Original Article

NEGATIVE TRUS – GUIDED BIOPSY OF PROSTATE IN DIFFERENT GROUPS OF RAISED PSA LEVEL

Muhammad Asif,[1] Hafiz Shahzad Ashraf,[2] Fazal-ur-Rehman Khan,[3] M. Nasir Ibrahim,[4] Nadir Hussain[5]

Abstract

Aims and Objectives

1. To determine the frequency of negative TRUS guided biopsy of Prostate in different groups of raised PSA level.
2. To determine the frequency of raised PSA level (> 4 ng/ml) in patients presenting with symptoms of enlarged prostate.

Study Design: Cross Sectional survey.

Setting: Department of Urology, Sheikh Zayed Hospital, Lahore.

Duration of Study: Six Months.

Sample Size: 90 cases.

Subjects and Methods: Ninety patients fulfilling the selection criteria were identified. All the patients underwent TRUS guided prostate biopsy and Results evaluated on the basis of biopsy report.

Results: This study included 90 patients. The age ranged from 48 – 80 years with a mean of 65.02 ± 8.32 years. PSA level range was from 4.7-230ng/ml; with mean PSA level of 24.12 ± 36.09.Out of 40 patients with PSA 4 – 10 ng/ml, 36 (90%) patient's TRUS guided biopsy was negative for malignancy. 26 (92.8%) out of 28 patients, with PSA 10 – 20 ng/dl the biopsy was negative, 9 (40.9%) out of 22 patients, biopsy was negative with PSA > 20 ng/ml. Among 19 patients having positive TRUS guided biopsy 12 (63.1%) had well differentiated adenocarcinoma; 6 (31.5%) had moderately differentiated adenocarcinoma and 1 (5.2%) had poorly differentiated adenocarcinoma.

Conclusion: Detection rate of carcinoma of prostate on TRUS guided biopsy according to serum PSA level is low in our setup, repeat serum PSA levels are recommended after a period of one month with or without cover of antibiotics so that unnecessary TRUS biopsies can be avoided.

Keywords: Transrectal ultrasound of the prostate, prostate cancer, prostate biopsy, prostate – specific antigen.

Asif M.[1]
Assistant Professor, Department of Urology
Sharif Medical City Hospital, Lahore

Ashraf H.S.[2]
Professor of Kidney Transplant Unit
Shaikh Zayed Hospital, Lahore

Khan F.R.[3]
Associate Professor
Department of Urology, Shaikh Zayed Hospital, Lahore

Ibrahim M.N.[4]
Kidney Transplant Unit, Shaikh Zayed Hospital, Lahore

Hussain N.[5]
Assistant Professor
Department of Urology, Shaikh Zayed Hospital, Lahore

Introduction

Most commonly found benign tumor in males is benign prostatic hyperplasia (BPH) and its incidence rises

as the age advances. The B.P.H is found in 20%, 50% and > 90% men at the age of 41 – 50, 51 – 60 and older than 80 years respectively on autopsy specimens.[1]

Carcinoma of prostate is the most common malignant tumor in males over age of 65 with an estimated 41000 American men dying from carcinoma of prostate annually. Most of patients are diagnosed at the time when the tumor has extended beyond the confines of the gland making it incurable. The magnitude of this problem in Pakistan is unknown,[2] however the lifetime risk of a diagnosis of prostate carcinoma is 17%.[3]

Carcinoma of the prostate most commonly arises from the peripheral zone of the gland, where about 60-70% of carcinomas originate. About 20% of prostate cancer arises in transition zone and 5 – 10% in central zone.

Several risk factors of prostate cancer, both genetic and environmental are important in the origin and evolution of prostate cancer. Advancing age, a prostate tumor in family, high fat diet, low plant – based diet, inflammation and infection are linked as causative factors.[4]

PSA is a proteolytic enzyme produced by prostatic tissue. It is prostate specific but not cancer specific. Normally it is less than ≤ 4 ng/ml. It is important in earlier diagnosis, monitoring of treatment and labelling of hormone refractory carcinoma of prostate.[5]

The carcinoma of prostate is graded on the basis of Gleason grades given by Gleason and Mellinger in 1974. The glandular pattern is given a score 1 – 5 histopathlogically. The two most frequent patterns are added to give a Gleason sum 2 – 10. Most frequent pattern is written first e.g. 3 + 4 = 7 where 3 is most prevalent pattern.[7]

Material and Methods

This Study is cross – sectional survey conducted in the Department of Urology, Shaikh Zayed Hospital Lahore. This study was completed in six months extending from October, 2010 to April, 2011. A total of 90 cases meeting the inclusion criteria were included in the study with confidence level of 95%, 8.5% margin of error and taking expected percentage of negative TRUS guided biopsy in patients having PSA level 10 – 20 ng/ml i.e. 20.31%. patients with enlarged prostate of > 20g, PSA > 4 ng/ml, age range 45 – 80 years and patients having lower urinary tract symptoms (i.e. Urinary frequency, urgency, Poor stream, nocturia, hesitancy) were included in the study while those with advanced metastatic disease (confirmed on CT Scan / bone scan) were excluded from the study. All the patients who fulfilled the inclusion criteria were selected from Outpatient Department of Urology, Shaikh Zayed Hospital Lahore. An informed consent was taken, PSA level assessed and patients categorized in three groups according to serum PSA level in group 1, group II and group III with PSA range 4 – 10 ng/ml, 11 – 20 ng/ml and > 20 ng/dl respectively. Then frequency of patients determined with PSA level 4 – 10 ng/ml, 11 – 20 ng/ml, > 20 ng/ml. All patients underwent TRUS guided prostate 8 core biopsy by a single radiologist. Negative (absence of prostatic carcinoma) TRUS guided biopsy results were collected on attached pre-designed computer based proforma in each group.

Results

This study included 90 patients. The age ranged from 48 – 80 years with a mean of 65.02 ± 8.32 years. Forty (44.44%), 28 (31.1%) and 22 (24.4) patients qualified the criteria of group I, II and III respectively. Detail of all three groups is given in table 1 while detailed outcome of TRUS guided prostatic biopsy in all three groups in table 2.

Table 1: Distribution of PSA levels by frequency and percentage.

Groups	PSA Levels (ng/dl)	No of patients (N)	Percentage (%)
Group I	4 – 10	40	44.4
Group II	11 – 20	28	31.1
Group III	> 20	22	24.4
Total		90	100.0

Table 2: TRUS guided biopsy results in different groups of PSA level.

Groups	PSA Level	Negative	Positive
Group I	04 – 10	36 (90.0%)	04 (10.0%)
Group II	11 – 20	26 (92.8%)	02 (07.1%)
Group III	> 20	09 (40.9%)	13 (59.1%)

Discussion

Most commonly found benign tumor in males is benign prostatic hyperplasia (BPH) and its incidence rises as the age advances. The B.P.H is found in 20%, 50% and > 90% men at the age of 41 – 50, 51 – 60 and older than 80 years respectively on autopsy specimens.[1]

Carcinoma of the prostate is one of the most common male malignant neoplasms in the world, especially in the West. Prostate cancer is diagnosed by DRE, PSA and TRUS guided prostate biopsy all over world. Best marker for diagnosis of prostatic malignancy is PSA. Incidence of prostate cancer is 15% at a PSA range of 4-10 with normal DRE. So at this PSA range 85% of patients undergo unwanted biopsies.

Initially sextant biopsy was used to diagnose carcinoma of prostate. Transrectal ultrasound has improved the method of taking prostatic biopsy, leading to increased diagnosis of prostatic malignancy. TRUS guided prostate biopsy was performed by Hodge et al in 1989. At that time sextant biopsy was gold standard for diagnosis of prostatic tumor.[8]

In our study, 90% of patients had negative yield for carcinoma on TRUS guided biopsy with PSA 4 – 10 ng/dl; 92.8% of patient's biopsies were negative with PSA of 11 – 20 ng/dl while 40.9% patient's biopsies were reported normal with PSA > 20 ng/dl. In another study by Seo HK, et al.[9] 83% of patients had negative TRUS biopsies with PSA 4 – 10 ng/dl; 74.1% negative rate in patients with PSA 11 – 20 ng/dl and 41.4% of patients had negative TRUS biopsy with PSA > 20 ng/dl. In a study by Choi JH, et al.[10] The negative rate of TRUS biopsy was 97% with PSA 4 – 10 ng/dl; 85% of the patients had negative TRUS biopsy with PSA 10 – 20 ng/dl and 64% of the patients had negative TRUS biopsy with PSA > 20 ng/dl. In a study by Yang WJ, et al.[11] The negative rate was 85.1% in patients with PSA 4 – 10 ng/dl; 65.9% negative rate with PSA 10 – 20 ng/dl and 6.2% of patients negative for carcinoma with PSA > 20 ng/dl.

Keeping in view all these studies, there is no significant difference especially in patients with PSA 4 – 10 ng/dl. However, there is small difference in patients with PSA 11 – 20 ng dl and > 20 ng/dl. Many reasons can be quoted for this difference. These include the number of cores in biopsy, high incidence of benign prostatic hyperplasia and chronic prostatitis in our population, low incidence of prostate cancer in our population and possibility of higher PSA levels in our population.

In our study, single 8 core prostatic biopsies were performed in all patients. Sextant biopsy gave 30% false negative results. This was due to lesser cores of prostate and more medial biopsies excluding lateral areas where 80% of Carcinoma of prostate generates. Later this modified to incorporate more lateral biopsies.[8]

Babaian RJ, et al,[12] showed that false negative biopsies are decreased by increasing number of prostatic biopsy cores, a new way of biopsy was introduced to include more lateral areas of prostate for biopsy. The 5-region method involves conventional sextant cores with 4 cores from lateral prostatic areas (2 on each side) and 3 mid line biopsies. In this way false negative rate is reduced by 35%. So, 5 – region (13 cores) biopsy should be recommended to get minimum false negative results.

In our study, we observed high incidence of benign prostatic hyperplasia and chronic prostatitis on histopathology that may be the one of the reasons for raised PSA levels. So, repeat PSA should be performed to avoid unnecessary biopsy. Renterghem K, et al.[13] Suggested that after a negative biopsy, patient may be advised antibiotics or diet supplements etc. for a certain period of time before repeating PSA levels and, if PSA is still elevated, repeat biopsy should be performed. Similarly, Eastham, et al,[14] suggested that an isolated PSA elevation should be re-measured before performing a prostate biopsy because of fluctuations in PSA that could represent a false – positive elevation in the test. In this study, PSA levels were not repeated before performing biopsy, so false elevation in PSA could not be ruled out. More studies in this regard can document if repeating PSA levels after a course of antibiotics carries any significance in our population.

The incidence of prostate cancer is different in our part of globe as compared to the west. As documented by Yang WJ, et al[11] and Seo, et al.[9] The incidence of prostate cancer is low in Korean population as compared with Americans. In a study by Yeole, et al.[15] The incidence of prostate cancer in India ranged from 3.38 – 6.98 / 100,000. In a Meta analysis of studies conducted in different regions in Iran, Mousavi[16] found that incidence of prostate cancer was 9.6 (3.2 to 16.0) per 100,000 in multi geographical settings. Bhurgri, et al,[17] studied the incidence of prostate cancer in Pakistan, which is probably the only large population based data available regarding prostate cancer incidence in our setup. They found the incidence of prostate cancer to be 10.1/100,000. In contrast to the studies conducted in our region, western and American

studies have documented a very high rate of prostate cancer.

Conclusion

As the detection rate of prostate cancer on TRUS guided biopsy according to serum PSA level is low in our setup, so, it is therefore recommended to repeat serum PSA levels after a period of time with or without cover of antibiotics so that unnecessary TRUS biopsies can be avoided.

Also, 5 region (13 cores) TRUS biopsy should be performed to decrease the false negative rate.

References

1. Presti C. Joseph, Kane J. Christopher, Shinohara Katsuto, Carroll R. peter: Neoplasms of the Prostate gland. In: Tanagho E, McAninch J, editors. Smith's General urology. 17th edition: McGraw Hill, 2008: 348-369.
2. Khan I.A, Nasir. M, Akbar M, Khattak. I, Khan A.N et al: Ca Prostate in clinically benign enlarged prostate. J Ayub Med Coll Abbottabad, 2008; 20 (2).
3. Carter H.B, Allaf M.E, Partin A.W: Diagnosis and Staging of Prostate Cancer. In: Wein A.J, Kavoussi L.R et al; editors. Cambell – Walsh Urology 9th edition Saunders Elsevier, 2007: 2912-2931.
4. Thompson IM, Ankerst DP, Chi C, et al. Assessing prostate cancer risk: results from the Prostate Cancer Prevention Trial. J Natl Cancer Inst. 2006; 98: 529-534.
5. M. Kwiatkowski, P. Stieber, AR Huber, F. Recher: Selective application of Tumor marker PSA. TherUmsch 2008 Sep; 65 (a): 493-501.
6. Ian M. Thompson and Donna P. Ankerst. Prostate – specific antigen in the early detection of prostate cancer. CMAJ. June, 19, 2007; 179 (13).
7. Borley Nigel, Feneley R. Mark: Prostate cancer: Diagnosis and Staging. Asian journal of Andrology, 2009; 11: 70-80.
8. KK Hodge, JE McNeal, MK Terris, et al. Incidence and clinical significance of false – negative sextant prostate biopsies. J Urol, 1998; 159: p. 1247.
9. Seo HK, Chung MK, Ryu SB, Lee KH; Detection rate of prostate cancer according to prostate-specific antigen and digital rectal examination in Korean men: a nationwide multicenter study, 2007 Dec; 70 (6): 1109-12.
10. Choi JH, Park HJ, Kwon HC; clinical value of prostatic biopsy in patients with elevated serum PSA. 1996 October; Vol. 37 No. 10, p.1110-1116, Korean J. Urol.
11. Yang WJ, Lee DH, Chung BH, Cho JS, Choi YD, Kim SJ, Cho IR, Kim HS, Kim CI, Hong SJ;Detection rate of prostate cancer on biopsy according to serum prostate – specific antigen in Korean men: a multicenter study. Urology, 2006 Feb; 67 (2): 333-6.
12. Babaian RJ, Camps JL. The role of prostate-specific antigen as part of the diagnostic triad and as a guide when to perform a biopsy. Cancer, 1991; 68: 2060–3.
13. Renterghem KV, Koeveringe GV, Achten R, Kerrebroeck PV. Clinical relevance of transurethral resection of the prostate in "asymptomatic" patients with an elevated prostate – specific antigen level. Eur Urol. 2007; 52: 819-26.
14. Eastham JA, Riedel E, Scardino PT, Shike M, Fleisher M, Schatzkin A, et al. Polyp Prevention Trial Study Group: Variation of serum prostate – specific antigen levels: An evaluation of year – to – year fluctuations. JAMA, 2003; 289: 2695-700.
15. Yeole BB. Trends in the Prostate Cancer Incidence in India. Asian Pacific J Cancer Prev. 2008; 9: 141-144.
16. Mousavi SM, Gouya MM, Ramazani R, Davanlou M, Hajsadeghi N, Seddighi Z. Cancer incidence and mortality in Iran. Annals of Oncology, 2009; 20: 556–563.
17. Bhurgri Y, Kayani N, Pervez S, Ahmed R, Tahir I, Afif M, et al. Incidence and trends of prostate cancer in Karachi South, 1995 – 2002. Asian Pac J Cancer Prev. 2009; 10: 45-8.