FREQUENCY OF CARCINOMA PROSTATE IN PATIENTS WITH CLINICALLY DIAGNOSED BENIGN PROSTATIC HYPERPLASIA (BPH) AND PROSTATE SPECIFIC ANTIGEN D" 4NG/ML

SHAFIQUR RAHMAN[1], SUDIP DAS GUPTA[2], SAJID HASAN[3], PRODYUT KUMAR SAHA.[4], AMANUR RASUL[4], M.A. AWAL[4]

[1]Dept. of Biochemistry, Comilla Medicla College, Comilla. [2]Dept. of Urology, Sir Salimullah Medical College, Dhaka. [3]Dept. of Urology, Bangabandhu Sheikh Mujib Medical University, Dhaka. [3]Dept. of Urology, Dhaka Medical College, Dhaka.

Abstract:

Objectives: *The present study was carried out in the Department of Urology, Sir Salimullah Medical College Mitford Hospital Dhaka between July 2009 to May 2010. To determine the frequency of prostate cancer in patients with BPH & PSA level d" 4 ngm/ml.*

Methods: *A total of 198 subjects aged above 50 years with serum PSA level of not more than 4.0 ng per milliliter , no suspicious nodule on digital rectal examination , homogenous echogenicity of prostate on ultrasonographic findings, peak urinary flow rate (Qmax) < 10ml/sec in uroflowmetry and no clinically significant coexisting conditions were included in the study. All the patients presented with obstructive urinary symptoms attended at four tertiary hospitals in Dhaka city during the study period were evaluated with clinical history, physical examination and some investigations. All the patients were treated with transurethral resection of prostate (TURP). Chips were collected carefully and sent for histopathology.*

Results: *The mean age was 65.1 ± 7.3 years. About 32% of patients had serum PSA level 2 ng/ml or less and 68.2% more than 2 ng/ml. The peak urinary flow rate was 7.2 ± 2.7 ml/sec. One hundred and ninety three (98%) patients were diagnosed as having benign prostatic hyperplasia (BPH) on histopathological examination and 5(2.5%) as having prostate carcinoma.*

Conclusion: *Prostate cancer is not rare among men with PSA levels of 4.0 ng per milliliter or less*

Key words: *BPH, Carcinoma prostate, PSA*

Bangladesh J. Urol. 2012; 15(2): 44-47

Introduction:

Prostate cancer is the second most common cause of cancer death for men[1]. From the available global statistics, in 2007, an estimated 782 600 new cases were diagnosed and 254, 000 patients died of carcinoma prostate[2].

The incidence rates show a 63 fold difference between countries, being lowest in Far East countries such as China- Shanghai (2.5 per 10^5) and highest in US blacks in Detroit (158 per 10^5). US blacks have a particularly high risk of prostate cancer with almost a two fold high incidence rate than that for US whites[3].The prevalence of cancer prostate increases with age. The probability of developing prostate cancer in men under the age of 40 years is 1 in 10,000; 1 in 103 for men of 40-59 years and 1 in 8 for men between 60 – 79 years of age[4]. The presence of prostate cancer may be indicated by symptoms, physical examination, prostate specific antigen (PSA), or biopsy. There is controversy about the accuracy of the PSA test and the value of screening. When first described in 1979, prostate-specific antigen (PSA) was considered a useful marker for assessing treatment responses and follow-up among patients with prostate cancer. After the publication of reports on several series in which the need for a biopsy of the prostate was based on the results of PSA tests, the potential of the PSA level as a screening tool was recognized. Further experience led to the consensus that a PSA level of

Correspondences: Dr. Md. Shafiqur Rahman, Comilla Meical College Hospital, E-mail: shafiq.uro@gmail.com

more than 4.0 ng per milliliter had predictive value for the diagnosis of prostate cancer[5]. Disease detection subsequently increased dramatically. In the past, most doctors considered a PSA level below 4.0 ng/mL as normal. In one large study, however, prostate cancer was diagnosed in 15.2 percent of men with a PSA level at or below 4.0 ng/mL. Among them approximately 2.3 percent overall, had high-grade cancers. Thus the previously defined predictive value of PSA seems to be doubtful for a higher yield of prostate cancer and needs to be re-fixed on the basis of recent study data.

There are limited data on the prevalence of prostate cancer among men with a PSA level of 4.0 ng per milliliter or less. The aim of the present study is to detect the frequency of carcinoma prostate in patients with PSA d" 4ng/ml.

Materials and Methods:

This study was a cross-sectional study. Total 198 patients with obstructive urinary symptoms were enrolled in this study. The study was carried out in the Department of Urology of Sir Salimullah Medical College Mitford Hospital, Dhaka medical college & Hospital, National institute of kidney diseases & urology (NIKDU), BSMMU Hospital Dhaka between July 2009 to May 2010. The patients aged above 50 years, serum PSA level not more than 4.0 ng per millilitre, prostate is enlarged but no suspected nodules on digital rectal examination, homogenous echogenicity of prostate on ultrasonographic findings, peak urinary flow rate (Qmax) < 10ml/sec in uroflowmetry were included in this study. Patients with clinically palpable suspicious nodule were excluded from the study. All the patients presented with obstructive urinary symptoms attended at four tertiary hospitals during the study period were evaluated with clinical history, physical examination and some investigations. Digital rectal examination was done to determine the prostate size and to exclude suspicious nodule. Routine investigations like complete blood count, urine routine and microscopic examination and culture sensitivity , serum creatinine, chest x-ray and echocardiography was done. Specific investigations like transadominal USG was done to detect any hydronephrotic change in the kidneys, urinary stone diseases, maximum cystrometric capacity, prostate size and echotexture, any hypoechoic lesion in the prostate and postvoidal residual urine. Uroflowmetry was done in all cases. A detailed data sheet was completed and this included particulars of the patients, history, results of physical examinations, relevant investigations as well as specific investigations. Unfortunately 2 patients were dropped out due to their refusal to do surgery. So finally 198 patients were enrolled for the study and all of them were treated with transurethral resection of prostate. Chips were collected carefully and sent for histopathology. Using computer software Statistical Package for Social Sciences (SPSS-13) data were processed and analyzed. The test statistics used for analysis of data were descriptive statistics, Chi-square Test or Fisher's Exact Probability Test and student's t Test. The level of significance is 0.05 and p-value < 0.05 was considered significant.

Results: Of 198 patients included in the study with symptoms of moderate and severe urinary tract obstruction, 193(97.5%) had benign enlargement of prostate and 5(2.5%) had prostatic carcinoma (Table I).

Table I

Distribution of the patients by diagnosis. (n=198)

Diagnosis	Frequency	Percentage
Malignant	05	2.5
Benign	193	97.5
Total	198	100.0

Among 198 patients half (50%) of the patients was in the range of 60 – 70 years, followed by 23.1% below 60 years, 21.2% between 70 – 80 years and rest 5.1% 80 years or more than 80 years. The mean age was 65.1 ± 7.3 years and the range was 52 to 90 years.

Table II

Distribution of patients by age

Age* (years)	Frequency	Percentage
< 60	46	23.1
60 – 70	100	50.0
70 – 80	42	21.2
e" 80	10	5.1
Total	198	100.0

*Mean = 65.1 ± 7.3 years; range = 52 – 90 years

Clinical presentations demonstrate that majority (94.4%) of the patients had poor urinary stream, 83.3% incomplete voiding and 86.4% frequency of micturation. Over three-quarter (76.8%) complained of dysuria, 75.3% nocturia and 70.7% urgency of micturation.(TableIII)

Table III

Distribution of the patients by clinical presentations (n = 198)

Clinical presentations	Frequency	Percentage
Poor urinary stream	187	94.4
Dysuria	152	76.8
Incomplete voiding	165	83.3
Frequency of micturation	171	86.4
Urgency of micturation	140	70.7
Nocturia	149	75.3

On per rectal digital examination prostate gland was found to be enlarged in all cases. Of them 65.0% had moderate enlargement, 20.0% had huge enlargement. Ultrasonographic findings demonstrate that all the patients had homogenous lesion. About 32% of patients had serum PSA level 2 ng/ml or less and 68.2% between 2 to 4 ng/ml. The peak urinary flow rate was 7.2 ± 2.7 ml/sec and the minimum and maximum flow rate were 4 and 9 ml/sec respectively (TableIV).

Table IV

Distribution of the patients by investigations (n = 198)

Investigations	Frequency	%	Mean ± SD	Range
USG of prostate				
Volume of prostate (gm)				
< 40	123	63	-	
40-60	30	15		
> 60	45	22		
Echo-pattern				
Homogenous	198	100		
Non-homogenous	0	0		
Serum PSA				
> 2 ng/ml	63	31.8	-	
2-4 ng/ml	135	68.2		
Peak urinry flow rate (ml/sec)			7.2± 2.7	4 - 9

One hundred and ninety three (98%) patients were diagnosed as having benign prostatic hyperplasia (BPH) on histopathological examination and 5(2.5%) as having prostate carcinoma(Figure I) . Gleason score demonstrate that 20% of patients had gleason score 5 after histopathological examination, 40% score 6 and another 40% score.

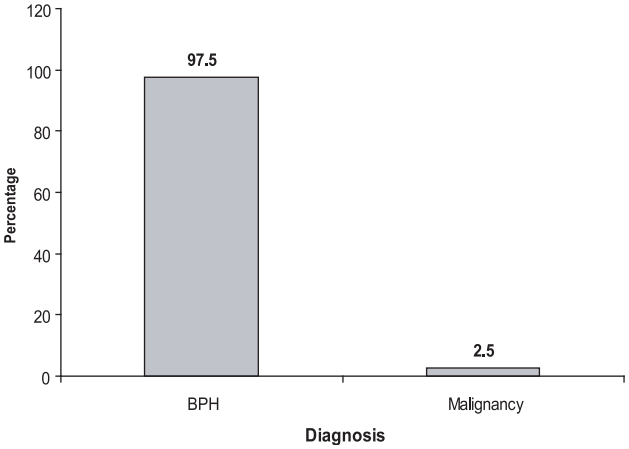

Fig.-1: *Distribution of patients by histopathological diagnosis (n= 198)*

Discussion:

In the present study 198 patients were evaluated on the basis of histopathological examination of post transurethral resection of prostatic chips. Among them mean age was 65.1 ± 7.3 years. Majority (94.4%) of the patients had poor urinary stream, 83.3% incomplete voiding and 86.4% frequency of micturation. Over three-quarter (76.8%) complained of dysuria, 75.3% nocturia and 70.7% urgency of micturation. Over 90% of the patients had severe lower urinary tract obstruction (LUTS) and 9.6% moderate obstruction in terms of International Prostate Symptom Score (IPSS). About 32% of patients had serum PSA level 2 ng/ml or less and 68.2% more than 2 ng/ml. The peak urinary flow rate and mean serum PSA were 10.2 ± 2.7 ml/sec and 2.6 ± 1.0 ng/ml respectively. Similar observation was made in Shaikh et al[6]. In our study we observed that 2.5% of the patients with PSA level 4 or < 4 ng/ml had histological evidence of prostate malignancy. **Garzotto** demonstrated that the risk of a positive biopsy was 4.9% (10 of 203 subjects) for men with a PSA d" 1.5[1]. Brawer et al. found cut off value for PSA as 4.0 g/ml in males > 50 years old, detection rate of malignancy was2.9%[7].These datas support using a lower PSA cutoff level for the detection of prostate cancer. Recently, it has been proposed that the normal PSA cutoff level be decreased to 2.5 or 3.0 ng/mL[8]. However, further study is needed to determine the net benefit of detecting cancers at this lower PSA level.

Conclusion:

The results of our study indicate that histopathologically detected prostate cancer is not rare among men with

PSA levels of 4.0 ng per milliliter or less. So patients with 4 or < 4 ng/ml should not be overlooked rather they should be kept under regular observation to find any malignant change. This study concludes that biopsy-detected prostate cancer is not rare among men with PSA levels of 4.0 ng per milliliter or less — the levels generally thought to be within normal range.

Conflict of Interest: None declared.

References:

1. Garzotto M, Beer TM, Hudson RG, Peters L, Hsieh YC & Barrera E 2005, 'Improved Detection of Prostate Cancer Using Classification and Regression Tree Analysis', *J Clinical Oncology*, Vol 23: 4322-4329.
2. Jemal A, Murray T, Ward E, Samuels A, Tiwari RC & Ghafoor A. Cancer statistics, 2005". *CA Cancer J Clin* 55 (1): 10–30.
3. ARC Worldwide Cancer Incidence Statistics—Prostate". *JNCI Cancer Spectrum*. Oxford University Press. December 19, 2001.
4. Stevens A, Milne R, Stein K, Robertson J, 1997, 'The diagnosis, management and costs of prostate cancer in England and Wales', Health Technology Assessment, vol.1, no. 3, pp-1-70.
5. Thompson IM, Ernst JJ, Gangai MP, Spence CR 1984. Adenocarcinoma of the prostate: results of routine urological screening. J Urol, vol. 132, pp.690-2
6. Shaikh AR, Siyal AR, Shaikh NA, 2000. 'Transuretheral resection of Prostate; Early experience in rural Sindh', The Professional vol. 07, no. 02
7. Brawer MK, Chetner MP, Beatie J, Buchner DM & Vessella RL 1992, 'Lange PH. Screening for prostatic carcinoma with prostate specific antigen', J Urol, vol.147: 841-5.
8. Punglia RS, D'Amico AV, Catalona WJ, Roehl KA & Kuntz KM 2003, 'Effect of verification bias on screening for prostate cancer by measurement of prostate-specific antigen', N Engl J Med, vol.349,pp.335-42
9. Ragde H, Aldape HC, Bagley CM Jr. Ultrasound-guided prostate biopsy: Biopty gun superior to aspiration. Urology 1988;32: 503-6.
10. Radhakrishnan S, TJ Dorkin TJ, Sheikh N and DR Greene DR, 2004, 'Role of transition zone sampling by TURP in patients with raised PSA and multiple negative transrectal ultrasound-guided prostatic biopsies', Prostate Cancer and Prostatic Diseases, 7: 338–342.
11. Osegbe, DN 1997, 'Prostate cancer in Nigerians: facts and nonfacts', *J Urol* , vol.157 : 1340–3.
12. Matlaga BR, Eskew LA, McCullough DL, 2003, 'Prostate biopsy: Indications and technique', J. Urol, 169: 12-19.
13. Hsing, AW; Tsao L & Devesa SS 2000, 'International trends and patterns of prostate cancer incidence and mortality', *Int J Cancer* , 85 : 60–7.
14. Huggins C, Steven RE & Hodges CV 1941, 'Studies on prostatic cancer', Arch. Sug. 43: 209–23.
15. Schulman CC, Ekane S & Zlotta AR 2001, 'Nutrition and prostate cancer: evidence or suspicion', *Urology*, 58: 318–34.
16. Shibata A, Ma J & Whittemore AS 1998, 'Prostate cancer incidence and mortality in the United States and the United Kingdom', J Natl Cancer Inst, 90: 1230-1.
17. Shimizu H, Ross RK, Bernstein L, Yatani R, Henderson BE, Mack TM, 1991, 'Cancers of the prostate and breast among Japanese and white immigrants in Los Angeles County', Br J Cancer, vol. 63, pp. 963-6.