Nephro-Urol Mon. 2011;3(3):186-190
Nephro-Urology Monthly
Journal home page: www.NUmonthly.com

Histopathological lesions in transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate specific antigen: A preliminary report

Muhammed Abrar Barakzai [1], Muhammed Mubarak [1*], Javed Iqbal Kazi [1]

[1] Histopathology Department, Sindh Institute of Urology and Transplantation, Karachi, Pakistan

ARTICLE INFO

Article Type:
Original Article

Article history:
Received: 16 Jan 2011
Revised: 17 Feb 2011
Accepted: 1 Mar 2011

Keywords:
Adenocarcinoma
Needle biopsy
Transrectal ultrasound
Prostate specific antigen

ABSTRACT

Background: Transrectal ultrasound (TRUS)-guided needle biopsies of prostate are considered the gold standard for the diagnosis of the prostatic cancer. Currently, there is no information on the spectrum of pathological lesions in TRUS biopsies of prostate in men from Pakistan.
Objectives: To determine the spectrum of pathological lesions in TRUS-guided needle biopsies of prostate in men with increased serum prostatic specific antigen (PSA) levels with or without symptoms of prostatism.
Patients and methods: A prospective study carried out at the Department of Histopathology, Sindh Institute of Urology and Transplantation (SIUT), Karachi from September 2001 to June 2002. Fifty four men underwent TRUS-guided prostate biopsies for suspected prostate cancer. Raised serum PSA levels were arbitrarily divided into mild (≥ 4 to 20 ng/ml), moderate (≥ 20.1 to 50 ng/ml) and marked elevations (≥ 50.1 to highest). In most cases, eight cores were taken per case. Each core was individually labeled and submitted for histopathological study.
Results: The mean age of patients was 66.9 ± 9.4 years (range: 5 2-100 years). The mean serum PSA was 97.1±119.4 ng/ml (range: 4-449 ng/ml). Mean number of cores obtained per case was 7.8±0.9 (range: 4-9). Overall, 30 (55.6%) cases showed benign lesions and 24 (44.4%), malignant. Benign lesions consisted of adenomyomatous hyperplasia. Fourteen of benign cases (46.6%) showed significant inflammatory changes. Among malignant lesions, all cancers were of moderate to high Gleason grades and scores. Mild serum PSA rise was seen in 26 (48.1%) patients; among these, 19 (73%) cases showed benign lesions and 7 (26.9%), malignant. Moderate serum PSA rise was seen in 14 (25.9%) cases; among these 9 (64.3%) were benign and 5 (35.7%) malignant. Fourteen (25.9%) patients had serum PSA ≥ 50.1 ng/ml. Among these, 12 (85.7%) had adenocarcinoma, 2 (14.3%) hyperplasia, one of the later with active prostatitis.
Conclusions: In conclusion, this is first study from Pakistan on the spectrum of pathological lesions in prostate TRUS-guided biopsies in men with suspected prostate cancer. The detection rate of prostate cancer is similar to that reported previously from around the world and rises with an increase in serum PSA level.

▸ *Implication for health policy/practice/research/medical education:*
This is the first study from Pakistan on the spectrum of pathological lesions observed in transrectal ultrasound guided prostate biopsies in men with suspected prostate cancer, and sheds light on the local perspective of this subject in the literature.

▸ *Please cite this paper as:*
Barakzai MA, Mubarak M, Kazi JI. Histopathological lesions in transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate specific antigen: A preliminary report. *Nephro-Urol Mon*. 2011;**3**(3):186-190.

* *Corresponding author at:* Muhammed Mubarak, Histopathology Department, Sindh Institute of Urology and Transplantation, 74200 Karachi, Pakistan. Tel: +92-219215752, Fax: +92-212726165.
E-mail: drmubaraksiut@yahoo.com

1. Background

Prostate cancer is the most common malignant tumour of solid organs in men through out the world (1). An estimated 217,730 cases of prostate cancer were likely to occur in USA alone in 2010, accounting for 28% of all new cases (2). It is also the second leading cause of cancer related deaths in men after lung cancer. An estimated 32,050 cases were likely to die of prostate cancer in USA alone in 2010, accounting for 11% of all cancer related deaths (2). The racial and regional differences in the incidence of prostate cancer are well established. Black men have approximately 2–3 fold higher incidence of prostate cancer compared to white men in USA (1). Asian men have very low age adjusted incidence rates as compared with their western counterparts (3). In Pakistan, the precise national population based data on the prevalence and incidence of prostate cancer are not available. However, recently, attempts have been made to establish regional tumour registries. In one such registry based in Karachi, prostate cancer was the fifth most common cancer in men in Karachi Division, occurring in 7.3% of all men (4). It was also the fifth most common tumour seen in northern areas (6.63%) in a hospital based study (5). Carcinoma of the prostate arises in the peripheral zone of the gland in approximately 70% of cases, classically in the posterior location (1). The diagnosis requires careful history, physical examination including digital rectal examination (DRE), serum prostate specific antigen (PSA) estimation and transrectal ultrasound (TRUS) and TRUS-guided needle biopsies of the prostate. Among these, the later are considered the gold standard for the tissue diagnosis of the prostatic cancer (3).

TRUS-guided needle biopsies of the prostate are the standard method for the early diagnosis of prostate cancer in most urology centers in the developed world (3). Hodge *et al.* (6-8) recommended systematic parasagittal sextant biopsies of the prostate with additional biopsies of hypoechoic areas outside the parasagittal plane under TRUS guidance for men with suspected prostate cancer. More recently, extended 10-12 core biopsy protocols have been developed and advocated by many researchers to be more sensitive for the early diagnosis of prostate cancer (9-21). However, the equipment and techniques TRUS-guided prostate biopsy are not widely available in most of the developing countries, including Pakistan. Sindh Institute of Urology and Transplantation (SIUT), Karachi, Pakistan, is the largest urology, nephrology and transplant center of Pakistan. Facilities and skills for TRUS-guided prostate biopsies are available at SIUT since last 20 years. However, there is little information in published literature on the histopathological findings in prostate TRUS-guided biopsies performed in men with suspected prostatic cancer from Pakistan. In addition, there is very scant data on the histopathologic characteristics such as grade, stage and extent of prostatic cancer in men from this country.

2. Objectives

This study was undertaken primarily to determine the spectrum of pathological lesions in prostate TRUS-guided biopsies from men with elevated serum PSA and secondarily to determine the histopathologic characteristics of prostate cancer in men from this country.

3. Patients and Methods

3.1. Patients

A prospective and descriptive study was carried out at the department of Histopathology, Sindh Institute of Urology and Transplantation (SIUT), Karachi from September 2001 to June 2002. The study patients included all consecutive adult or elderly males, who presented to SIUT prostate clinic with complaints of prostatism. Their detailed physical examination and DRE were performed, followed by appropriate laboratory investigations including determination of serum PSA. Serum PSA levels were arbitrarily divided into mild (≥ 4 to 20 ng/ml), moderate (≥ 20.1 to 50 ng/ml) and marked elevations (≥ 50.1 to highest) and correlated with various clinical and biopsy findings.

3.2. Biopsy technique

TRUS guided needle biopsies of the prostate gland were performed only in those patients who had serum PSA levels ≥ 4 ng/ml and/or abnormal DRE suspicious for prostate cancer. Ultrasound guidance was provided by a diagnostic ultrasound machine (Sonolayer 270 Toshiba) with 7 MHz, biplanar transrectal probe. Biopsies were obtained with patient in right or left lateral decubitus position and the prostate was imaged in the sagittal plane. Biopsies were obtained using an automatic biopsy gun (Manan Promag 2.2) and 18 gauge biopsy needle. Mostly eight cores were taken in each patient, one each from the predetermined sites so that to include all major zones of the prostate tissue. Ninth core was only taken from the suspected area (if present). In a few small prostates, lesser number of cores was also obtained. Each core was individually labeled with the specific site from which it was obtained as per our protocol. Only first time biopsies were included. Repeat biopsies were not included in the analysis.

3.3. Pathologic study

The biopsy specimens were processed and studied at the department of Histopathology, SIUT. Gross examination of the biopsies included precise length and diameter and colour of the cores. The biopsies were processed for paraffin embedding, cut at 3-5 um and stained by haematoxylin and eosin (H&E) for detailed microscopic examination. The later was done by two pathologists, first independently and then jointly to arrive at consensus diagnosis. The histological types of the lesions in each core

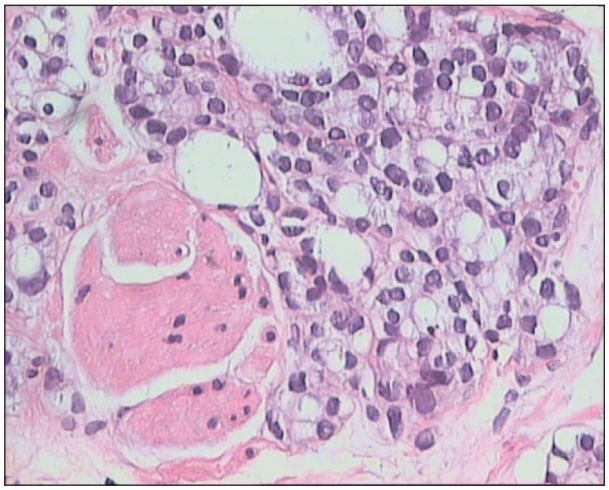

Figure 1. High magnification image showing a few glandular lumina with focal areas of loss of glandular differentiation, a pattern consistent with Gleason grade 4 adenocarcinoma of the prostate (H&E, × 400).

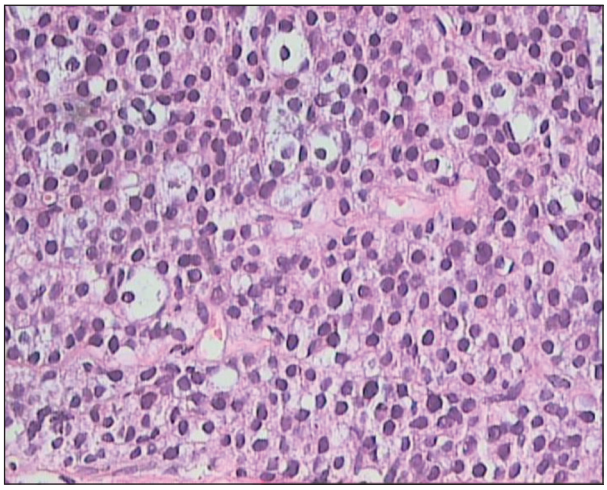

Figure 2. High magnification image showing solid pattern of growth and lack of any glandular differentiation, as seen in Gleason grade 5 adenocarcinoma of the prostate (H&E, ×400).

of the biopsy were determined and recorded separately in the report. The histopathological grading and scoring by Gleason system was done in all cases of adenocarcinoma of prostate. Demographic, clinical and laboratory data of each patient was taken from the clinical charts. Histopathological features were noted from original biopsy reports. The grading system for prostate carcinoma devised by Gleason was used. The primary and secondary patterns were combined to give a tumour score, referred to as Gleason score (22). The core biopsies were graded and scored according to revised WHO criteria for the grading and scoring of needle biopsies of the prostate (23).

3.4. Statistical analysis

Statistical analysis was carried out using IBM compatible SPSS for Windows version 10 (SPSS, Chicago, IL, USA). Simple descriptive statistics such as mean ± SD were used for continuous variables such as age and clinical and laboratory parameters. Percentages were used for categorical data. For comparisons of prostate cancer and the non-cancer group, independent-samples T test and Chi - square tests were used. A p value of less than 0.05 was considered significant.

4. Results

The main clinical and laboratory features of all patients and the cancer and non-cancer groups are shown in *table 1*. The mean age of all patients was 66.9 ± 9.5 years; range was from 52 to 100 years. There was no significant difference in the mean age of the 2 groups (p, 0.57). The main presenting symptoms of the patients were: retention of urine in 20 (37%) patients, weak stream in 18 (33.3%), frequency in 15 (27.7%), urgency in 9 (16.6%), hematuria in 7 (12.9%), incomplete emptying in 6 (11.1%), nocturia in 6 (11.1%), hesitancy in 4 (7.4%), and post void dribbling in 3 (5.5%) patients, in variable combination. Overall 92% patients were symptomatic at the time of presentation.

The mean serum PSA value was 54.8 ± 88.5 ng/ml; range was 4 to 449 ng/ml. The mean PSA was significantly higher in the cancer group (p, 0.001) than in the benign group. Mean number of cores obtained in each case was 7.8 ± 0.9. There was no significant difference in the mean number of cores obtained in the 2 groups (p, 0.24). In most cases (79.6%), eight cores were obtained. Minimum number of cores obtained per case was 4 and maximum 9. Of 54 cases, 24 (44.4%) revealed adenocarcinoma and the remaining 30 (55.6%) showed adenomyomatous hyperplasia with or without associated active prostatitis. The rate of cancer detection increased significantly with increasing serum PSA level. Of 30 benign cases, 14 (46.6%) cases showed hyperplasia with active prostatitis. Among 24 patients with adenocarcinoma, six patients (11.1%) had grade 3, seven (13%) grade 4 *(Figure 1)* and remaining eleven (20.4%) patients had grade 5 *(Figure 2)*. Most of the patients having grade ≥ 3 showed markedly high levels of serum PSA. Similarly, on Gleason scoring, four patients (7.4%) had score 6, two (3.7%) score 7, five (9.3%) score 8, seven (13%) score 9 and six (11.1%) had score 10 *(Table 2)*. Most of the patients having Gleason score ≥ 6 also showed markedly high levels of serum PSA. Twenty eight out of 54 patients (51.8%) had serum PSA ≥ 20.1 ng/ml. Of these, 17 (60.7%) patients had prostatic adenocarcinoma, and 11 (39.3%) benign changes. When higher cut off value of serum PSA was used at ≥ 50.1 ng/ml, fourteen out of 54 (25.9%) patients showed this degree of increase in serum PSA. Among these, 12 (85.7%) had adenocarcinoma, 2 (14.3%) hyperplasia, one of the later with active prostatitis. In our study, only 16.6% (4/24) prostate cancer patients had biopsy Gleason scores of less than 7 and there was no clinically insignificant cancer.

Of the 30 (55.5%) cases with benign lesions, 14 (46.6%) patients had adenomyomatous hyperplasia with active

Table 1. Comparison of clinical and laboratory characteristics among patients with and without cancer on prostate core biopsies

	Positive Biopsy	Negative Biopsy	p-value	Total
Patients [No. (%)]	24 (44.4)	30 (55.6)		54
Age [Mean ± SD (range)]	67.7 ± 11 (52-100)	66.3 ± 8.1 (53-93)	0.57	66.9 ± 9.5 (52-100)
Age Range [No. (%)]			0.72	
50 – 60 (year)	8 (33.3)	10 (33.3)		18 (33.3)
61 – 70 (year)	10 (41.7)	15 (50)		25 (46.2)
> 70 (year)	6 (25)	5 (16.7)		11 (20.3)
Mean PSA level (ng/ml)	97.1 ± 119.4	20.9 ± 18.4	0.001	54.8 ± 88.5 (4-449)
PSA Range [No. (%)]			0.001	26 (48.1)
4 – 20	7 (29.2)	19 (63.3)		14 (25.9)
20.1 – 50	5 (20.8)	9 (30)		14 (25.9)
> 50.1	12 (50)	2 (6.7)		
Cores [Mean ± SD (range)]	7.6 ± 1.2 (4-9)	7.9 ± 0.4 (6-9)	0.34	7.8 ± 0.9

prostatitis and of these, 6 (42.8%) patients had chronic non specific active prostatitis, 3 (21.4%) had chronic granulomatous inflammation, 2 (14.2%) patients had severe acute prostatitis with abscess formation, one patient (7.1%) each had xanthogranulomatous inflammation, candida infection, and foreign body granulomatous reaction. The three patients with chronic granulomatous inflammation showed no caseation necrosis and negative results for acid fast bacilli on Ziel-Nelson staining and thus were labeled as idiopathic granulomatous prostatitis.

5. Discussion

Although, this is a small scale study of relatively short duration, it is the first to report on the spectrum of pathological lesions found in TRUS-guided biopsies of the prostate in men with elevated serum PSA and/or symptoms of prostatism from Pakistan. As such, it may be considered as a foundation on which further large scale studies may be conducted to accurately characterize the spectrum of pathological lesions in such biopsies in general and prostate cancer in particular. The prostate cancer is seen typically in elderly men and its frequency rises with increasing age (1). In this context, the mean age of our patients is concordant with that reported previously in local and international studies (2-21). However, no significant rise in cancer incidence was seen in our patients with increasing age, as in other studies (1). This may partly be due to the small size of the sample in the present study. In our study, most patients were symptomatic; 92% presented with lower urinary tract symptoms (LUTS) commonly knows as prostatism. Very few patients (8%) presented for screening of the prostate cancer at asymptomatic stage. This is understandable given the low level of awareness of this cancer among the general population.

The overall cancer detection rate in TRUS-guided biopsies in our series was 44.4%. This corresponds fairly well with many previously reported series from around the world (3-21). In a study from China, cancer detection rate was 40% (3). In the study by Levine *et al.* (16) cancer was detected in 31% of cases. Presti *et al.* observed prostate cancer in 42% of the TRUS-guided biopsies (18). All these studies included patients with raised serum PSA associated with or without prostatism, as in our study. However, different levels of serum PSA and different biopsy strategies were employed in these studies, which are reflected in slight differences in cancer detection rates. In a significant number of patients with raised serum PSA, TRUS-guided biopsies showed benign hyperplastic or inflammatory lesions rather than cancer. The proportion of benign lesions was greater in patients with mild or moderate elevations of serum PSA. In contrast, cancer was more frequent in cases with marked elevations in serum PSA. Similar observations have been noted in previous investigations as well. These findings show that simply a rise in serum PSA levels ≥ 5 ng/ml does not indicate that a patient has prostate cancer because benign conditions such as hyperplasia and prostatitis can also increase the serum PSA levels (24, 25).

In our study, 14 (25.9%) patients had PSA levels of ≥ 50 ng/ml, of which 12 (85.7%) patients had adenocarcinoma, 2 (14.3%) patients had hyperplasia; one of the later had active prostatitis. There were only two patients out of 14 with PSA levels ≥ 50 ng/ml and their biopsies revealed benign changes. This is an interesting finding which shows that patients with markedly elevated serum PSA levels are more likely to harbor adenocarcinoma in their biopsies than benign changes, as in previous studies (3). There was one patient in our study who had PSA level of 80 ng/ml and revealed benign changes with active prostatitis. In our study, we obtained eight cores according to slightly modified protocol proposed by Presti *et al.* (18). An additional core was taken from the suspicious area in a few cases only. It was observed that the levels of serum PSA increased with increasing Gleason grade and score of the tumour. In our study, majority of cancers (22/24: 91.6%) belonged to intermediate to high grade category. Similarly, scores were also moderate to high in majority of cases. Most of the patients having grade 3 or above

Table 2. Histopathological characteristics of prostate cancer observed in 24 patients with raised serum prostate specific antigen levels.

	Patients [No. (%)]
Biopsy Gleason grade	
3	6 (11.1)
4	7 (13)
5	11 (20.4)
Biopsy Gleason score	
6	4 (7.4)
7	2 (3.7)
8	5 (9.3)
9	7 (13)
10	6 (11.1)
Positive biopsy cores	
1	3 (12.5)
2	1 (4.2)
3	1 (4.2)
4	1 (4.2)
5	2 (8.3)
7	2 (8.3)
8	11 (58.3)

showed markedly high levels of PSA. In conclusion, this is the first report on the spectrum of pathological lesions in TRUS biopsies of prostate in patients with symptoms of prostatism and high serum PSA from Pakistan. The detection rate of prostate cancer is almost similar to that reported previously in literature with similar biopsy indications from different parts of the world. Further long duration and large scale studies are needed to accurately characterize this common cancer of men in our population.

Financial support

None declared.

Conflict of interest

None declared.

References

1. Epstein JI. The lower urinary tract and male genital system. In: Robbins SL, Kumar V, Abbas AK, Cotran RS, Fausto N, editors. Robbins and Cotran pathologic basis of disease. 8th ed. Philadelphia: Saunders/Elsevier; 2010. p. 982-1004. .
2. Jemal A, Siegel R, Xu J, Ward E. Cancer statistics, 2010. *CA Cancer J Clin.* 2010;**60**(5):277-300.
3. Dai B, Ye DW, Kong YY, Shen YJ, Wang BH. Individualized prostate biopsy strategy for Chinese patients with different prostate-specific antigen levels. *Asian J Androl.* 2008;**10**(2):325-31.
4. Bhurgri Y. Epidemiology of cancers in Karachi (1995-1999). Karachi: *Pharmacia and Upjohn.* 2001.
5. Ahmad M, Khan AH, Mansoor A. The pattern of malignant tumours in northern Pakistan. *J Pak Med Assoc.* 1991;**41**(11):270-3.
6. Hodge KK, McNeal JE, Stamey TA. Ultrasound guided transrectal core biopsies of the palpably abnormal prostate. *J Urol.* 1989;**142**(1):66-70.
7. Hodge KK, McNeal JE, Terris MK, Stamey TA. Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *J Urol.* 1989;**142**(1):71-4; discussion 4-5.
8. Stamey TA. Making the most out of six systematic sextant biopsies. *Urology.* 1995;**45**(1):2-12.
9. Durkan GC, Sheikh N, Johnson P, Hildreth AJ, Greene DR. Improving prostate cancer detection with an extended-core transrectal ultrasonography-guided prostate biopsy protocol. *BJU Int.* 2002;**89**(1):33-9.
10. Philip J, Ragavan N, Desouza J, Foster CS, Javle P. Effect of peripheral biopsies in maximising early prostate cancer detection in 8-, 10- or 12-core biopsy regimens. *BJU Int.* 2004;**93**(9):1218-20.
11. Philip J, Hanchanale V, Foster CS, Javle P. Importance of peripheral biopsies in maximising the detection of early prostate cancer in repeat 12-core biopsy protocols. *BJU Int.* 2006;**98**(3):559-62.
12. Beurton D, Barthelemy Y, Fontaine E, Chartier E, Lamotte F, Franc B. Twelve systematic prostate biopsies are superior to sextant biopsies for diagnosing carcinoma: a prospective randomized study. *Br J Urol.* 1997;**80**(2):239-42.
13. Chen ME, Troncoso P, Johnston DA, Tang K, Babaian RJ. Optimization of prostate biopsy strategy using computer based analysis. *J Urol.* 1997;**158**(6):2168-75.
14. Chang JJ, Shinohara K, Bhargava V, Presti JC, Jr. Prospective evaluation of lateral biopsies of the peripheral zone for prostate cancer detection. *J Urol.* 1998;**160**(6 Pt 1):2111-4.
15. Eskew LA, Bare RL, McCullough DL. Systematic 5 region prostate biopsy is superior to sextant method for diagnosing carcinoma of the prostate. *J Urol.* 1997;**157**(1):199-202; discussion -3.
16. Levine MA, Ittman M, Melamed J, Lepor H. Two consecutive sets of transrectal ultrasound guided sextant biopsies of the prostate for the detection of prostate cancer. *J Urol.* 1998;**159**(2):471-5; discussion 5-6.
17. Norberg M, Egevad L, Holmberg L, Sparen P, Norlen BJ, Busch C. The sextant protocol for ultrasound-guided core biopsies of the prostate underestimates the presence of cancer. *Urology.* 1997;**50**(4):562-6.
18. Presti JC, Jr., Chang JJ, Bhargava V, Shinohara K. The optimal systematic prostate biopsy scheme should include 8 rather than 6 biopsies: results of a prospective clinical trial. *J Urol.* 2000;**163**(1):163-6; discussion 6-7.
19. Hoedemaeker RF, van der Kwast TH, Boer R, de Koning HJ, Roobol M, Vis AN, et al. Pathologic features of prostate cancer found at population-based screening with a four-year interval. *J Natl Cancer Inst.* 2001;**93**(15):1153-8.
20. Keetch DW, Catalona WJ, Smith DS. Serial prostatic biopsies in men with persistently elevated serum prostate specific antigen values. *J Urol.* 1994;**151**(6):1571-4.
21. Gupta NP, Ansari MS, Dass SC. Transrectal ultrasound guided biopsy for detecting early prostate cancer: An Indian experience. *Indian J Cancer.* 2005;**42**(3):151-4.
22. Gleason DF. Histologic grading of prostate cancer: a perspective. *Hum Pathol.* 1992;**23**(3):273-9.
23. Montironi R, Mazzuccheli R, Scarpelli M, Lopez-Beltran A, Fellegara G, Algaba F. Gleason grading of prostate cancer in needle biopsies or radical prostatectomy specimens: contemporary approach, current clinical significance and sources of pathology discrepancies. *BJU Int.* 2005;**95**(8):1146-52.
24. Catalona WJ. Clinical utility of measurements of free and total prostate-specific antigen (PSA): *a review. Prostate Suppl.* 1996;**7**:64-9.
25. Yuan JJ, Coplen DE, Petros JA, Figenshau RS, Ratliff TL, Smith DS, et al. Effects of rectal examination, prostatic massage, ultrasonography and needle biopsy on serum prostate specific antigen levels. *J Urol.* 1992;**147**(3 Pt 2):810-4.