WHO grade group 2 or 3 and summated Gleason score of 7 (n=17, 17.0 %) The least grade described by ISUP/WHO grade group 1 and summated Gleason score of 5 was seen among 5 patients (5.0%).

The mean and middle upsides of prostate specific antigen of members with prostate cancer were 43.2 + 34.6 ng/mL and 36.0 ng/ml separately with 95% confidence interval 36.3-50.0 ng/mL. The greater part (88.0%) of the members with prostate cancer had serum prostate specific antigen levels > 4 ng/mL. Greater part of the members had prostate specific antigen values going from 31-40 ng/ml (22.0%). The prostate specific antigen values >4.0-≤10 ng/mL was seen in 6.0% of participants, values 11-20 ng/mL were seen in 9.0% members, and values 21 - 30 ng/ml in 12.0 % of members. **(Table no.2)**

TABLE NO.2: Distribution of Prostate-specific antigen findings among participants with prostate cancer

PROSTATE SPECIFIC ANTIGEN (ng/ml)	**NUMBERS (n)**	**PERCENTAGE %**
< 4.0	12	12
4-10	06	6
11-20	09	9
21-30	12	12
31-40	22	22
41-50	08	8
51-60	04	4
61-70	05	5
71-80	04	4
81-90	-	-
91-100	10	10
101-110	02	2
111-120	04	4
121-130	02	2
TOTAL	**100**	**100**

The mean and median values of prostate volume for members with prostate cancer were 116.8 + 3378.2 cm and 98.0 cm individually with 95% confidence interval to 132.3 cm. Prostatic volume of 26.0-50 cm and 76-100 cm were the two most prevalent prostate size assessment with each comprising 18.0%. The second driving prostatic volume went from 101.0 to 125.0 cm were seen among 12.0 % of the members.

The mean and median of prostate specific antigen density were 0.31 + 0.23 ng/mL/cm and 0.31 ng/mL/cm separately with 95% confidence interval to 0.25 to 0.35 ng/mL/cm. The greater part (27.0%) of the members with prostate cancer had serum Prostate Specific Antigen density levels of 0.01-0.10 ng/mL/cm. The second and third largest number of prostate cancer members had Prostate

Specific Antigen density upsides of 0.31-0.40 ng/mL/cm (17.0 %) and 30.41-0.50 ng/ml/cm (16.0 %) **(Table no.3)**

TABLE NO.3: Distribution of Prostate-specific antigen density findings among participants with prostate cancer

PROSTATE SPECIFIC ANTIGEN DENSITY ($ng/ml/cm^3$)	**NUMBERS (n)**	**PERCENTAGE %**
0.01-0.10	27	27
0.11-0.20	11	11
0.21-0.30	12	12
0.31-0.40	17	17
0.41-0.50	16	16
0.51-0.60	4	4
0.61-0.70	4	4
0.71-0.80	9	9
TOTAL	**100**	**100**

To assesses the connections among's Prostate specific antigen density, and prostate cancer evaluating frameworks (Gleason Score and ISUP/WHO grade group), the Prostate Specific Antigen Density shows weak negative relationships with Gleason grading score (r = - 0.071) and ISUP/WHO grade bunch (r = - 0.12), demonstrating negligible relationship with prostate cancer severity, and these connections are not statistically significant. **(Table no. 4a)**

The ANOVA **(Table no. 4b)** looks at the changeability of Prostate Specific Antigen Density across Gleason scores, uncovering a critical relationship for the Prostate Specific Antigen Density (F-value: 6.83, $p<0.001$). The Prostate Specific Antigen Density was most elevated for summated Gleason score of 10 (0.5 ± 0.18) and least for score of 8 (0.13 ± 0.15), with transitional scores (5, 7, and 9) showing covering implies. This demonstrates that the Prostate Specific Antigen Density shifts altogether with prostate cancer and may assist with recognizing among Gleason scores.

This ANOVA **table 4c** assesses the relationship of Prostate Specific Antigen Density with ISUP/WHO grade group of prostate adenocarcinomas, uncovering a huge relationship for the Prostate Specific Antigen Density (F-value: 5.33, p=0.001). For the Prostate Specific Antigen Density, Prostate adenocarcinoma ISUP/WHO Grade Group 3 showed the most elevated mean (0.47±0.18), while Grade Group 4 had the least (0.13±0.15). Prostate adenocarcinoma ISUP/WHO Grade Group1, 2, and 5 showed covering implies (0.36±0.09, 0.34±0.2, and 0.3±0.24, separately), as demonstrated by shared superscripts (a, b) in **Table 4b**. This proposes that Prostate Specific Antigen Density fluctuates fundamentally with cancer grade, with unmistakable contrasts between specific groups.

Table 5 sums up univariate logistic regression results for factors anticipating cancer risk. Age (Odd Ratio [OR]: 1.10, 95% CI: 1.04-1.17, p=0.002) and Prostate Specific Antigen Density (OR: 34.43, 95% CI: 3.07-386.82, p=0.004) were positively connected with prostate cancer. Multivariate analysis adapts to co-operations between variables. Prostate Specific Antigen Density (OR:2.36, p=0.48) was not statistically significant, affirming its non-defensive impact. Age showed a pattern toward significance (OR: 1.13, p=0.09), proposing a perplexing exchange among these variables in prognosticating cancer risk (Table 5). A Receiver Operating Characteristic (ROC) examination (figure 1) shows the demonstrative diagnostic closeness of Prostate Specific Antigen Density in distinguishing prostate cancer. The Area Under the Curve (AUC) for the Prostate Specific Antigen Density was 0.9 (95% CI: 0.83-0.97), showing solid symptomatic execution for anticipating prostate cancer. The optimal cutoff point of 0.052 yielded a sensitivity of 85.0 % and a false positive rate (1-specificity) of 8.0%. Prostate Specific Antigen Density metric had p-values <0.001, affirming its factual importance and expected clinical application in distinguishing and prognosticating prostate disease.

TABLE NO. 4a: Association between Prostate Specific Antigen Density and the Grading system

VARIABLES	PROSTATE SPECIFIC ANTIGEN DENSITY	GLEASON SCORE	ISUP/WHO GRADE
Prostate specific antigen density	1		
Gleason score	-0.071	1	
ISUP/ WHO grade	-0.12	.96	1

TABLE NO. 4b: Association between Prostate Specific Antigen Density and Severity of Prostate cancer in relation to Gleason's Grading Score

VARIABLE	GLEASON SCORE	N	MEAN	F-VALUES	P-VALUES
Prostate Specific Antigen Density	5	5	0.36±0.09	6.83	<0.001
	7	24	0.42±0.2		
	8	17	0.13±0.15		
	9	47	0.28±0.24		
	10	7	0.5±0.18		

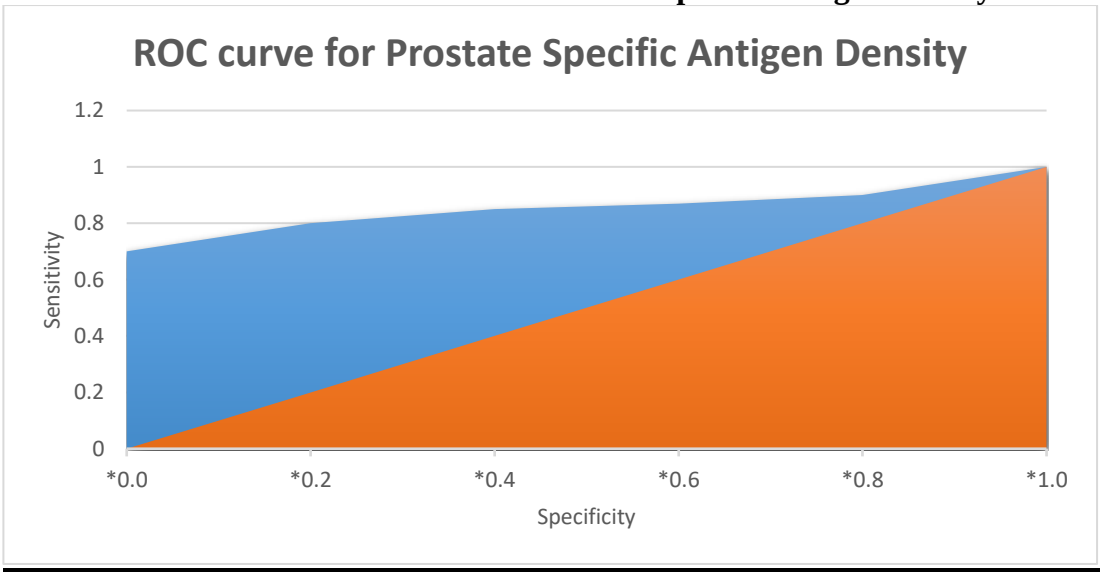
TABLE NO. 4c: Association between Prostate Specific Antigen Density and Severity of Prostate cancer in relation to ISUP/WHO Grade group

VARIABLE	ISUP/WHO Grade Group	N	MEAN	F-VALUES	P-VALUES
Prostate Specific Antigen Density	1	5	0.36±0.09	5.33	<0.001
	2	10	0.34±0.2		
	3	14	0.47±0.18		
	4	17	0.13±0.15		
	5	54	0.3±0.24		

TABLE NO. 5: Univariate and Multivariate Logistic Regression Analysis

UNIVARIATE REGRESSION ANALYSIS				MULTIVARIATE REGRESSION ANALYSIS			
Variables	**B**	**Odd Ration (95% CI)**	**P-value**	**Variables**	**B**	**Odd Ration (95% CI)**	**P-value**
Age	0.1	1.10 (1.04–1.17)	0.002	Age	0.12	1.13 (0.98-1.2)	0.09
Prostate specific antigen density	3.54	34.43 (3.07-386.8)	0.004	Prostate specific antigen density	0.86	2.36 (0.23-24.6)	0.48

FIGURE NO. 1: ROC cure for Prostate Specific Antigen Density



DISCUSSION

Prostate cancer is still of perhaps of the most well-known disease in men that is related with preventable mortality. Subsequently, prostate specific antigen density, a diagnostic device that has been displayed to assume a crucial part in determination and prognosticating prostate cancer. Acknowledgment of intriguing side effects, digital rectal examination, prostate specific antigen, transrectal ultrasonography and transrectal ultrasounds can directed prostate biopsy are correlative diagnostic boundaries alongside prostate specific antigen density for detection of prostate cancer.[16-17]

In study, the mean and median ages for every one of the members with prostate cancer was 65.1 years and 64.0 years. These discoveries concur somewhat with mean ages of 69.5 years, 52.9 years, 68.2 years and 71.3 years as well as a median age of 66 years revealed by Aisuodionoe-Shadrach in Abuja, Nigeria, Abonyo, et al in Kenya and Ngwu, et al in Uturu separately.[18,19,20] Our research showed that 98.0 % of members with prostate cancer were matured 50 years or more. Subsequently, clearly prostate cancer is bound to foster in older men, and the gamble of creating prostate cancer increments bit by bit from the age of 40 years. This declaration recommends that age actually stays the most grounded risk factor for prostate cancer independent of the geological area.[21]

In the record study, frequency of prostate cancer was 26.2% with all cases being adenocarcinoma. This recurrence is lower than 34.0%, 42.9%, 53.2%, 54.9%, 59.6%, 65.0% and 67.2% revealed by Jeon, et al in South Korea, Yusim, et al in Isreal and Sebastianelli, et al in Italy separately.[22,23,24] Then again, Ikuerowo, et al in Lagos, South-West Nigeria recorded a much lower pace of 12.6 % for prostate cancer. Most patients (95.0%) had clinically significant prostate cancer, ISUP/WHO grade group ≥ 2 (Gleason score ≥ 7) which is additionally affirmed by the after effects of our study wherein most of patients gave progressed prostate adenocarcinoma including high grade growth showed by ISUP/WHO grade group 5 and summated Gleason score of 9 (47.0%), ISUP/WHO grade group 4 and summated Gleason score of 8 (17.0 %) and ISUP/WHO grade group 5 and summated Gleason score of 10 (7.0%) at the hour of conclusion. The finding of Danacioglu, et al in Turkey, Ikuerowo, et al and Ngwu, et al in Nigeria halfway concurs with the file review with prostate adenocarcinoma ISUP/WHO grade bunch 5 being the most widely recognized growth grade. This is anyway not the same because of much lower pace of half for clinically significant prostate adenocarcinoma announced by Yusim, et al in Israel. From the previous, it very well may be shown that the clinically significant prostate adenocarcinoma with high cancer grade are definitely more normal than the clinically inconsequential prostate adenocarcinoma.[25]

The mean and median upsides of prostate-specific antigen for members with prostate cancer were 43.2 ng/mL and 36.0 ng/ml individually. Most of the members had serum prostate specific antigen levels > 4 ng/mL (88.0%) and values going from 31-40 ng/ml (22.0%). These discoveries vary from mean of 45.2 ng/ml and 94.9ng/ml revealed by Abonyo et al in Kenya and Ogbetere, etalin Auchi, Nigeria separately yet higher than worth of 5.6ng/ml announced by Amin sharifi, et al in USA.[26-27] Then again, median value of 18ng/ml recorded by Abonyo et al is a lot of lower than what was gotten in our study. As per Ikuerowo et al in Nigeria showed that 95% of members analyzed of prostate cancer had serum all out prostate specific antigen level of above10ng/L. Albeit a rising serum prostate - specific antigen level above 4.0ng/ml might act as an indicator of prostate cancer most times; this is anyway frequently tested by the possible gamble of false positivity or negativity related with resultant over-diagnosis, under-determination, and overtreatment of prostatic cancer. What's more, it has been shown that rising prostate specific antigen isn't completely limited to prostate cancer as conditions like urinary tract contaminations, benign prostate hyperplasia, intense and ongoing urinary maintenance, awful prostate biopsy, and enthusiastic advanced assessment. Accordingly, it is many times recommended that patients with raised serum prostate specific antigen level ought to be likewise have reciprocal auxiliary symptomatic examinations like prostate specific antigen thickness, transrectal ultrasonography and transrectal ultrasound check directed prostate biopsy to preclude mirroring benign prostate lesions.[28]

In the study, the mean and median values of prostate-specific antigen density were 0.31 + 330.23 ng/mL/cm and 0.31 ng/mL/cm separately with the larger part (27.0%) of the members with prostate

malignant growth having serum Prostate Specific Antigen Density levels of 0.01-0.10 ng/mL/cm. As opposed to our research, Nath, et al in Meghalaya recorded a much lower mean values of 0.15 ± 0.01 for Prostate Specific Antigen Density while Ogbetere, et al detailed a somewhat high mean value of 0.42ng/mL/cm. Besides, median values of 0.10 ng/ml/cm and 0.15 ng/ml/cm were recorded by Yusim, et al in Israel and Amin sharifi, et al in USA separately; these discoveries are anyway 50 - 60% not as much as what was gotten in our study, despite the fact that greater part of our members had serum Prostate specific antigen density levels of 0.01-0.10 3ng/mL/cm (27.0 %) that adjusts to the finding of 35.1 % of the members in a concentrate by Abonyo et al detailing level of <0.15 ng/mL/cm.[29,20,31] The distinction in discoveries might be to some degree made sense of by the various strategies involved at many focuses in examination of factors for Prostate Specific Antigen Density like prostate specific antigen and prostatic volume. The Prostate Specific Antigen Density shows frail negative correlation with Gleason grading Score (r = - 0.071) and ISUP/WHO grade group (r = - 0.12), demonstrating negligible relationship with prostate cancer severity, and these connections are not statistically significant. Members with prostate cancer showed fundamentally higher Prostate Specific Antigen Density (0.31±0.23 versus 0.05±0.06) contrasted with members with non-cancer prostatic lesions (p-values <0.001). The ANOVA investigation shows a significant relationship between the Prostate Specific Antigen Density and Gleason grading scores of prostate adenocarcinomas (F-value: 6.83, p<0.001) with the mean Prostate Specific Antigen Density value being highest for summated Gleason score of 10 (0.5 ± 0.18) and least for score of 8 (0.13 ± 0.15). This outcome shows that the Prostate Specific Antigen Density changes fundamentally with prostate cancer severity and may assist with recognizing different Gleason scores. The ANOVA examination uncovers a significant relationship between the Prostate specific antigen density and ISUP/WHO grade gathering of prostate adenocarcinoma (F-value: 5.33, p=0.001) with the prostate adenocarcinoma ISUP/WHO Grade group 3 displaying the most elevated mean of 0.47±0.18. This finding recommends that Prostate Specific Antigen Density shifts essentially with cancer grade, with particular contrasts between specific grade groups; this concurs with finding of Sebastianelli, et al, in their research.[32]

In the record study, univariate logistic regression showed positive relationship of age and Prostate Specific Antigen Density with prostate cancer (p=0.002 and p=0.004 separately) though a multivariate analysis showed that Prostate Specific Antigen Density was not genuinely connected with prostate cancer (p =0.024) contrasted with age which show a pattern towards significant relationship with prostate cancer (p = 0.09). These discoveries recommended that a complicated exchange of factors, for example, age and Prostate Specific Antigen Density in prognosticating prostate cancer risk. These discoveries concur with the aftereffects of positive correlation among's Prostate Specific Antigen Density and prostate cancer detailed by Sebastianelli, et al in Italy, Avci, et al in Turkey and Joan, et al in South Korea.[33,34] In the study, the Area Under the curve (AUC) for the density was 0.9 (95% CI: 0.83-0.97, p<0.001), showing solid diagnostic execution for prognosticating prostate cancer. As per studies led by Yanai, et al in Japan, Park, et al in North Korea, Agbo et al in Nigeria, Morote, et al in Spain, Sinan, et al in Turkey, and Zou, et al in China, region under bend of prostate specific antigen density was 0.698, 0.764, 0.84, 0.764 and 0.770 and 0.900 separately (p <0.001) for prognosticating prostate cancer.[35,36] These discoveries contrast somewhat and our research and those of Yusim, et al in Israel, with the area under curve being 0.64 (p=<0.001) for prediction of clinically significant prostate cancer. Besides, significance of Prostate Specific Antigen Density in prognosticating prostate cancer was explained by a concentrate by Presti, et al in USA. Our research recorded a density cutoff point of 0.052 ng/ml/cm with a sensitivity of 85.0 % and a false positive rate of 8.0 %. This outcome moderately adjusts with a finding of density cutoff point of under 0.08 ng/ml/cm with a 96% negative predictive value for prostate cancer in a study by Amin sharifi, et al in USA. Then again, Avci, et al in Turkey and Yanai, et al in Japan recorded the best removed upsides of density of 0.11 and 0.20 ng/ml/cm separately.[37,38]

Agbo, et al in North Focal locale of Nigeria, showed a Prostate Specific Antigen Density cutoff point of 0.12 ng/ml/cm with a sensitivity and specificity of 95.0% and 62.0% separately.[39] Abonyo, et al in Kenya detailed density of 0.23 with a sensitivity and specificity of 82.9% and 222.2%.[40] A

concentrate by Jeon, et al, in South Korea demonstrated that a prostate specific antigen density of 0.15 ng/mL/cm as the significant cutoff value for prognosticating positive target biopsy in groups with negative orderly biopsy. The changeability in density cutoff point, sensitivity and negative positive qualities detailed in the various researches could likely be illustrated to the way that fluctuated prostate specific antigen kits delivered by various organizations could have been utilized, number of clumps of prostate specific antigen tests run during the research, as well as proficiency and precision of deciding prostatic volume utilizing shifting strategies and aptitude. From the previous, clearly prostate specific antigen density worked on the presentation of prostate specific antigen to identify significant cancer (AUC 0.58 to 0.68) and any cancer (AUC 0.55 to 0.69, each $p<0.001$). Moreover, density plays had an impact in prognosticating clinically insignificant prostate cancer, and guide educated choice on conduction regarding prostate biopsy and forestall unjustifiable prostate biopsy. Albeit a higher cutoff point comparable to a higher specificity with a propensity to decrease in false positive outcomes has been recommended to diminish pointless prostate biopsy; this is anyway presented with the resultant low sensitivity that could make the more hazardous issue of passing up a major opportunity patient with cancer. Accordingly, it is relevant to adjust the factors of prostate discovery rate, particularity and negative positive values to stay away from compromise one way or another.

CONCLUSION

A moderately lower Prostate Specific Antigen Density level comparative with other tantamount examinations was gotten as the slice off worth to prognosticating prostate cancer while assessing patients with brought or typical prostate specific antigen up in our populace. Prostate specific antigen density showed measurable importance in cancer discovery with further developed identification rate, sensitivity and false positive rates.

RECOMMENDATIONS

A Prostate Specific Antigen density of 0.052 ng/ml/cm should be adopted as the cut-off value for prognosticating prostate cancer in Pakistani population.

ETHICAL APPROVAL:

Ethical approval was taken from the Review Broad of the Mekran Medical College, turbat.

PATIENT'S CONSENT:

Informed written consent was taken from each patients for participating in the study, and publication of study results.

CONFLICT OF INTEREST:

The study has no conflict of interest to declare by any author.

AUTHOR'S CONTRIBUTION:

1. Literature search, conduct of study and editing.
2. Literature search, ethical approval and manuscript writing.
3. Sampling and results writing.
4. Statistics writing.
5. Literature review and discussion editing.
6. Review and editing.

REFERENCES

1. Agbo CA, et al. Usefulness of Prostate Specific Antigen Density in Prostate Cancer Detection among Men with PSA of 4-10 ng/ml. Ann Med Health Sci Res. 2020;10: 1138-1141.
2. Abonyo C., Ndaguatha P, Owillah FA. To assess the correlation between prostate specific antigen density and prostate biopsy results of patients with raised prostatic specific antigen levels at the

Kenyatta National Hospital. East African Medical Journal.2020; 97(8):2975-2982.
3. Munteanu VC, Munteanu RA, Gulei D, Schitcu VH, Petrut B, Berindan Neagoe I, Achimas Cadariu P, Coman I. PSA Based Biomarkers, Imagistic Techniques and Combined Tests for a Better Diagnostic of Localized Prostate Cancer. Diagnostics (Basel).2020;10:806.
4. Okuja M, Ameda F, Dabanja H, Bongomin F, Bugeza S. Relationship between serum prostate specific antigen and transrectal prostate sonographic findings in asymptomatic Ugandan males. African Journal of Urology.2021;27:e58.
5. Ikuerowo SO, Omisanjo OA, Bioku MJ, Ajala MO, MordiVP, EshoJO. Prevalence and characteristics of prostate cancer among participants of a community-based screening in Nigeria using serum prostate specific antigen and digital rectal examination. Pan Afr Med.J.2013; 15:129.
6. Ogbetere FE, Irekpita E. Detection rate of prostate cancer following 12-core extended biopsy in a Semi-urban Nigerian Tertiary Hospital. Urology Annals.2021;13:150-155.
7. Soronen V, Talala K, Raitanen J, Taari K, Tammela T, Auvinen A. Digital rectal examination in prostate cancer screening at PSAlevel 3.0-3.9 ng/ml: long-term results from a randomized trial. Scand J Urol. 2021;55(5):348-353.
8. Beyer K, Moris L, Lardas M, Haire A, Barletta F, Scuderi S, et al. Diagnostic and prognostic factors in patients with prostate cancer: a systematic review protocol. BMJ Open. 2021;11:e040531.
9. Mensah JE, Akpakli E, Kyei M, Klufio K, Asiedu I, Asante K, et al. Prostate-specific antigen, digital rectal examination, and prostate cancer detection: Astudy based on more than 7000 transrectal ultrasound-guided prostate biopsies in Ghana. Translational Oncology;2024; 51:102163.
10. Ying Y, He W, Xiong Q, Wang Z, Wang M, Chen Q, et al. Value of digital rectal examination in patients with suspected prostate cancer: a prospective cohort analysis study. Transl Androl Urol.2023;12(11):1666-1672.
11. Zhu J, Wu X, Xue Y, Li X, Zheng Q, Xue X, et al. Prospective analysis of the diagnostic accuracy of digital rectal examination and magnetic resonance imaging for T staging of prostate cancer. J Cancer Res Ther. 2023;19(4):1024-1030.
12. Sarkar D, Jain P, Gupta P, Pal DK. Correlation of digital rectal examination and serum prostate-specific antigen levels for detection of prostate cancer: Retrospective analysis results from a tertiary care urology center. J Cancer Res Ther. 2022;18(6):1646-1650.
13. Elijah A. Udoh, Okon E. Akaiso, Albert E. Uk pong. Accuracy of digital rectal examination to diagnose prostate cancer confirmed by needle biopsy reports: A 3–year hospital-based study. Ibom Medical Journal.2020;13(3):156-163.
14. Bouras, S. Digital rectal examination in prostate cancer screening: a critical review of the ERSPC Rotterdam study. Afr J Urol. 2023;30, 51:1-6.
15. Morote J, Paesano N, Picola N, Muñoz-Rodriguez J, Ruiz-Plazas X, Muñoz-Rivero MV, et al. The Role of Digital Rectal Examination for Early Detection of Significant Prostate Cancer in the Era of Magnetic Resonance Imaging. Life. 2024; 14(11):1359.
16. Matsukawa A, Yanagisawa T, Bekku K, Parizi MK, Laukhtina E, Klemm J, et al. Comparing the performance of digital rectal examination and prostate-specific antigen as a screening test for prostate cancer: a systematic review and meta-analysis. European Urology Oncology. 2024; 7 (4):697-704.
17. Krilaviciute A, Becker N, Lakes J, Radtke JP, Kuczyk M, Peters I, et al.. Digital Rectal Examination Is Not a Useful Screening Test for Prostate Cancer. European Urology Oncology, 2023; 6(6):566-573.
18. Aisuodionoe-Shadrach OI, Eniola SB, Nwegbu MM, Kolade-Yunusa HO, Okereke OO, Yunusa T. Determination of Serum Prostate Specific Antigen Levels Amongst Apparently Healthy Nigerian Males in a University and University Hospital Community in the Federal Capital Territory. Cancer Control.2022; 29:10732748221081366.
19. Mumuni S, O'Donnell C, Doody O. The Risk Factors and Screening Uptake for Prostate Cancer:

A Scoping Review. Healthcare(Basel).2023;11(20):2780
20. Cirulli GO, Davis M, Stephens A, Chiarelli G, Finati M, Corsi N, et al. Impact of Prostate-Specific Antigen Screening Pattern on Prostate Cancer Mortality Among Non-Hispanic Black and Non-Hispanic White Men: A Large, Urban Health System Cohort Analysis. J Urol. 2024;212(4):560-570.
21. Hamdy FC. Prostate-Specific Antigen Testing for Prostate Cancer Screening-Is the Message Getting Through? JAMA Oncol. 2022; 8(1):47-49.
22. Narain TA, Sooriakumaran P. Beyond Prostate Specific Antigen: New Prostate Cancer Screening Options. World J Mens Health. 2022;40(1):66-73.
23. Ko, YH, Kim BH, Jung W, Ha JY, Shin TJ, Kwon SY, et al. Delaying a Biopsy With Serial Prostate-Specific Antigen Checkup Helps to Identify a Significant Prostate Cancer: A Strategy to Evade UnnecessaryProcedures.JUrolOncol.2022;20(3):177-185.
24. Tidd Johnson A, Sebastian SA, Co ELF, Afaq M, Kochhar H, Sheikh M, et al. Prostate cancer screening: continued controversies and novel biomarker advancements. Curr Urol. 2022;1–10.
25. Ngwu PE, Achor GO, Eziefule VU, Orji JI, Alozie FT. Correlation between Prostate Specific Antigen and Prostate Biopsy Gleason Score. Annals of Health Research. 2019; 5:243-248.
26. Chang TH, Lin WR, Tsai WK, Chiang PK, Chen M, Tseng JS, et al. Zonal adjusted PSA density improves prostate cancer detection rates compared with PSA in Taiwanese males was with PSA< 20 ng/ml. BMC Urol.2020;20(1):151.
27. Park DH, Yu JH. Prostate-specific antigen density as the best predictor of low- to intermediate-risk prostate cancer: a cohort study. Transl Cancer Res 2023;12(3):502-514.
28. Erdogan A, Polat S, Keskin E, Turan A. Is prostate volume better than PSA density and free/total PSA ratio in predicting prostate cancer in patients with PSA2.5-10 ng/mL and 10.1-30 ng/mL? Aging Male. 2020;23(1):59-65.
29. Zou BZ, Wen H, Luo HJ, Luo WC, Xie QT, Zhou MT. Value of serum free prostate-specific antigen density in the diagnosis of prostate cancer. Ir J Med Sci. 2023;192(6): 2681-2687.
30. Zhang Q, Li H, Song Z, Kong S, Zhao S, Fan S, Qin F, Ma J. Potential diagnostic value of multiple indicators combined with total prostate-specific antigen in prostate cancer. J Int Med Res. 2023;51(10):3000605231204429.
31. Omri N, Kamil M, Alexander K, Alexander K, Edmond S, Ariel Z, et al. Association between PSA density and pathologically significant prostate cancer: The impact of prostate volume. Prostate2020;80(16):1444-1449.
32. Nath C, Barman B, Phukan P, Sailo SL, Dey B, Nath I, et al, Prostate-Specific Antigen Density: A Measurement to Differentiate Benign Hypertrophy of Prostate from Prostate Carcinoma. Journal of Laboratory Physicians. 2020;12(1):44-48.
33. Yusim I, Krenawi M, Mazor E, Novack V, Mabjeesh NJ. The use of prostate specific antigen density to predict clinically significant prostate cancer. Sci Rep.2020;10(1):20015.
34. Arafa MA, Farhat KH, Rabah DM, Khan FK, Mokhtar A, Al-Taweel W. Prostate-specific Antigen Density as a Proxy for Predicting Prostate Cancer Severity: Is There Any Difference between Systematic and Targeted Biopsy? Saudi J Med Med Sci.2023;11(4):299-304.
35. Drevik J, Dalimov Z, Uzzo R, Danella J, Guzzo T, Belkoff L, et al. Utility of PSA density in patients with PI-RADS 3 lesions across a large multi-institutional collaborative. UrolOncol.2022;40(11):490.e1-490.e6.
36. Rajendran I, Lee KL, Liness Thavaraja L, Barrett T. Risk stratification of prostate cancer with MRI and prostate-specific antigen density-based tool for personalized decision making, British Journal of Radiology. 2024; 97(1153):113–119.
37. Avci S, Çağlayan V, Önen E, Kiliç M,Gül A, Öner S. The effectiveness of prostate specific antigen density in predicting prostate cancer and clinically significant prostate cancer in patients aged 70 year sandover. Turkish Journal of Geriatrics.2020;23(2):197-205.
38. Zou, BZ., Wen, H., Luo, HJ. et al. Value of serum free prostate-specific antigen density in the diagnosis of prostate cancer. Ir J Med Sci. 2023;192:2681–2687.
39. Danacioglu, YO, Keser, F, Efiloğlu, Ö, Culpan, M., Polat, S., Atis, R. G., & Yildirim, A. The

efficiency of prostate-specific antigen density measurement using three different methods on the prediction of biochemical recurrence. The Aging Male.2021;24(1):15–23.

40. Presti JC Jr, Hovey R, Carroll PR, Shinohara K. Prospective Evaluation of Prostate Specific Antigen and Prostate Specific Antigen Density in the Detection of Non palpable and Stage T1C Carcinoma of the Prostate. Journal of Urology [Internet]. 2024;156(5):1685–90.