Global Academic Journal of Medical Sciences

Available online at www.gajrc.com
DOI: 10.36348/gajms.2022.v04i06.010

OPEN ACCESS

ISSN: 2706-9036 (P)
ISSN: 2707-2533 (O)

Original Research Article

A Comparative Study between Transrectal Ultrasound Guided 6-Core and 12-Core Prostate Biopsy for Detection of Prostate Cancer

Dr. Md. Asaduzzaman[1*], Dr. Md. Mostakim Maoya[2], Dr. Md. Shaheen Reza[3], Dr. Munshi Akid Mostofa[4], Dr. Md. Masud Rana[5], Dr. Md. Tanuwar Islam Chowdhury[6]

[1]Assistant Registrar, Department of Urology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
[2]Specialist, Department of Urology, Evercare Hospital, Dhaka, Bangladesh
[3]Assistant Professor, Department of Urology, Sheikh Hasina Medical College and Hospital, Tangail, Bangladesh
[4]Assistant Registrar, Department of Urology, National institute of Cancer Research and Hospital, Dhaka, Bangladesh
[5]Assistant Professor, Department of Urology, Bangladesh Medical College & Hospital, Dhaka, Bangladesh
[6]Assistant Registrar, Department of Urology, Shaheed Suhrawardy Medical Hospital, Dhaka, Bangladesh

***Corresponding Author**
Dr. Md. Asaduzzaman
Assistant Registrar, Department of Urology, Rajshahi Medical College Hospital, Rajshahi, Bangladesh
Email ID:
drasad42@yahoo.com

Article History
Received: 28.10.2022
Accepted: 06.12.2022
Published: 22.12.2022

Abstract: ***Background:*** Prostate cancer is common in urological practice. Diagnosis of prostate cancer depends on biopsy of the prostate. For the last two decade TRUS guided 6 core (sextant) biopsy is being considered as standard for prostate biopsy. Various studies in different countries showed the drawback of sextant biopsy. The debate remains alive on number of biopsy core which is appropriate for obtaining representative tissue. Moreover, more number of needle biopsy may be associated with more complication. ***Methods:*** In this hospital based Quasi experimental study, a total of 50 patients were allocated into two groups by purposive sampling technique where 6 core prostate biopsy in one group and 12 core biopsy in another group. Baseline demographic and clinical data were recorded. Post procedural morbidity & histopathological findings were recorded. All the collected data were compiled. Further Statistical analyses of the results were obtained by using Microsoft Xcel, 2010 and web based computer software - Graph Pad Software, 2017. A probability value (p) of less than 0.05 was considered to indicate statistical significance. ***Results:*** The baseline characteristics like age, S.PSA, prostate volume & DRE findings were similar in two groups. Cancer detection rate was not significantly different between the 6 core biopsy group and 12 core biopsy group (48% Vs 60%, p=0.395). Dysuria with difficulty in micturition and hematuria after biopsy significantly more in 12 core biopsy group (24% Vs 44% and 32% Vs 60% respectively). Other post procedural complications like fever, perrectal bleeding was found statistically not significant between two groups ***Conclusion:*** Trans rectal ultrasound guided 6 core biopsy is equally effective as Trans rectal ultrasound guided 12 core biopsy for detection of prostate cancer.

Keywords: N/A. Prostate cancer, Prostate biopsy, TRUS guided 6 core, Sextant biopsy, Needle biopsy

INTRODUCTION

Prostate cancer is the second most common cancer and the sixth leading cause of cancer death worldwide, with an estimated 899,000 cases and 258,000 deaths annually [1]. Its incidence varies widely between countries and ethnic populations. The incidence is highest in African Americans and jamaicans of African descent [2]. The ability to diagnose carcinoma of prostate has been enhanced by the discovery of prostate specific antigen (PSA) as

a screening tumor marker. Using serum PSA combined with digital rectal examination (DRE) on an annual basis physicians are diagnosing carcinoma of prostate at an earlier stage [3]. Digital rectal examination of the prostate has long been the sole method of physically examining the prostate. Nodularity, hardness or irregularity on digital rectal examination has led to the clinician to perform biopsy of the prostate to determine the presence or absence of carcinoma. Before the era of systemetic 6 core biopsy the diagnosis of prostate cancer relies on three methods: digital rectal examination, needle biopsy and open perineal biopsy [4]. The next major advancement in prostate needle biopsy was the use of transrectal ultrasonography (TRUS). Weaver *et al.,* described the use of TRUS versus digitally guided biopsy in patients with abnormal DRE findings. Digitally guided biopsy missed more than 50% of adenocarcinomas compared with TRUS guided biopsy [4]. The systematic TRUS guided sextant biopsy has revolutionized the ability to detect carcinoma of prostate during which biopsies are taken parasagitally from base, mid zone and apex in both side. This sextant biopsy scheme significantly improved cancer detection over digitally directed biopsy [5]. Several authors showed the drawback of sextant biopsy. They showed that traditional sextant biopsy may fail to detect a significant proportion of clinically important tumors [6]. Some author shows 12 core biopsy can detect 30% more prostate cancer in compare to 6 core biopsy without increasing significant morbidity [7]. Diagnosis of prostate cancer requires obtaining cancerous tissue from the prostate gland during biopsy. The optimum number of biopsy core needed to detect prostate cancer remains controversial. Many investigators have insisted that large number of biopsy core should be obtained. Others have reported that detection rate of prostate cancer is not significantly increased by taking more than 6 biopsy core, 6 core biopsy was as effective as 12 core biopsy [8]. However, TRUS-guided prostate biopsy has some potential risk of infectious complications, such as pyuria, bacteruria & fever, hemorrhagic complications, minor complication including vasovagal syncope and major complication such as structural damage to surrounding structure and septicaemia [4]. The incidence of infectious complications after TRUS guided biopsy is rising. One large retrospective study reveals a fourfold increase in infection related hospitalizations between the 1996 and 2005 study periods [9]. Several authors have been proposed to explain the higher incidence of infection in recent years. These theories include a trend towards biopsies with more needle passes; more repeat biopsies after the adoption of active surveillance protocol [10] and increase prevalence of antibiotic resistant bacteria in the rectum and genitourinary tract [11]. A large study suggests fluroquinolone resistant rectal flora and the number of biopsy cores taken were independent predictors of infection following TRUS guided prostate biopsy [12]. Prostate cancer is not uncommon in Bangladesh. The study has designed to compare the effectivity of 6 core and 12 core prostate biopsy for detection of prostate cancer and also morbidity associated with the procedure in Bangladeshi men.

OBJECTIVES

General Objectives

- To find more effective prostate biopsy technique for diagnosis of prostate cancer with acceptable morbidity.

Specific Objectives

- To compare the detection rate of prostate cancer between transrectal ultrasound guided 6 core and 12 core prostate biopsy.
- To compare the post procedural morbidity in between two procedures like, Per rectal bleeding, Haematuria, Fever, Dysuria with voiding difficulty, Sepsis.

MATERIALS AND METHODS

This is a hospital based quasi experimental study. Purposive sampling method was applied to collect the target sample. A total 50 sample selected, 25 in group A and 25 in group B were selected. The patients who were attending in the Department of Urology, Dhaka Medical College Hospital (DMCH) Dhaka, Bangladesh having raised serum PSA or abnormal DRE findings or both. The study conducted during July 2017 to June 2018.

Inclusion Criteria

- Hard in consistency or nodularity or focal induration of prostate in DRE.
- Raised serum PSA > 4 ng /ml.

Exclusion Criteria

- Patients with bleeding disorder.
- Patient with anorectal pathology or painful anal conditions.
- Acute UTI or prostatitis.
- Patient with previous prostate biopsy or prostate surgery.

Study Procedure

This hospital based prospective study was conducted in male patients who are potential candidates for prostate biopsy attending in urology department during the period from July 2017 to June 2018 at Dhaka Medical College Hospital. All male patient aged over 50 years having lower urinary tract symptoms (LUTS) attending to urology OPD was evaluated by history, clinical examination and

necessary investigations to identify the potential candidates for prostate biopsy and potential participants was counseled for prostate biopsy. Total 50 patients were included for the study as per inclusion and exclusion criteria. Patients then allocated randomly into two groups; Group-A, where trans rectal ultrasound guided 6 core biopsy was taken and Group-B, where transrectal ultrasound guided 12 core biopsy was taken. In history Age of the patients, history of LUTS like frequency, urgency, hesitancy, nocturia, poor urinary flow, incomplete voiding and dysuria all were recorded. History of anorectal diseases like pain, per rectal bleeding was taken. History of overall general health including bleeding disorder and diabetes mellitus was taken. Drug history with special attention to anti-thrombotic and anti-coagulant medication like aspirin, clopidogrel and warfarin was taken. Overall general examination as well as examination of urinary system and anorectal region was done. DRE was done to see the size, consistency and nodularity of prostate prior to biopsy. All investigations mentioned below were done for evaluation of the patients. Urine routine & Microscopic exam & culture and sensitivity (Before and 72 hours after the procedure)-to exclude UTI. Ultra sonogram of urinary system- to see prostate size, echogenicity of prostate and any other patology of urinary system with other findings. Complete blood count- for evidence of infection. Blood sugar-to exclude diabetes mellitus. Serum prostate specific antigen level –to see the blood level of this tumor marker for prostate cancer. Prothombin time, Bleeding time & clotting time– to exclude bleeding disorder.

Ethical Consideration

All the patients included in this study were informed about the risk & benefit of the study and informed written consent was taken from each patient as per instructions of the ethical committee.

Data Analysis

After meticulous checking and rechecking all the collected data were compiled. Then statistical analysis (chi square test, Student's unpaired 't' test) was done using computer software Microsoft Xcel, 2010 (Microsoft Corporation, Washington, U.S.) and web based computer software - Graph Pad Software, 2017 (Graph Pad Software, Inc, USA). Necessary help was taken from the resource personnel in the field of statistics. A probability value (p) of less than 0.05 was considered to indicate statistical significance. The results were presented in tables, figures and diagrams. The summarized findings were then presented in the form of tables and graphs.

RESULTS

Table I showed, age ranged of study population from 52 to 80 years. Participants were divided into two groups. Group A underwent 6-core biopsy and group B underwent 12-core prostate biopsy for detection of prostate cancer.

Table I: Distribution of the patients with age (N=50)

Group	Age range (in years)	Mean ±SD	P value
A (n=25)	55-80 yrs.	66.04±7.63	0.218
B (n=25)	52-80 yrs.	65.56±7.70	

Table II showed, for group A mean volume was 53.08±17.38 gram and for group B it was 52.12±18.46 gram respectively.

Table II: Distribution of the patients with volume of prostate (N=50)

Group	Volume of prostate (gram)	Mean ±SD	p-value
A(n = 25)	25-123	53.08±17.38	0.85
B(n = 25)	23-120	52.12±18.46	

Table III showed, serum PSA level was measured in all patients. PSA level was 4.85- 83.68 ng/ml for group A and 5.3- 85.9 for group B. For group A mean PSA level was 41.13±24.76 ng/ml and for group B it was 41.26±24.93 ng/ml.

Table III: Distribution of the patients with prostate specific antigen level (N=50)

Group	PSA level (ng/ml)	Mean ±SD	P-value
A(n = 25)	4.85-83.68	40.53±22.37	
B(n = 25)	5.3-85.9	41.26±24.93	0.91

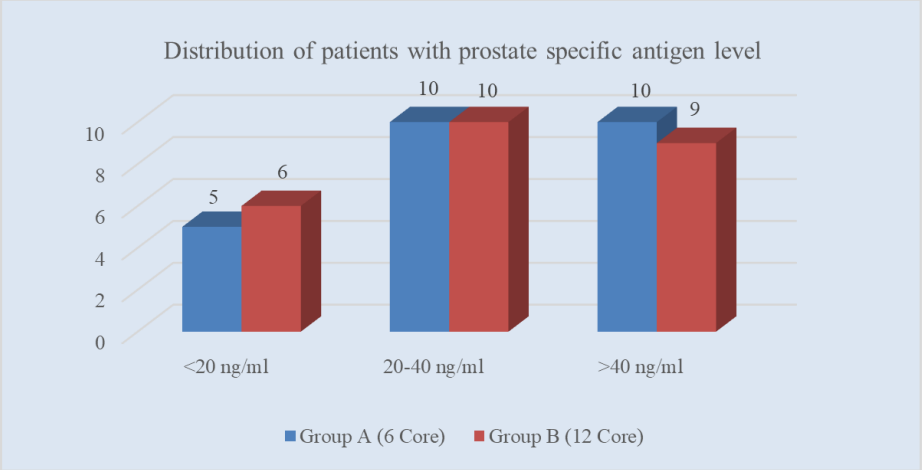

Figure I: Bar chart showed group wise patients prostate specific antigen leveldistribution (N=50)

Table IV showed, digital rectal examination was done in all patients. In group A 19(76%) patients were found normal DRE findings other than enlarged prostate and 6(24%) patients were found abnormal DRE findings, e.g. hard consistency or nodule in the prostate. Similarly, in group B 20(80%) patients were found normal DRE findings other than enlarged prostate and 5(20%) patients were found abnormal DRE findings, e.g. hard in consistency, focal induration or nodule in the prostate.

Table IV: Digital rectal examination findings (N=50)

Group	Normal DRE	Abnormal DRE	P-value
A(n = 25)	19	6	
B(n = 25)	20	5	0.73

Table V showed, in group A 1(4%) patent developed fever (temperature >100° F) and in group B 3(12%) developed fever upto the follow-up period of 72 hours. In group A 5(20%) patient developed dysuria and in group B 10(40%) complained of dysuria after 72 hours follow-up. In group A 8(32%) patient complained of macroscopic hematuria and in group B 15(60%) complained of macroscopic hematuria after 2 hours of prostate biopsy. In group A 3(12%) patient complained of per rectal bleeding and in group B 5(20%) complained of per rectal bleeding after 02 hours of prostate biopsy.

Table V: Comparison of Post procedural complications (N=50)

Group	Fever	Dysuria	Urinary retention	Sepsis	Hematuria	Per rectal bleeding
A (n=25)	1(4.0%)	4(16.0%)	0(0.0%)	0(0.0)	8(32.0%)	3(12.0%)
B (n=25)	3(12.0%)	11(44.0%)	1(4.0%)	0(0.0)	15(60.0%)	5 (20.0%)
P-value	0.6	0.031	1.0	0.00	0.047	0.7

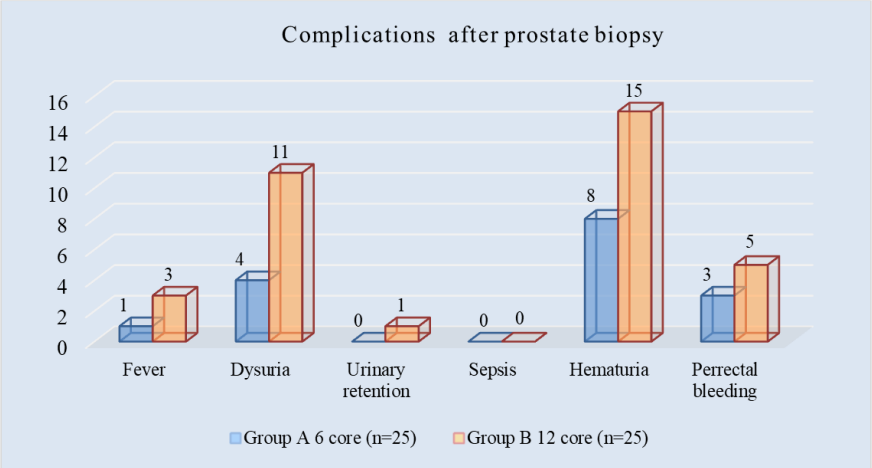

Figure II: Bar chart showed group wise comparison of Post procedural complications (N=50)

Table VI showed, in group A 1(4%) patent developed fever (temperature >100° F) and in group B 3(12%) developed fever up to the follow-up period of 72 hours after trans rectal ultrasono guided (TRUS) prostate biopsy.

Table VI: Comparison of Post procedural fever up to 72 hours (N=50)

Group	Fever	Without fever	'x2'	p-value
A (n=25)	1(4.0%)	24 (96.0%)	0.271	0.60
B (n=25)	3(12.0%)	22 (88.0%)		

Table VII showed, in group A 4(16%) patent developed dysuria and voiding difficulty and in group B 11(44%) developed dysuria and voiding difficulty up to the follow-up period of 72 hours after trans rectal ultrasono guided (TRUS) prostate biopsy.1 patient in group B developed urinary retention for this he was admitted in hospital. In group A no patient developed urinary retention.

Table VII: Comparison of Post procedural dysuria and voiding difficulty after 72 hours (N=50)

Group	Dysuria	Without dysuria	'x2'	p-value
A (n=25)	4(16.0%)	21 (84.0%)	4.67	0.031
B (n=25)	11 (44.0%)	14 (56.0%)		

Table VIII showed, in group A 8(32%) patent developed hematuria and in group B 15(60%) complained macroscopic hematuria after 02 hours of trans rectal ultrasono guided (TRUS) prostate biopsy. Group A patients underwent 6 core prostate biopsy and group B patients underwent 12 core prostate biopsy.

Table VIII: Comparison of Post procedural macroscopic hematuria after 2 hours of trans rectal ultrasono guided prostate biopsy (N=50)

Group	Hematuria	Without Hematuria	'x2'	p-value
A (n=25)	8 (32.0%)	17 (68.0%)	3.95	0.047
B (n=25)	15 (60.0%)	10 (40.0%)		

Table IX Showed, In group A 03 (12%) patient continued perrectal bleeding and in Group B 05(20%) complained per rectal bleeding after 02 hours of trans rectal ultrasono guided (TRUS) prostate biopsy. Group A patients underwent 6 core prostate biopsy and Group B patients underwent 12 core prostate Biopsy (table IX).

Table IX: Comparison of Post procedural per rectal bleeding after 02 hours of trans rectal ultrasono guided prostate biopsy (N=50)

Group	Per rectal bleeding	Without Per rectal bleeding	'x2'	p-value
A (n=25)	3 (12.0%)	22 (88.0%)	0.149	0.70
B (n=25)	5 (20.0%)	20 (80.0%)		

Group A patients underwent Transrectal ultrasound guided 6 core prostate biopsy and Group B patients underwent TRUS guided 12 core biopsy for the diagnosis of prostate cancer. All histopathology reports were collected. For group A carcinoma prostate was diagnosed in 12(48%) patients and for group B it was diagnosed in 15(60%) patients. Benign prostatic hyperplasia was diagnosed in 10(40%) patients in Group A and 08(32%) patients in Group B. Prostatitis were diagnosed in 03(12%) patients in Group A and 02(8%) patients in Group B.

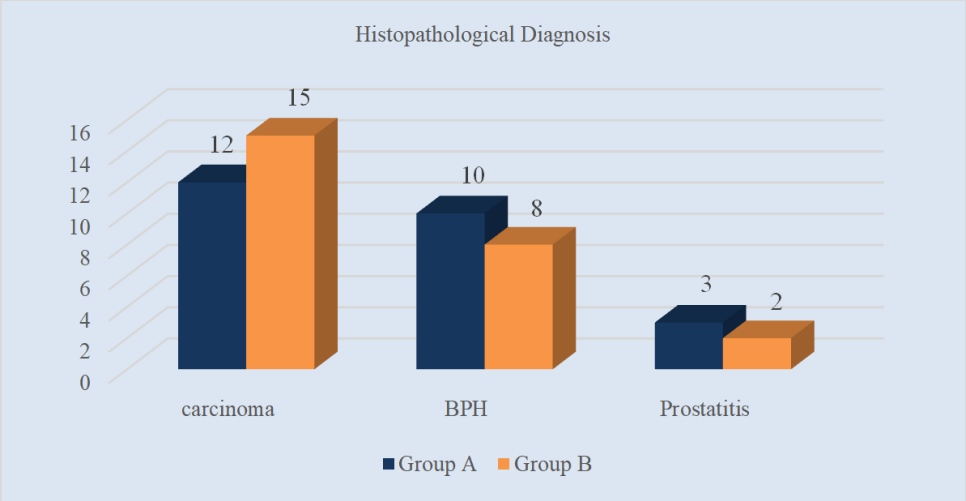

Figure III: Bar chart Showed Group Wise Histopathological Diagnosis (N=50)

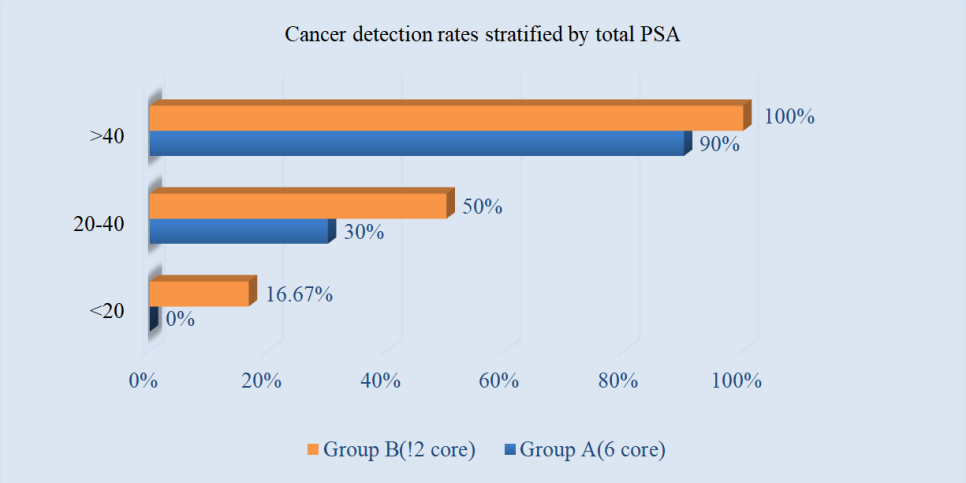

Figure IV: Bar chart Showed Cancer detection rates stratified by total PSA (N=50)

Table X Showed, In Group A 12 cases were diagnosed as carcinoma prostate and 13 cases were diagnosed as other disease. In Group B 15 cases were diagnosed as carcinoma prostate and 10 cases were diagnosed as other disease (Table-X).

Table X: Comparizon of efficacy of two procedures (N=50)

Group	Carcinoma	Non- malignancy	'x²'	p-value
A (n=25)	12(48.0%)	13(52.0%)	0.725	0.395
B (n=25)	15(60.0%)	10(40.0%)		

Table XI: Prostate cancer detection rate stratified by total PSA (N=50)

Total PSA (ng/ml)	Group A (6 core)	Group B (12 core)	P-value
<20 ng/ml	0/5(0.0%)	1/6(16.67%)	1.0
20-40 ng/ml	3/10(30.0%)	5/10(50%)	0.65
>40 ng/ml	9/10(90.0%)	9/9(100%)	1.0

So TRUS guided 6 core prostate biopsy is equally effective to TRUS guided 12 core biopsy in detection of prostate cancer. Three advances established transrectal ultrasonography (TRUS) as the preferred approach for prostate biopsy, first was the development of high frequency transducers, allowing greater resolution and identification of hypoechoic area. The second advance was the spring –driven biopsy device that converted prostate biopsy into a quick OPD procedure. Finally, description of the sextant biopsy method looks much of the subjectivity out of prostate biopsies [13].

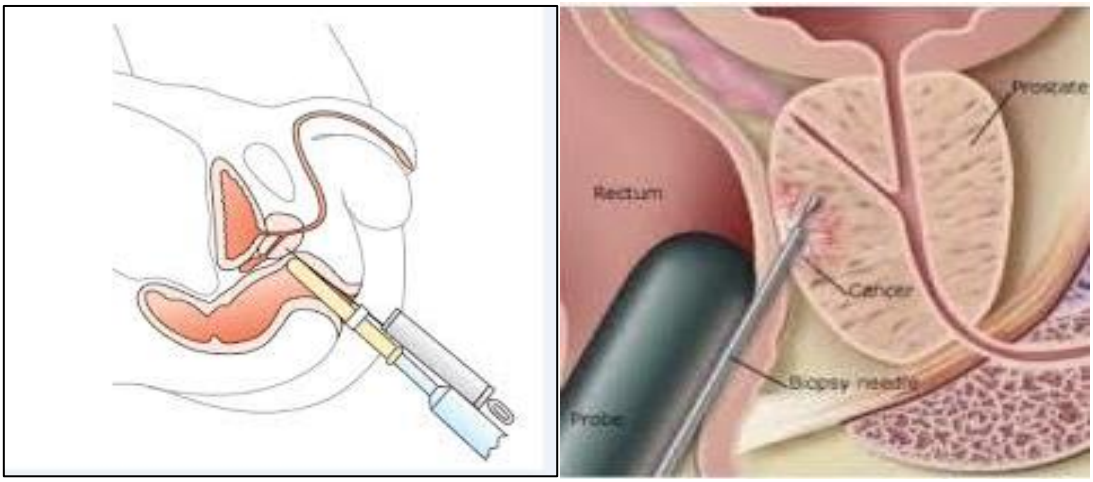

Figure V: TRUS guided prostate biopsy

TRUS requires a endorectal probe, a console and a monitor screen. Prostate images are usually displayed in two planes, the transverse plane and the sagittal plane [14]. The limitation of TRUS in prostate cancer detection are that most hypoechoic lesion found on TRUS are not cancer and that 50% of non-palpable cancers less than 1 cm in greatest dimension are not visualized by ultrasound. Although hypoechoic area on TRUS are more than twice as likely to contain cancer as isoechoic areas 25% to 50% of cancer would be missed if only hypoechoic areas were biopsied. Therefore, any patient with DRE suspicious for cancer or a PSA elevation should undergo prostate biopsy regardless of TRUS findings. The main function of TRUS is to guide the needle in different region of prostate to obtain proper tissue sample [15].

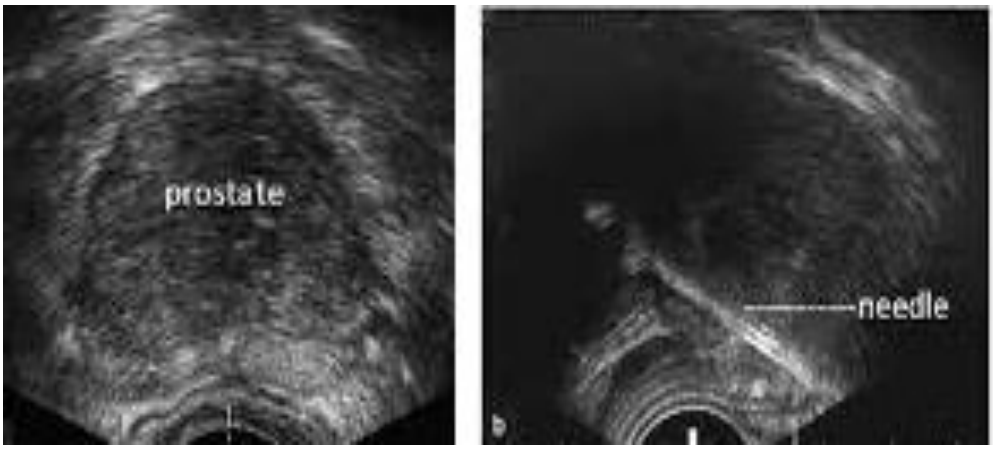

Figure VI: Trans rectal ultrasound scan of prostate and prostate biopsy [16]

DISCUSSION

This study compared the detection rate of prostate cancer and post procedural morbidity between 6 core prostate biopsy and 12 core prostate biopsy. Present study was conducted in similar background of age, prostate volume, DRE findings and serum PSA value. Group A underwent TRUS guided 6 core biopsy and Group B patients underwent TRUS guided 12 core biopsy. Mean age in the study was similar to other study conducted by different investigators. Age limit was similar as prostate cancer is more prevalent after 60 years of age; e.g. study of Ahmed *et al.,* (2006) mean age was 64 years for 6 core and 63 years for 12 core biopsy group [17]. Serum PSA was measured for all patients before prostate biopsy. In this study mean serum PSA was 44.29 ng/ml for group A and 41.26 ng/ml for group B. Mean serum PSA in this study is similar in both groups but high in respect to other study. 80% patient in group A and 76 % in group B were presented with High PSA (>20 ng/ml), The reason of high PSA in this study was that the patient came to urology OPD, Dhaka Medical college hospital in late and when symptomatic. During first evaluation volume of prostate was measured by USG. In this study mean volume was 53.08 gm for group A and 52.12 gm for group B patients. Digital rectal examination was done in all patients. In Group A, 6(24%) patients were seen abnormal DRE findings, e.g. hard in consistency or nodule in prostate.

Similarly, in group B, 5 (20%) patients were seen abnormal DRE findings. Most of the patients in this study underwent prostate biopsy is due to raised PSA level. In current study, carcinoma prostate was diagnosed in 12(48%) patients in group A and 15(60%) patients in group B. Cancer detection was 48 % for 6 core prostate biopsy (group A) and 60% for 12 core prostate biopsy (group B). Cancer detection rate was higher in both groups. Prakash *et al.,* (2013) found higher cancer detection rate up to 59.09% in patients with PSA level greater than 20.1ng/ml [18]. In this study mean S. PSA >40 ng/ml. Here, Cancer detection rate is higher in group B then group A (60% Vs 48%) but this is not statistically significant (p> 0.05). The result of this study was similar to the study done by Kim *et al.,* (2004) [4]. In Korea. (14.4% Vs 17.2%). Korea was a geographical area of low incidence of prostate cancer like Bangladesh. This study was different from some other study. Ahmed *et al.,* (2006) was conducted a study in Egypt [17]. That study showed cancer detection rate was 24.8% for 6core prostate biopsy and 36.4% for 12 core biopsy (p=0.039). In this study cancer detection rate >90% in both groups when S.PSA >40ng/ml (90% Vs 100%). Which is similar to the study conducted by (Fuganty *et al.,* (2002) [19]. They showed Bx12core does not increases prostate cancer detection over Bx6core among patients with high serum PSA and palpable nodule. (Fenely *et al.,* (1997) showed that sextant biopsy could detect the tumor in 36%, 44% and 100% of the cases in which the lesion occupied 2.5%, 5% and 20% respectively of the gland volume [20]. In this study S.PSA is high (average >40ng/ml). Lesion may occupy > 20% volume in most of the cases. This study was conducted in Dhaka medical college hospital. The maximum patient came in DMCH was poor and neglected. Patients came here in late stage when they were symptomatic. They did not come here for screening of prostate cancer. They presented with high PSA. That may be the probable explanation of high cancer detection rate and insignificant difference of cancer detection rate among the two groups. Post procedural morbidity was evaluated and compared in between two groups. In group A, 1(4%) patient developed fever (Temperature> 1000F) and in group B 3(12%) developed fever up to the follow up period of 72 hours. group A, 03(12%) patient complained per rectal bleeding and in group B,05(20%) patient complained per rectal bleeding after 2 hours of prostate biopsy. No significant difference was seen between two groups. In group A, 4(24%) patient complained dysuria and voiding difficulty and in group B,11(44%) patient complained dysuria and voiding difficulty after 72 hours follow up. Among them 1 patient in group B developed retention of urine for which he was admitted. In group A, 8(32%) patient complained naked eye hematuria and in group B,15(60%) patient complained hematuria after 2 hours of prostate biopsy. This difference was significant in between two groups. So, Dysuria with voiding difficulty and haematuria were significantly increase in 12 core group in compare to 6 core groups In this study, minor complications like dysuria with voiding difficulty and hematuria after 2 hours of biopsy was significantly increase in 12 core biopsy group but comments cannot be drawn with this small study.

Limitation of the Study

- Sample size was small; a large sample may help to get a more accurate result.
- High PSA among the study population which may influence the study result.
- The study conducted in a single center in Dhaka city which might not be representative to the whole population

CONCLUSION AND RECOMMENDATION

The result of this study shown that the cancer detection rate is almost equal in trans rectal ultrasound guided 6 core and 12 core prostate biopsy. Post procedural morbidity is less in 6 core prostate biopsy. Further prospective randomized multi-centric study should be performed in future with large sample size.

REFERENCES

1. Center, M. M., Jemal, A., Lortet-Tieulent, J., Ward, E., Ferlay, J., Brawley, O., & Bray, F. (2012). International variation in prostate cancer incidence and mortality rates. *European urology*, *61*(6), 1079-1092.
2. Siegel, R., Ma, J., Zou, Z., & Jemal, A. (2014). Cancer statistics, 2014. *CA: a cancer journal for clinicians*, *64*(1), 9-29.
3. Catalona, W. J., M'Liss, A. H., Scardino, P. T., Richie, J. P., Ahmann, F. R., Flanigan, R. C., ... & Southwick, P. C. (1994). Selection of optimal prostate specific antigen cutoffs for early detection of prostate cancer: receiver operating characteristic curves. *The Journal of urology*, *152*(6), 2037-2042.
4. Silletti, J. P., Gordon, G. J., Bueno, R., Jaklitsch, M., & Loughlin, K. R. (2007). Prostate biopsy: past, present, and future. *Urology*, *69*(3), 413-416.
5. Hodge, K. K., McNeal, J. E., Terris, M. K., & Stamey, T. A. (1989). Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. *The Journal of urology*, *142*(1), 71-74.
6. Naughton, C. K., Miller, D. C., Mager, D. E., Ornstein, D. K., & Catalona, W. J. (2000). A prospective randomized trial comparing 6 versus 12 prostate biopsy cores: impact on

cancer detection. *The Journal of urology*, *164*(2), 388-392.

7. Levine, M. A., Ittman, M., Melamed, J., & Lepor, H. (1998). Two consecutive sets of transrectal ultrasound guided sextant biopsies of the prostate for the detection of prostate cancer. *The Journal of urology*, *159*(2), 471-476.
8. Kim, J. W., Lee, H. Y., Hong, S. J., & Chung, B. H. (2004). Can a 12 core prostate biopsy increase the detection rate of prostate cancer versus 6 core?: a prospective randomized study in Korea. *Yonsei medical journal*, *45*(4), 671-675.
9. Nam, R. K., Saskin, R., Lee, Y., Liu, Y., Law, C., Klotz, L. H., ... & Narod, S. A. (2010). Increasing hospital admission rates for urological complications after transrectal ultrasound guided prostate biopsy. *The Journal of urology*, *183*(3), 963-969.
10. Gonzalez, C., Averch, T., & Boyd, L. AUA / SUNA White paper on the Incidence, Prevention and Treatment of complications related to Prostate Needle Biopsy. *Linthicum: American Urological Association Education and research,* 1012.
11. Carignan, A., Roussy, J. F., Lapointe, V., Valiquette, L., Sabbagh, R., & Pepin, J. (2012). Increasing risk of infectious complications after transrectal ultrasound–guided prostate biopsies: time to reassess antimicrobial prophylaxis?. *European urology*, *62*(3), 453-459.
12. Papagiannopoulos, I. A., Sideris, V. I., Boschmann, M., Koutsoni, O. S., & Dotsika, E. N. (2013). Anthropometric, hemodynamic, metabolic, and renal responses during 5 days of food and water deprivation. *Complementary Medicine Research*, *20*(6), 427-433. Doi: 10.1159/000357718.
13. Terris, M. K. (1999). Sensitivity and specificity of sextant biopsies in the detection of prostate cancer: preliminary report. *Urology*, *54*(3), 486-489.
14. Applewhite, J. C., Matlaga, B. R., Mccullough, D. L., & Hall, M. C. (2001). Transrectal ultrasound and biopsy in the early diagnosis of prostate cancer. *Cancer control*, *8*(2), 141-150.
15. Carrol, P., & Shinohara, K. (2002). Transrectal ultrasound guided prostate biopsy. *J Urol*, 164, 203-207.
16. Dessouky, B. A. E. M., El-Fattah, W. A., & Gaffer, S. T. (2013). The role of transrectal ultrasound-guided biopsy in diagnosis of prostate cancer. *Menoufia Medical Journal*, *26*(2), 163-169.
17. Elabbady, A. A., & Khedr, M. M. (2006). Extended 12-core prostate biopsy increases both the detection of prostate cancer and the accuracy of Gleason score. *European urology*, *49*(1), 49-53.
18. Prakash, V. S., Mohan, G. C., Krishnaiah, S. V., Vijaykumar, V., Babu, G. R., Reddy, G. V. B., & Mahaboob, V. S. (2013). Ten-core versus 16-core transrectal ultrasonography guided prostate biopsy for detection of prostatic carcinoma: a prospective comparative study in Indian population. *Prostate international*, *1*(4), 163-168.
19. Fuganti, P. E., Tobias-Machado, M., Pinto, M. A., Simardi, L. H., & Wroclawski, E. R. (2002). Twelve core prostate biopsy versus six systematic sextant biopsies. *Braz. J. Urol*, *28*, 207-213.
20. Feneley, M. R., & Parkinson, M. C. (1997). Biopsy diagnosis of prostatic cancer--current areas of concern. *Journal of clinical pathology*, *50*(4), 265-266.