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Urology

PROPORTION OF PROSTATIC CANCER IN PATIENTS WITH PROSTATE-SPECIFIC ANTIGEN MORE THAN 4 NG/ML IN INDIAN POPULATION – A CROSS-SECTIONAL STUDY FROM TERTIARY HEALTH CARE CENTRE.

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ABSTRACT **Objective:** To estimate the proportion of prostate cancer and to assess the association between prostate specific antigen level with diagnosis, tumour aggressiveness and bony metastasis in patients with prostate-specific antigen more than 4 ng/ml. **Method:** It is a Hospital based descriptive cross-sectional study in the Department of Urology, Government Medical College, Thiruvananthapuram. **Results:** Total 110 patients were analysed for TRUS guided prostate biopsy. Mean age of the patients was 69.79 ± 7.3 years. Of these patients, 30% were diagnosed with prostate cancer, with the proportion of prostate cancer increasing with higher PSA levels, reaching 100% in those with PSA levels over 100ng/mL. We also found a positive correlation between PSA levels and the incidence of skeletal metastasis . The study found that the proportion of patients with PSA levels between 4.1 to 10 ng/mL, 10.1 to 20 ng/mL, and 20.1 to 50 ng/mL was significantly lower in patients with a Gleason score greater than 7 compared to those with a score of 7 or less. In our study, we found that the mean±SD of Free/Total (%) PSA in benign prostatic hyperplasia (BPH) was 20.56±4.4, which was significantly higher than in prostate cancer (CA prostate) (10.77±1.46) with a p-value of <.0001. **Conclusion:** In our research, we have found a significant association between PSA levels and the likelihood of being diagnosed with prostate cancer, as well as the aggressiveness of the tumor, the extent of local spread, and the presence of skeletal metastases. Our results indicate that the proportion of prostate cancer is about 30%. Furthermore, our study reveals that when PSA levels exceed 50 ng/mL, the probability of a prostate cancer diagnosis is higher than that of benign prostatic hyperplasia (BPH).

KEYWORDS : Prostate Cancer , PSA, TRUS.

INTRODUCTION

The prevalence of prostate cancer is increasing in asia.[1-4] Prostate cancer Incidence varies by race/ ethnicity, with African-Americans experiencing a 73% higher incidence rate than whites.[5] Currently, common tool for diagnosis of prostate cancer are prostate-specific antigen (PSA) and Digital rectal examination (DRE). Combination of both DRE and PSA leads to greater detection of prostate cancer. If abnormal results are shown either or both tests, biopsy is indicated for a tissue diagnosis of prostate cancer. The high sensitivity and low specificity of PSA testing in diagnosis of prostate cancer is problem in clinical practice.[6-9] Use of PSA testing alone has reduced specifically owing to the influence of prostate volume and other factors such as infection and manipulation. Even with this disadvantage, however, PSA measurement is still used in clinical practice given that no new biomarker are currently accepted for diagnosis of prostate cancer. The general cut-off for the PSA level is 4ng/ml. With the use of this cut-off, the cancer detection rate ranges from 35% to 42.3% for 10-12 core biopsy.[10-12] A greater PSA level may relate to a greater likelihood of positive tissue diagnosis, a higher Gleason score, and a greater likelihood of bone metastasis

METHODS

This descriptive cross sectional study was conducted at Department of Urology in Government Medical College, Thiruvananthapuram between August 2022 to May 2023 to estimate proportion of prostate cancer in patients with prostate specific antigen more than 4 ng/ml. Patients who met the following criteria were included in study group: with age more than 50 years with lower urinary tract symptoms and PSA more than 4 ng/ml, age less than 50 years with family history of prostate cancer.

Patients in the Department of Urology who have undergone Prostatic biopsy with repeat PSA greater than 4 ng/ml. All patients who will undergo prostatic biopsy, intravenous cefoperazone and sulbactam-wasgiven 1 hour prior to the procedure. After biopsy oral cephalosporin was prescribed for 5 days. Per rectal/ Trans rectal ultra sound guided biopsy was performed by using biopsy needle (20 cm, 18G) From 12 different points of basal, middle lobe, apex, right and left lobe of the prostate. It was tried to sample from the peripheral area of the above points where the cancer risk is more than other areas. In the next visit, according to their pathology findings further investigation like Magnetic resonance imaging and Bone scan was advised according to standard protocol. Patient's details like name, age, PSA level, biopsy findings, Gleason score, MRI findings and bone scan findings was recorded in proforma. The patients was divided into subgroups by baseline PSA level as follows: 4.1-10, 10.1-20, 20.1-50, 50.1-100 and more than 100.

Data was entered into Microsoft excel and analysed using SPSS ver 25.0. Quantitative variables was summarized as mean and standard deviation, median and inter quartile range. Qualitative variables such as frequency, percentage and 95% confidence intervals was calculated. Chi square test of significance was done to find out the association between PSA levels with diagnosis, tumour aggressiveness and bone metastasis.p value less than 0.05 was considered significant.

RESULTS

Out of 110 patients, 54(49.09%) patients belonged to age group 61-70 years, 35(31.82%) to age group 71-80 years, 11(10.00%) to age group 51-60 years. Age group 81-90 years had only 10 out of 110 patients (9.09%).Mean value of age (years) of study subjects was 69.79 ± 7.3. A positive biopsy result was found in 33 patients (30 %). In this study we found association of PSA with final diagnosis. PSA corresponded very well with prostate cancer diagnosis. In patients group with PSA 4.1 to 10,10.1 to 20,20.1 to 50,50.1 to 100,more than 100 ng/ml, proportion of prostate cancer was 12.5%,17.6 %,19.04%,73.3% and 100% respectively. In our study there was significant association of PSA level with aggressiveness of cancer. Median (25th-75th percentile) of PSA in Gleason score >7 was 100 which was significantly higher as compared to Gleason score <=7 (p value <0.0001). we found significant association of skeletal metastasis with PSA level. Median of PSA level in patients with skeletal metastasis was 123 which was significantly higher as compared to patients without skeletal metastasis. (p value <0.0001).

Table 1:- Association Of PSA Level With Diagnosis

PSA level (ng/mL)	BPH(n=77)	CA prostate (n=33)	Total	P value
4.1 to 10	28 (36.36%)	4 (12.12%)	32 (29.09%)	<.0001*
10.1 to 20	28 (36.36%)	6 (18.18%)	34 (30.91%)	
20.1 to 50	17 (22.08%)	4 (12.12%)	21 (19.09%)	
50.1 to 100	4 (5.19%)	11 (33.33%)	15 (13.64%)	
>100 ng/mL	0 (0%)	8 (24.24%)	8 (7.27%)	

‡ Mann Whitney test, * Fisher's exact test

Table 2:- Association Of PSA With Different Variables

PSA level	Skeletal metastasis	Locally advanced	Gleason score	P value

	Present	Absent	Yes	No	>7	<=7	
4.1 to 10	0 (0%)	4 (21. 05%)	0 (0%)	4 (23. 53%)	0 (0%)	4 (23. 53%)	0.0001
10.1 to 20	0 (0%)	7 (36. 84%)	0 (0%)	7 (41. 18%)	0 (0%)	7 (41. 18%)	0.0001
20.1 to 50	1 (7. 14%)	3 (15. 79%)	1 (6. 25%)	3 (17. 65%)	1 (6. 25%)	3 (17. 65%)	0.0001
50.1 to 100	6 (42. 86%)	5 (26. 32%)	8 (50 %)	3 (17. 65%)	8 (50%)	3 (17. 65%)	0.0001
>100	7 (50%)	0 (0%)	7 (43. 75%)	0 (0%)	7 (43. 75%)	0 (0%)	0.0001
Mean ± SD	155.59 ± 95.79	34. 28 ± 32.79	146. 89 ± 92.41	28. 2 ± 28.57	145.76 ± 93.22	29.27 ± 30.68	0.0001
Median(25th-75th percentile)	123 (88.75-199.5)	17.66 (12.2-52.7)	100 (83.25-198.5)	17.65 (10.4-26)	100 (82.5-198.5)	17.65 (10.4-26)	0.0001

In prostate cancer patients mean free/total percent PSA was 10.77 %, which was significantly lower than BPH patients.

DISCUSSION

Prostate cancer diagnosis commonly relies on the use of Digital Rectal Examination (DRE) and Prostate-Specific Antigen (PSA) testing. Since the introduction of PSA testing in 1986, there have been changes in screening practices resulting in earlier detection and treatment of prostate cancer, leading to an overall increase in survival rates [5-8]. The usefulness of PSA testing has been demonstrated in early diagnosis, assessing treatment response, and determining tumour progression [11-13]. However, there are limitations to PSA testing, including the risk of over diagnosis and negative biopsies due to poor specificity. Other conditions such as prostatic hyperplasia, prostatitis, and recent ejaculation can also affect PSA levels, and a PSA level above 4.0 ng/mL is generally considered the cut-off point for further investigation [14].

In a study using PSA levels to identify non-organ-confined disease, the incidence of extra prostatic extension was found to increase with higher PSA levels [15]. Free PSA is typically lower in prostate cancer than in benign prostatic hyperplasia, and a ratio of free PSA to total PSA (%fPSA) greater than 25% lowers the chance of prostate cancer compared to a %fPSA less than 10% [16].

In our study, we examined 110 patients with PSA levels above 4ng/ml, with a mean age of 69.79±7.3 years. Of these patients, 30% were diagnosed with prostate cancer, with the proportion of prostate cancer increasing with higher PSA levels, reaching 100% in those with PSA levels over 100ng/mL. We also found a positive correlation between PSA levels and the incidence of skeletal metastasis.

In a study by Singh et al., a positive relation was found between PSA levels and the incidence of bone metastasis [17]. Similarly, Chybowski et al documented that the PSA level was correlated with the risk of bone metastasis in 521 patients [18]. In both studies, the PSA concentration was found to be the best predictor for bone metastases among other clinical and pathological parameters. However, the incidence of positive bone metastases with lower serum PSA levels in Singh et al.'s study was much higher than in the United States and Canada .

The study conducted by Lojanipiwat et al [19]. found that the prostate-specific antigen (PSA) level is significantly associated with locally advanced prostate cancer and tumor aggressiveness. The study also found that abnormal findings on a digital rectal exam (DRE), such as the presence of a hard nodule, are significantly associated with a higher proportion of patients diagnosed with prostate cancer.

Specifically, the study found that the proportion of patients with a PSA level between 50.1 and 100 ng/mL and greater than 100 ng/mL was significantly higher in patients with locally advanced prostate cancer compared to those without (50% vs. 17.65% and 43.75% vs. 0%, respectively). The median PSA level in patients with locally advanced disease was 100 ng/mL (83.25-198.5), which was significantly higher than the median PSA level in patients without locally advanced disease (17.65 ng/mL, 10.4-26) (p-value < .0001).

Regarding tumor aggressiveness, the study found that the proportion of patients with PSA levels between 4.1 to 10 ng/mL, 10.1 to 20 ng/mL, and 20.1 to 50 ng/mL was significantly lower in patients with a Gleason score greater than 7 compared to those with a score of 7 or less (0% vs. 23.53%, 0% vs. 41.18%, and 6.25% vs. 17.65%, respectively). The same pattern was observed in patients with a PSA level between 4.1 to 10 ng/mL, 10.1 to 20 ng/mL, and 20.1 to 50 ng/mL, where the proportion of patients with lower PSA levels was significantly lower in those with a Gleason score greater than 7 compared to those with a score of 7 or less (0% vs. 23.53%, 0% vs. 41.18%, and 6.25% vs. 17.65%, respectively) (p-value < 0.0001).

Additionally, the study found that the proportion of patients diagnosed with prostate cancer was significantly higher in those with abnormal DRE findings, such as a hard nodule, compared to those without (96.43% vs. 7.32%). The proportion of patients with PSA levels between 50.1 to 100 ng/mL and greater than 100 ng/mL was also significantly higher in patients with abnormal DRE findings compared to those without (35.71% vs. 6.10% and 25% vs. 1.22%, respectively). The median PSA level in patients with abnormal DRE findings was 78.65 ng/mL (21.74-111.5), which was significantly higher than the median PSA level in patients without abnormal DRE findings (12.1 ng/mL, 8.675-21) (p-value < .0001).

Similar studies have also found an association between PSA levels and the diagnosis and aggressiveness of prostate cancer. A study by Makarov et al.[20] found that higher PSA levels were associated with a greater risk of prostate cancer mortality, and a study by Ross et al.[21] found that PSA screening was associated with a lower risk of prostate cancer mortality.

In our study, we found that the mean±SD of Free/Total (%) PSA in benign prostatic hyperplasia (BPH) was 20.56±4.4, which was significantly higher than in prostate cancer (CA prostate) (10.77±1.46) with a p-value of <.0001 (Table 7). Our findings support those of Catalona et al. [22], who included a total of 773 men (379 with prostate cancer and 394 with benign prostatic disease) aged 50 to 75 years with a palpably benign prostate gland, PSA level of 4.0 to 10.0 ng/mL, and histologically confirmed diagnosis. They found that a 25% free PSA cutoff detected 95% of cancers while avoiding 20% of unnecessary biopsies and cutoff of 25% or less free PSA is recommended for patients with PSA values between 4.0 and 10.0 ng/mL and a palpably benign gland, regardless of patient age or prostate size.

Additionally, we compared our results to those of Lojanipiwat et al.,[19] who conducted a retrospective study among 1116 patients who underwent TRUS-guided prostate biopsy. The patients were divided into subgroups by baseline PSA level as follows: ≤4, 4.1–10, 10.1–20, 20.1–50, 50.1–100, and >100 ng/mL. A positive biopsy result was found in 395 patients (35.39%). The PSA level corresponded well with the diagnosis of prostate cancer and a positive bone scan, but moderately well with Gleason score as shown by AuROC for diagnosis of prostate cancer (0.82), positive bone scan (0.88), and Gleason score >7 (0.78). The specificity of a PSA level of 4.1– 10, 10.1–20, 21.1–50, 50.1–100, and >100 ng/mL in the diagnosis of prostate cancerwas 9.3, 55.5, 87.5, 98.2, and 99.7, respectively. They concluded that there was a strong correlation of PSA level with tumor diagnosis, tumor aggressiveness, and bone metastasis. The prevalence of prostate cancer in this cohort was 35.39%. The chance of a diagnosis of prostate cancer was greater than that for benign prostatic hyperplasia when the PSA level was higher than 20 ng/mL.

In another study, Boegemann M et al compared the diagnostic accuracy of PSA and prostate health index (PHI) for detecting prostate cancer [23]. They found that PHI had a higher diagnostic accuracy than PSA and could improve the detection of prostate cancer in patients with PSA levels between 2-10ng/ml. Similarly, in a study by Wei et al., a panel of plasma miRNAs was found to be a potential non- invasive biomarker for early detection and prognosis of prostate cancer, with better sensitivity and specificity than PSA alone [24].

In summary, while PSA testing is a useful tool for the early detection and management of prostate cancer, it has limitations, including poor specificity and the risk of overdiagnosis. Other biomarkers such as PHI and plasma miRNAs may provide better diagnostic accuracy and are promising areas of future research.

REFERENCES

1. Baade PD, Youlden DR, Cramb SM, Dunn J, Gardiner RA, Epidemiology of prostate cancer in the Asia-Pacific region. Prostate Int 2013;1:47-58.
2. Ito K prostate cancer in Asian men. Nat Rev Urol 2014;11:197-212.
3. Nomura AM, Kolonel LN, Prostate cancer: a current perspective. Epidemiol Rev 1991;13:200-27.

4. Williams S, ChiongE,Lojanpiwat B, Umbas R, Akaza H; Asian oncology summit2013. Management of prostate cancer in Asia: resource stratified guidelines from Asian oncology summit 2013. Lancet Oncol 2013;14e524-34.
5. Siegel R, Ma J, Zou et al:Cancer statistics, 2014, CA cancer J Clin 64(1):9- 29,2014.
6. Thompson IM, Ankrest DP. Prostate-specific antigen in early detection of prostate cancer.CMAJ 2007;176:1853-8.
7. Roobol MJ, Kranse R, Bangma CH, van Leenders AG, Blijenberg BG, van Schaik RH, et al. Screening of prostate cancer:results of Rotterdam section of the European Randomised study of screening for prostate cancer. EurUrol 2013;64:530-9.
8. Schroder FH, van der Mass P, Beemsterboer P, Kruger AB, Hoedmaeker R, Rietbergen J, et al. Evaluation of the digital rectal examination as a screening test for prostate cancer. J Natl cancer Inst 1998;90:1817-23.
9. Schroder FH, Carter HB, Wolters T, van der bergh RC, Gosselaar C, Bangma CH, et al. Early detection of prostate cancer in 2007. Part1: PSA and PSA kinetics. EurUrol 2008;53:468-77.
10. Mistry K, Cable G. Meta-analysis of Prostate- specific antigen and digital rectal examination as screening tests for prostate carcinoma. J Am Board FamPract 2003;16:95-101.
11. Obort AS, Ajadi MB, Akinloye O. Prostate –specific antigen: any successor in sight? Rev Urol 2013;15:97-107.
12. Parkin DM, Bray F, Ferlay J, Pisani P. Global cancer statistics, 2002. CA Cancer J Clin. 2005 Apr;55(2):74–108.
13. Coleman MP, Quaresma M, Berrino F, Lutz J-M, De Angelis R, Capocaccia R, et al. Cancer survival in five continents: a worldwide population-based study (CONCORD). Lancet Oncol. 2008 Aug;9(8):730–56.
14. Oesterling JE, Rice DC, Glenski WJ, Bergstralh EJ. Effect of cystoscopy, prostate biopsy, and transurethral resection of prostate on serum prostate- specific antigen concentration. Urology 1993;42:276-82.
15. Partin AW, Pearson JD, Landis PK, Carter HB, Pound CR, Clemens JQ, et al. Evaluation of serum prostate-specific antigen velocity after radical prostatectomy to distinguish local recurrence from distant metastases. Urology 1994;43:649-59.
16. Benson MC, Whang IS, Pantuck A, Ring K, Kaplan SA, Olsson CA, et al. Prostate specific antigen density: a means of distinguishing benign prostatic hypertrophy and prostate cancer. J Urol 1992;147(3 Pt 2):815-6.
17. Singh O P, Yogi V et al, Role of serum prostate-specific antigen as predictor for bone metastases in newly diagnosed prostate cancer.Journal of Cancer Research and Therapeutics 2019 15(1):39-41
18. Chybowski FM, Keller JJ, Bergstralh EJ, Oesterling JE. (1991) Predicting radionuclide bone scan findings in patients with newly diagnosed, untreated prostate cancer: Prostate specific antigen is superior toall other clinical parameters. J Urol; 145: 313-8.
19. Lojanapiwat B, Anutrakulchai W, Chongruksut W, Udomphot C. Correlation and diagnostic performance of the prostate-specific antigen level with the diagnosis, aggressiveness, and bone metastasis of prostate cancer in clinical practice. Prostate Int. 2014 Sep;2(3):133-9.
20. Makarov DV, Trock BJ, Humphreys EB, Mangold LA, Walsh PC, Epstein JI, Partin AW. Updated nomogram to predict pathologic stage of prostate cancer given prostate-specific antigen level, clinical stage, and biopsy Gleason score (Partin tables) based on cases from 2000 to 2005. Urology. 2007 Jun;69(6):1095-101.
21. Ross KS, Carter HB, Pearson JD, Guess HA. Comparative efficiency of prostate-specific antigen screening strategies for prostate cancer detection. JAMA. 2000 Sep 20;284(11):1399-405.
22. Catalona WJ, Partin AW, Slawin KM, Brawer MK, Flanigan RC, Patel A, Richie JP, deKernion JB, Walsh PC, Scardino PT, Lange PH, Subong EN, Parson RE, Gasior GH, Loveland KG, Southwick PC. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. JAMA. 1998 May 20;279(19):1542-7.
23. Boegemann M, Stephan C, Cammann H, Vincendeau S, Houlgatte A, Jung K, Blanchet JS, Semjonow A. The percentage of prostate-specific antigen (PSA) isoform [-2]proPSA and the Prostate Health Index improve the diagnostic accuracy for clinically relevant prostate cancer at initial and repeat biopsy compared with total PSA and percentage free PSA in men aged ≤65 years. BJU Int. 2016 Jan;117(1):72-9.
24. Wei J, Gao W, Zhu CJ, Liu YQ, Mei Z, Cheng T, Shu YQ. Identification of plasma microRNA-21 as a biomarker for early detection and chemosensitivity of non-small cell lung cancer. Chin J Cancer. 2011 Jun;30(6):407-14. doi: 10.5732/cjc.010.10522. PMID: 21627863; PMCID: PMC401341