ORIGINAL ARTICLE

OUTCOME OF TRANS RECTAL ULTRASOUND GUIDED TWELVE CORE BIOPSY OF PROSTATE FOR THE DETECTION OF PROSTATE CANCER- A SINGLE CENTRE EXPERIENCE

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Background: This study was conducted to determine the outcome of trans-rectal ultrasound (TRUS) guided biopsy of prostate for the detection of prostatic carcinoma in a single tertiary care hospital in Pakistan. **Methods:** This is a retrospective study including three hundred and eighty-three patients who underwent trans rectal ultrasound guided biopsy of prostate in a single tertiary care hospital. Indications for biopsy were raised prostate specific antigen (PSA), abnormal digital rectal examination (DRE) and/or both. Twelve core biopsy of prostate was done. **Results**: The overall detection rate of prostate cancer was 59%. Prostate cancer detection in various PSA ranges of 0–3.99, 4–9.99, 10–19.99 and >20 ng/ml are 22.22%, 37.88%, 50.0% and 89.9%. PSA density >0.15ng/ml^2 can diagnose 74.5% of patients with cancer. Prostate cancer detection rate based on abnormal DRE is 64.6% compared to 60.8% detected by PSA>4 ng/ml. **Conclusion**: In conclusion raised PSA, smaller prostate volume, abnormal DRE and raised PSA density are associated with greater chances of detection of prostate carcinoma.

Keywords: Digital rectal examination; Prostate cancer; Prostate Specific antigen; Prostate volume, Trans rectal ultrasound

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INTRODUCTION

Prostate carcinoma is currently the most commonly diagnosed cancer and second leading cause of death in men. There is life time risk of 16% to be diagnosed with prostatic carcinoma. Incidence is lowest in Asian men.[1] According to first Karachi cancer registry report prostate carcinoma is the fifth most common cancer in Pakistani men.[2]

There are increased chances of recurrence free survival and cancer specific survival if prostatic carcinoma is diagnosed in early stages.[3] Currently the screening and diagnostic tools are digital rectal examination, PSA and trans rectal biopsy of prostate.[4] PSA had revolutionized the diagnosis of carcinoma of prostate but it has relative lower specificity when in the range of 4–10ng/ml.[5]

Benson and colleagues described the concept of PSA density to increase the detection rate and avoid unnecessary prostate biopsies.[1,5] TRUS guided biopsy of prostate is the gold standard for diagnosis of prostate carcinoma. It is indicated if there is abnormal DRE, raised PSA or both. Currently 10–12 cores biopsy is the standard.[3] With development of advanced equipment and technology refinements, TRUS guided prostatic biopsy is easy, quick and less painful procedure.[5] Therefore it is one of the most commonly performed procedures in Urology practice with more than one million procedures done each year in United States and Europe.[6]

Despite being one of the most common malignancies, there is lack of basic data on the detection rate of prostate cancer and post procedure complication rates in Pakistani men. We hereby share our experience of TRUS guided 12 core prostate biopsy in Pakistani men in a tertiary care hospital. To our knowledge this is the largest data base study of Pakistani men describing the detection rate, value of different diagnostic tools and complications after TRUS guided biopsy of prostate.

MATERIAL AND METHODS

This retrospective study was done in Urology department of Shifa International Hospital Islamabad. The study included all male patients who underwent TRUS guided biopsy of prostate from January 2013 to December 2015. Indications of biopsy were PSA >4 and/or abnormal DRE (induration, irregularity, nodularity and asymmetry). Data was collected by chart review method. All those patients who underwent prostate surgery, previous biopsy or already known prostate cancer patients were excluded from study. All patients had PSA level measured once or twice before TRUS biopsy.

For prostate biopsy patients were placed in left or right lateral position. Per rectal enema was

given six to eight hours before procedure while tablet Levofloxacin 500 mg was given per orally four hours before procedure. Lignocaine gel 2% was used as local anaesthetic/lubricant. Prostate volume was measured by cranio caudal, transverse and antero posterior lengths of prostate using trans rectal ultrasound. Twelve core biopsy was taken with automatic 18 G needle (BARD, MONOPTY, USA). All biopsy specimens were fixed in formalin. PSA density was calculated by dividing PSA level with TRUS measured prostate volume. Data was collected regarding patient age, PSA, DRE findings, prostate volume, histopathology outcome and post procedure complications. Mean±SD was calculated for quantitative variables like age PSA and prostate volume by frequency and percentage was calculated for qualitative variables like DRE findings, biopsy report. We used SPSS version 16.0. For comparison between the prostate cancer and the non-cancer groups, we used the independent sample t- and chi-square tests. A *P*-value of less than 0.05 was considered significant.

RESULTS

Three hundred and eighty-three men underwent TRUS guided prostate biopsy. Most common presentation was lower urinary tract symptoms as in 288/383 (75.2%) while 57/383 (14.9%) presented with previously known raised PSA, 26/383 (6.8%) with haematuria and 12/383 (3.1%) were asymptomatic. Their mean age was 66.3±8.74 years, median prostate volume was 55.30 ml and median serum PSA level was 13 ng/ml (mean 48.36±132.55 ng/ml and range of 0.24–1462 ng/ml). The systemic 12 core biopsies were performed on 157/383 (41%) of men without cancer compared to 226/383 (59%) men with cancer (p<0.001). Men with prostate cancer were older (68.63 vs 62.95 years, p<0.001) and higher PSA levels (17.75 vs 10.18 ng/ml, p<0.0001) despite having smaller prostates (51 vs 66 ml, p<0.0001). They were also more likely to have suspicious DRE findings (64.6% vs 35.4% p=0.002). (Table-1)

Out of the 365/383 (95.30%) men with serum PSA >4 ng/ml, 222/365 (60.8%) had positive biopsy. Serum PSA was categorized into four main groups: 0–3.99 ng/ml, 4–9.99 ng/ml, 10–19.99 ng/ml and >20 ng/ml. Their corresponding cancer detection rates were 4/18 (22.2%), 50/132 (37.88%), 47/94 (50%) and 125/139 (89.9%).

Cancer detection rate according to prostate volume groups, i.e., <35 ml, 35–70 ml and >70 ml is 50/66 (75.8%), 147/228 (64.5%) and 29/89 (32.6%) respectively (p<0.001). (Table-2)

Patients with only PSA density >0.15ng/ml^2 are 271 (70.81%) and the detection rate was 202 (74.5%); (Table-2). But when a cut off of PSA >4 ng/ml was used, the detection rate of prostatic cancer in patients with PSA density >0.15 ng/ml^2 remains almost same as 202/270 (74.8%). Corresponding cancer detection rate of cancer with PSA density >0.15 ng/ml^2 in respect to PSA categories of 4–9.99, 10–19.99 and >20 ng/ml were 31/52 (59.6%), 46/80 (57.5%) and 125/138 (90.6%). (Table-4)

Similarly, detection rate with abnormal DRE in different PSA ranges (0–3.99, 4–9.99, 10–19.99 and >20 ng/ml) were 04/18 (22.2%), 25/69 (36.2%), 35/58 (60.3%) and 100/109 (91.7%). (Table-5)

Among post procedure complications, 09 (2.3%) developed haematuria, 07 (1.8%) had UTI, 03 (0.8%) had sepsis, 04 (1.0%) had retention of urine, 03 (0.8%) had haematochezia, 03 (0.8%) patients had abdominal pain.

Table-1: Patients Characteristics

Demographics	Total	Men without cancer	Men with cancer	*p*-value
Patients n (%)	383 (100%)	157 (41%)	226 (59%)	
Age (years, mean ±SD)	66.3±8.74	62.95±7.57	68.63±8.76	<0.001
Abnormal DRE	254 (66.3%)	90(35.4%)	164 (64.6%)	0.002
Prostate Volume (ml) Median Mean±SD	 55.3 58.15±26.19	 63 67.11±31.10	 50 51.93±19.97	<0.001
Serum PSA (ng / ml) Median Mean±SD	 13 48.36± 132.55	 8.48 10.18±6.67	 14.50 74.89±167.55	<0.001
PSA Density (ng /ml^2) Median Mean±SD	 0.25 0.92±2.43	 0.09 0.18±0.17	 0.48 1.43±3.06	<0.001

Table-2: Prostate cancer detection rate based on the PSA density

PSA Density (ng/ml^2)	Total Patients	Benign	Malignant	*p*-value
<0.15	112 (29.24%)	88 (78.6%)	24 (21.4%)	
>0.15	271 (70.8%)	69 (25.5%)	202 (74.5%)	<0.001

Table-3: Prostate cancer detection rate based on the prostate volume

Prostate volume (ml)	Total Patients	Benign	Malignant	*p*-value
<35	66 (17.2%)	16 (24.2%)	50 (75.8%)	
35-70	228 (59.5%)	81 (35.5%)	147 (64.5%)	<0.001
>70	89 (23.2%)	60 (67.4%)	29 (32.6%)	

Table-4: Overall prostate cancer detection rates based on serum PSA levels and PSA Density

PSA (ng/ml)	Patients	Cancer detection	PSA Density <0.15ng/ml2		PSA Density >0.15 ng/ml	
			Incidence	Cancer detection	Incidence	Cancer detection
0–3.99	18 (4.7%)	4 (22.22%)	17	04 (23.5%)	01	- (0%)
4.00–9.99	132 (34.5%)	50 (37.88%)	80	19 (23.8%)	52	31 (59.6%)
10.00–19.99	94 (24.5%)	47 (50%)	14	01 (7.1%)	80	46 (57.5%)
>20.00	139 (36.3%)	125 (89.9%)	01	-- (0%)	138	125 (90.6%)

Table-5: Overall prostate cancer detection rates based on serum PSA levels and DRE findings

PSA (ng/ml)	Patients	Cancer detection	Normal DRE		Abnormal DRE	
			Incidence	Cancer detection	Incidence	Cancer detection
0–3.99	18 (4.7%)	4 (22.22%)	--	-- (0%)	18	4 (22.2%)
4.00 – 9.99	132 (34.5%)	50 (37.88%)	63	25 (39.7%)	69	25 (36.2%)
10.00–19.99	94 (24.5%)	47 (50%)	36	12 (33.3%)	58	35 (60.3%)
>20.00	139 (36.3%)	125 (89.9%)	30	25 (83.3%)	109	100 (91.7%)

DISCUSSION

Prostatic specific antigen is diagnostic and screening tool for early detection of prostate. It is a glycoprotein excreted by both normal and abnormal tissue. It was first used as diagnostic tool in 1986. It caused 75% reduction in the cancer related morbidities and metastasis since 1990s. Currently PSA>4 ng/ml is considered as the cut off value.[1] But it is observed that up to 15% of patients with PSA<4 can have prostate carcinoma[7]. While PSA can be raised due to causes other than prostatic carcinoma, i.e., BPH, prostatitis, urological manipulation and after ejaculation.[8]

PSA density, introduced by Benson and colleagues to increase the specificity of PSA and to decrease the un necessary biopsies particularly in patients with a PSA in grey zone (4–10).[1,5] It is based on the concept that cancer cells produce more PSA per unit volume than non-cancerous cells. Different cut-off values are used in different studies from 0.1–0.15.[9] There are a very few studies with limited data describing the prostate carcinoma detection rate, their detection tools and their strengths and weaknesses used for Pakistani men. In this study we retrospectively analysed the detection rate and diagnostic tools for prostatic carcinoma in patients undergoing prostate biopsy from Jan 2013 to Dec 2015 in a single tertiary care hospital. As there are no regional or national cancer screening program in Pakistan. This study will help in devising the screening strategies for this common tumour in future. The results of our study will provide the characteristics of patients with prostate cancer in our setup and will help the urologist and patients in making decisions regarding indication for prostate biopsy and know the possible risks.

In our study the mean age of the patients was 66.30±8.74 years that is comparable with national (67.11±8.9[10] and 63.5±8.5[11] years) and regional studies (68.2±8.9[12] and 64.1±7.4[13], 68.4±8.0[14] years) but higher than the in western studies as 62 years.[15] This may be due to the late presentation of patients and lack of screening program in our country. The overall detection rate in our study is 226/383 (59%) which is higher than the most of the local and international studies. Ramsha *et al*[10] and Deepak Par Kash *et al*[11] in their study of Pakistani men showed detection rate of 99/203 (48.8%) and 151/300 (50.3%) respectively, using 08 core biopsy models. Elvin *et al*[12] in their study of 841 Singaporean men with TRUS guided 12 core prostatic biopsy described the detection rate of prostatic carcinoma as 35.1%. Detection rate was 27.6%[14] 33.3%[23] and 44.5% in studies from china[14], US[15] and Turkey[16]. Higher detection rate can be described to increase in the number of cores taken on TRUS prostate biopsy, improvement in technique of biopsy, increasing incidence, lack of screening program and advanced disease at presentation.

As in our study patients with prostatic carcinoma are older and with higher mean PSA than the patients with benign outcome. It is consistent with many other studies.[10,12,17] DRE is considered as relevant and important tool for detection of prostate cancer.[12] Detection rate in abnormal DRE findings alone is 64.6% that is superior to PSA >4 ng/ml alone as 60.8%. Detection rate increased to 67.79% when we combined abnormal DRE and PSA >4 ng/ml. Lee *et al*[12] described the detection rate of prostate carcinoma with only abnormal DRE as 59.2% that increased to 69.9% when it was combined with PSA >4 ng/ml. In the study by JYC Teoh *et al*[14], cancer detection rate increased in all PSA ranges with abnormal DRE as compared to normal DRE. Similar findings were shown in our study for PSA range of 10–19.99 and >20 ng/ml but it did not show increasing trend for PSA range 0–3.99 ng/ml and 4–10 ng/ml. Abnormal DRE is not sensitive for intermediate PSA levels (4.00-9.99 ng/ml).[12] Vis *et al*[18] proposed that PSA values may replace the DRE as screening test in patients with low PSA levels. They described as to diagnose a single case of clinically significant prostate cancer 289 DREs are needed while 96 DREs may be needed to diagnose any prostate cancer. Prostate cancer detection rate in prostate volume group of <35 ml (75.8%) is higher than the prostate volume group of 35–70 ml (64.5%) and >70 ml (32.65%). Tanaka *et al*[17] in their study described decreasing prostate cancer detection with rising prostate volume. Young Min Kim *et al*[19] described the prostate volume as the most important predicting factor in men with PSA>4.0. Tang

P *et al*[20] found that men with prostate volume >60 ml had substantially decreased risk of prostate cancer as compared to those with PV <60 ml. Similar findings were described by YS Wu *et al*[21] and Inpyeong Hwang *et al*[22] in their cohort of Chinese and Korean men respectively. In patients with serum PSA level of 4.00–9.99 ng/mL, the detection rate of overall prostate cancer is 37.88%. This rate is higher than 17.6% and 19.1 % described by Ramsha *et al*[10] and Deepak *et al*[11] in Pakistani men. While it was 20.9%[12] and 26.1%[23] in Singaporean and American men using twelve and six core biopsy respectively. Detection rate is increased with increasing PSA levels as there was 50% in PSA group 10–19.99 ng/ml and highest in group with PSA>20ng/ml (89.9%). Similar trend was described by Deep Par Kash *et al*[11] as 19.1%, 28.3% and 74.6% in PSA ranges of 4–10 ng/ml, 10.01–20 ng/ml and >20 ng/ml, respectively. While JYC Teoh *et al*[14] described the detection rate as 27.8%, 59.6% and 93.7% in patients with PSA of 10.1–20 ng/ml, 20.1–50ng/ml and >50 ng/ml respectively.

Prostate cancer detection rate in patients with PSA density >0.15 ng/ml^2 is 74.5% which is higher than the detection rate when considering only PSA >4 ng/ml that is 60.8%, but increased slightly (74.8%) in combination group (PSA>4 ng/ml and PSA density >0.15 ng/ml^2). Higher detection rate is described with increasing PSA density in various study models.[5,22,24]

In our study detection rate of prostate cancer was increased when raised PSA density was considered with different ranges of raised PSA levels. This increase is significant in PSA range 4.0–9.99 ng/ml (37.88–57.5%). Raised PSA density increases the diagnostic efficacy of PSA for prostate detection in both western (2.5–10 ng/ml) and Chinese (10.1–20 ng/ml) grey zones of PSA values.[5,25] Zheng *et al*[26] in his study model of 44 patients with prostate carcinoma and 193 with benign prostatic hyperplasia concluded that PSA density is better predictor than PSA for diagnosis of prostate cancer in men with PSA range of 4–10 ng/ml. Similarly, Sasaki R *et al*[27] found that raised PSA and PSA density as most powerful predictors for prostatic cancer in all PSA ranges while PSA density is more accurate in PSA range of 4.1–10.0 ng/ml.

Total complication rate in our study is 7.57%. Among them 3.65% had infectious complications and 1.82% needed in hospital admission. Kam *et al*[28] in his cohort of 1083 patients, who underwent TRUS guided biopsy of prostate, described overall complications as 6.8% and among them 4.9% needed hospitalization. In another study described hospital admission rate due to post TRUS prostate biopsy sepsis as1.5% (12/804)[12]. Generally, incidence of infectious complication, requiring hospital admission, range from 0.6–4.1%.[29]

Other complications in our cohort were haematuria (2.3%), haematochezia (0.8%) and abdominal pain (0.8%). Chiang IN *et al*[30] in his analysis of 1875 patients who underwent TRUS guided biopsy of prostate described acute prostatitis in 3.8%, acute urinary retention in 2.1%, haematuria in 1.9%, rectal bleeding in 0.2%, epididymitis in 0.2%, sepsis in 0.05% and vasovagal syncope in 0.05% of patients. Complications in our study were comparable to most of the previous studies.

CONCLUSION

In our current retrospective study, we endeavoured to evaluate the detection of prostate carcinoma by using serum PSA levels, DRE findings, prostate volume and PSA density. The detection rate is higher than most of the studies in literature. Raised PSA density is better predictor of prostatic carcinoma than raised PSA. The incidence of prostatic carcinoma increased with raise in PSA levels. PSA density >0.15 ng/ml^2 increases the detection rate of prostatic carcinoma when combined with different PSA ranges particularly with PSA range 4–9.99 ng/ml. Abnormal DRE also increases the detection rate with raised PSA but not in PSA range 4–9.99 ng/ml. Risk of prostate carcinoma increased with decreasing prostate volume. Large prostate volume is more associated with benign disease. Infectious complications after biopsy are the most common complications. Limitations in our study are as it is retrospective study. Our study lacks data on the cancer detection rate in men with PSA 0–3.99 ng/ml. Caution should be taken in making any firm conclusions in this group for our local population.

Conflict of Interest: The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

MW: study conception and design, literature review, data collection, statistical analysis, manuscript writing. DS: Data collection and entry, manuscript review. AM: Data collection and entry. MAK: Data collection, manuscript review. MWI: Manuscript review. SA: Manuscript review

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