OCCURRENCE OF CARCINOMA PROSTATE IN DIFFERENT LEVELS OF SERUM PSA ≥ 2.5 NG/ML IN BANGLADESH

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Abstract

Background: *Prostate cancer is the most common cancer in men. Serum prostate-specific antigen (PSA) is the screening test for the prostate cancer. This test is usually done for the first step in any prostate cancer diagnosis. Prostate biopsy is the procedure for final diagnosis of carcinoma prostate.*

Objective: *To detect the occurrence of prostate cancer at different level of serum PSA ≥2.5ng/ml*

Method: *This hospital based cross sectional analytical study was conducted between the periods of January 2012 to April 2013. A total of 105 patients with features of lower urinary tract symptoms with enlarged prostate attending to the Department of Urology, National Institute of Kidney Diseases & Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka were purposively selected as study population. Patients more than 50 years old with lower urinary tract symptoms at S. PSA level ≥ 2.5 ng/ml and enlarged prostate in DRE were selected as study population. Patients with bleeding disorder, anorectal pathology, active UTI or prostatitis or urethral stricture were excluded from this study. DRE was done to see the size, consistency and nodularity of prostate. Those who had enlarged prostate found on DRE having S. PSA levele" 2.5 ng/ml, they were sent for biopsy.*

Result: *The mean age of the patients was 66.87±10.13 years with a range of 51-92 years. Among 105 patients 19 (18.10%) were in the age group of 51-60 years, 35 (33.33%) were in the age group of 61 - 70 years, 27 (25.71%) were in the age group of 71 - 80 years and 24 (22.86%) were in the age group >80 years. Among 105 patients 45 (42.9%) had malignant lesion and 60 (57.10%) had benign lesion. Mean serum PSA level among the patients with histopathological findings benign and malignant were 7.87±5.18 and 27.42±22.25 ng/ml respectively. Out of 45 patients with malignant lesion, 3(16.7%) had serum PSA level within 2.50-2.99 ng/ml, another 5(14.3%) had 4.00-9.99 ng/ml, 11(56.0%) had serum PSA level within 10.00-20.00 ng/ml and 26(57.8%) There is a statistically significant difference observed in serum PSA level among the patients with histopathological findings benign and malignant (P<0.001).*

Conclusion: *For early diagnosis of prostate cancer cut-off value of serum PSA≥ 2.5 ng/ml may be used as an indication for prostate biopsy.*

Key words: *Prostate cancer, PSA (prostate-specific antigen), cut-off value, prostate biopsy*

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Introduction

Prostate cancer is the most common and the second leading cause of male deaths in the United States. A number of 30,068 African Americans were diagnosed as new cases of prostate cancer, 15,950 in Caribbean islands and 39,460 in Africa[1]. In Korea, 202,053 cases and 72,046 deaths occurred during 2010 with 960,654 prevalent cancer cases identified by January 2011[2]. The estimated lifetime risk of disease incidence is 17.6% for Whites and 20.6% for African Americans, with a lifetime risk of death of 2.8% and 4.7% respectively[3].

Worldwide, prostate cancer is the fourth most common cancer with markedly varying incidence and mortality rates among and within countries[4].

The disease is uncommon before the age of 50 years, the frequency climbs steeply with age to peak or plateau around 9th decade for both incidence and mortality[5]. Once it metastasizes outside the gland, the disease is unfortunately fatal. Early diagnosis and treatment improves survival.

In the absence of effective treatment options for advanced prostate cancer, intensive efforts to detect low stage, curable cancers may help to improve cancer-specific survival[6]. Digital rectal examination (DRE) has been used for diagnosis and screening for prostate cancer since the early 1900s, and its importance is well-established. But there remains a considerable proportion of prostatic mass not detectable by rectal examination even in the presence of symptomatic disease[7].

Wang Y *et al.* in 2013 isolated prostate specific antigen (PSA) from prostate tissue that appears to be the best serum marker for prostate cancer. This noninvasive serological test has brought a new light in the diagnosis of prostate cancer[8]. The widespread use of serum PSA (S. PSA) testing has increased detection rate of early stage cancers and partially responsible for the recent decrease in prostate cancer mortality rates in the United States[9].

A S. PSA cut-off value of 4ng/ml is generally used for recommending a prostate biopsy[10]. According to a study, cancer is detected in initial or early follow-up biopsies in more than one third of man with serum PSA levels greater than 4 ng/ml[11]. It is informative that cancer cells liberate 10 times more PSA than benign ones due to lack of basement membrane[6]. Though prostate cancer may be found without the presence of elevated PSA in serum, its presence poses a relative higher risk of the presence of prostate cancer. When PSA is elevated in serum, the cancer must be proved by prostate biopsy. Initially, a threshold of 4.0ng/ml was the recommended level at which a person should undergo prostate biopsy. Others recommended the value within 4.0-10ng/ml to fall within “diagnostic gray zone”. Conventionally cut-off value has taken as 4.0ng/ml for indication of prostate biopsy. Using the cut-off value of 4.0ng/ml, the sensitivity, specificity and positive predictive value (PPV) were 89.88%, 37% and 49% respectively. By raising the cut-off value to 10ng/ml, the specificity and PPV increase to 66% and 63% respectively, while the sensitivity is reduced a little to 83.7%. Even some researchers had diagnosed prostate cancer while S. PSA was <2.5ng/ml[12]. So there is a possibility of diagnosing prostatic cancer when S. PSA is ≥2.5ng/ml.

Prostate cancer is not uncommon in Bangladesh. But information about the relationship between the S. PSA level and presence of cancer has to be evaluated with more scientific evidence. Therefore present study was designed to determine the presence of prostate cancer at different levels of serum PSA which will help in early diagnosis, effective treatment, increase survival and decrease disease specific mortality and to set up a new cut-off value for prostate biopsy.

Method:

This hospital based cross sectional analytical study was conducted between the periods of January 2012 to April 2013 in the Department of Urology, National Institute of Kidney Diseases & Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka. A total of 105 patients with features of lower urinary tract symptoms with enlarged prostate attending to Department of Urology, National Institute of Kidney Diseases & Urology (NIKDU), Sher-E-Bangla Nagar, Dhaka were purposively selected as study population. Patients more than 50 years old with lower urinary tract symptoms at S. PSA levele” 2.5 ng/ml and enlarged prostate in DRE were selected as study population. Patients with bleeding disorder, anorectal pathology, active UTI or prostatitis or urethral stricture were excluded from this study. After proper counseling and consent, DRE was done to see the size, consistency and nodularity of prostate. Those who had enlarged prostate found on DRE having S. PSA levele” 2.5 ng/ml, they were sent for biopsy. Before taking biopsy patients were again judged by inclusion and exclusion criteria.

Results:

The study was carried out in the inpatient department of NIKDU to assess the relationship of PSA level with the occurrence of prostatic cancer. The results of the study are given below.

Table I

Age of the patients (years)

Age of the patients (years)	Frequency	Mean ± SD* (%)	Minimum – maximum
51-60	19 (18.10)	70.85 ± 16.24	51-92
61-70	35 (33.33)		
71-80	27 (25.71)		
>80	24 (22.86)		

*SD = Standard deviation

The age of the patients was recorded in the study. Table 1 is showing that the patients were nearly 71 years of age on average with a standard deviation (SD) of around 16 years. The minimum age was 51 years and the maximum was 92 years. The patients were mostly concentrated within the age group of 61-70 years (33.33%) followed by 71-80 years (25.71%), which means half of the patients in this study were from 61-80 years. More than one fifth (22.86%) of the patients were above 80 years or so and 19 (18.10%) patients were from 51-60 years.

Table II

Distribution of patients by different Serum PSA levels (ng/L)

Serum PSA	Frequency	Mean ± SD (%)	Minimum – maximum
≥2.5-3.99	18 (17.14)	16.24 ± 17.87	2.60-120.40
4-9.99	35 (33.33)		
10-20	25 (23.81)		
>20	27 (25.71)		

Blood was drawn to investigate the level of S. PSA which is shown in Table 2. The patients had 16.24 ng/L of S. PSA on average with a very high SD of 17.87. At a minimum of e"2.5 ng/L the patients were included for prostatic biopsy. The lowest level was 2.6 ng/L and the highest was 120.4 ng/L. At S. PSA level 2.6-3.99 ng/ml, there were 18 (17.1%) patients, at S. PSA level 4-10, there were 35 (33.3%), at S. PSA 10-20, there were 25(23.8%) and there were 27(25.7%) patients with S. PSA above 20.

Table III

Age of the patients at different PSA level

PSA level	Mean±SD	25th percentile	50th percentile	75th percentile
≥ 2.5-3.99	68.61±10.68	61.25	66.50	76.50
4-9.99	69.40±9.09	63.00	70.00	76.00
10-20	71.20±9.64	63.00	73.00	80.00
>20	73.89±11.55	61.00	74.00	85.00

Table III is showing the association of S. PSA level at different ages of patients. It shows that within S. PSA 2.6-3.99 ng/L the mean age of the patients was 68.61±10.68 years median age was 66.5 years, age at 25th percentile was 61.25 years and age at 75th percentile was 76.5 years; within S. PSA 4-10 ng/L the mean age was 69.40±9.09years median age was 70 years, age at 25th percentile was 63 years & age at 75th percentile was 76 years; within S. PSA 10-20 ng/L the mean age was 71.20±9.64 years, age at 25th percentile was 63 years and age at 75th percentile was 80 years; when the S. PSA was above 20 ng/L the mean age was 73.89±11.55 years median age was 74 years, age at 25th percentile was 61 years & age at 75th percentile was 85 years.

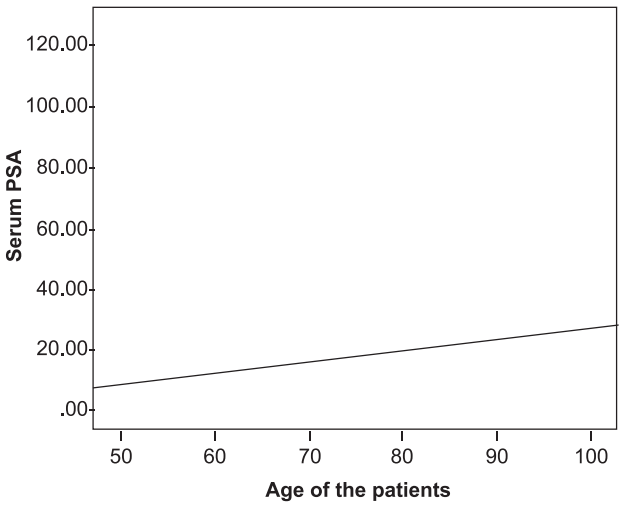

Fig.-1: *Correlation of Serum PSA with age of patients* F=50.6, p=0.03

Figure: 1 is showing the correlation of Serum PSA with age of the patients and a linear relationship was found to exist. The regression analysis showed a significant positive correlation (F=50.6, p=0.03) and the equation of the relationship was as follows

Serum PSA level = (-10.565) + 0.378age

Table IV

Distribution of patients according to biopsy results

Biopsy results	Frequency	%
Benign	60	57.1
Malignant	45	42.9
Total	105	100.0

Table IV is showing the biopsy result where benign hyperplasia was detected in 60 (57.1%) patients and cancer was found in 45(42.9%) patients

Table V

Biopsy result by age group

Age group	Biopsy results		Total	÷^{2}, p
	Benign (%)	Malignant (%)		
51-60 years	13 (68.4)	6 (31.6)	19	2.85, 0.42
61-70 years	22 (62.9)	13 (37.1)	35	
71-80 years	13 (48.1)	14 (51.9)	27	
>80 years	12 (50.0)	12 (50)	24	
Total	60 (57.1)	45	105	

χ^2 =2.8, p not significant

The age group was checked with the biopsy results. Table 6 is showing that there were 31.6% patients in age group 51-60 years diagnosed as having malignant tumour in histopathology, which increased to 37.1% in age group 61-70 years, further increased to nearly 52% in age group 71-80 years and just 50% in age group >80 years, all compared with benign enlargement proportion in the same age group respectively. Though there was a gradual increase of malignant proportion with increasing age group, the association was not statistically significant.

Table VI

Biopsy result by Serum PSA

	Biopsy results	N	Mean±SD	t, p
PSA	Benign	60	7.86±5.18	5.78,
	Malignant	45	27.42±22.25	<0.001

t=5.78, p<0.001

Table VI shows that the cancer patients were much higher level than the patients with benign hypertrophy by nearly 20 units. Serum PSA level of benign patients was 7.86±5.18 ng/ml while that of the cancer patients was 27.42±22.25 ng/ml. The difference of level between the benign and cancer patients was significant.

Table VII

Serum PSA group levels with biopsy results

PSA (ng/ml)	Biopsy results		Total	÷^{2}, p
	Benign	Malignant		
e" 2.5-3.99	15 (83.3%)	3 (16.7%)	18(100.0%)	48.21,
4-9.99	30 (85.7%)	5 (14.3%)	35(100.0%)	<0.001
10-20	14 (56.0%)	11(44.0%)	25(100.0%)	
>20	1 (3.7%)	26 (96.3%)	27(100.0%)	

χ^2 =48.21, p<0.001

Table VII shows the Serum PSA with biopsy results. When Serum PSA was very low (2.6-3.99 ng/ml) biopsy showed positive result in 16.7% patients, Serum PSA 4-10 biopsy positive 14.3%, Serum PSA10-20 biopsy positive 44.0% and when Serum PSA was above 20 ng/ml biopsy was positive in 96.3% cases. The association of higher biopsy level with increasing rate of cancer patients was highly significant.

Table VIII

Logistic regression analysis to assess cancer by S. PSA adjusted by age

Variables	OR (95% CI)	P
Age	1.03 (0.99-1.08)	0.18
Serum PSA	13.13 (4.98-34.64)	<0.001

As age and Serum PSA became significant with biopsy result, both the variables were put to logistic regression model (Table VIII). It was found that Serum PSA was highly significant after adjusted by age with very high odds of over 13. The odds ratio (OR) with 95% confidence interval (CI) of the logistic regression model is shown in Table VIII.

Discussion:

This was a cross sectional study conducted on a total of 105 patients who had a positive DRE finding and a Serum PSA level ≥ 2.5 ng/ml. All the patients then had to go for TRUS guided histopathological examination of

prostatic tissue obtained to detect the presence of cancer.

The mean age was 70.85 ± 16.24 years (range 51-92 years) and mostly concentrated within the age group of 61-70 years (33.33%) followed by 71-80 years (25.71%). Researchers in California (Jacobsen SJ *et al.* 2012)[13] conducted a prospective study to assess serum PSA and the occurrence of prostatic cancer. The overall age of inclusion of the respondents was within 40-79 years. This study included patients from 51 years and above. They showed that the Serum PSA increases at increasing age. So this study also gave more or less similar impression of increasing serum PSA while age is increasing. Gilligan *et al.* in 2004 showed that the disease was uncommon before the age of 50 years, following steep with age to peak or plateau around 9th decade for both incidence and mortality[5].

The present study shows that within serum PSA 2.6-3.99 ng/ml the mean age of the patients was 68.61±10.68 years and median age was 66.5 years; within serum PSA 4-10 ng/ml the mean age was 69.40±9.09 years and median age was 70 years; within serum PSA 4-10 ng/ml the mean age was 71.20±9.64 years and median age was 73 years; within serum PSA above 20 ng/ml the mean age was 73.89±11.55 years and median age was 74 years. In this study it is seen that with increase age Serum PSA level also increased.

Benign hyperplasia was detected in 57.1% patients and cancer was found in 42.9% patients. While looking at different levels of Serum PSA with malignancy, there were 16.7% patients with PSA level from 2.6-3.99 ng/ml, 14.3% from 4-10ng/ml, 44% from 10-20 ng/ml and 96.3% patients had their PSA >20ng/ml. A Serum PSA cutoff value of >4ng/ml was recommended for biopsy by Catalona et al. (1997)[10] and supported by Shekariz *et al*. (2001)[11]. But this study revealed some more patients 16.7%, would have been missed had we been considering the cut-off value of 4 ng/ml. So this study could bring about the fact of screening patients with a cutoff value >2.5 ng/ml instead of 4ng/ml.

Conclusion:

The study finds out prostate cancer with serum PSA at a level of ≥ 2.5 ng/ml as was the objective of this study. So it can be concluded that prostate cancer could be detected with the marker serum PSA level as low as e" 2.5 ng/ml.

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