

Frequency of Prostatic Adenocarcinoma in Men with Clinical suspicion of malignancy using TURP/Trans rectal Prostate Needle Biopsies with emphasis on Gleason score/grade.

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Abstract

Background: Prostatic pathologies have always stayed the reason of concern in men above 50 years of age; the most dreaded of these is prostatic carcinoma. Progress in medical field has led to development of new investigative and treatment modalities in this domain. The current study is aimed at determining the frequency of prostatic adenocarcinoma in men with clinical suspicion of malignancy using transurethral resection of the prostate (TURP)/trans rectal prostate needle biopsy, using modified Gleason scoring system.

Methods: A descriptive cross-sectional study of histopathological findings of 178 specimens was conducted for men undergoing TURP/trans rectal needle biopsy during a period of 3 years from January 2014 to January 2017 at Benazir Bhutto Hospital, Rawalpindi, Pakistan.

Results: The histopathological findings of TURP/trans rectal prostatic needle biopsies of 43(24.2%) specimens confirmed prostatic adenocarcinoma. Of the rest 133 (74.7%) were diagnosed as benign prostatic hyperplasia, and 2 (1.1%) squamous metaplasia. Mean age of all patients was 65.8±9.02 years. The tagging of the 43 cases of prostatic adenocarcinoma on the basis of Gleason score disclosed that 17 cases (39.5%) had Gleason grade pattern IV followed by 13 cases of Gleason grade pattern III (30.2%) and 8 cases of Gleason grade pattern II (18.6%).

Conclusion: Prostatic adenocarcinoma was noted in 24.2% of our patients with clinical suspicion of prostatic malignancy. Grade IV and II Gleason grade was noted in majority of these patients.

Keywords: Prostatic adenocarcinoma, Gleason score/grade, TURP, trans rectal needle biopsy.

Introduction

Prostate cancer is the second most commonly diagnosed cancer in men worldwide¹. The American Cancer Society's estimates for prostate cancer in the United States for 2017 are about 180,890 new cases of prostate cancer with about 26,120 deaths from prostate cancer. Prostate cancer alone accounts for one out of 5 diagnosis.² In Pakistan, there was unavailability of precise data on the incidence and prevalence of prostate cancer. However, tumour registries have been established in the recent past. Prostate cancer was the seventh most common cancer in men living in Karachi division (7.3%). However, it was the fifth most common tumour (6.63%) in northern areas as seen in a hospital based study.³ In another study in Punjab, the incidence of prostate cancer in men is 3.8%.⁴ Trans rectal ultrasound guided prostate biopsy is presently the 'gold standard' for the diagnosis of prostate cancer. Over the last decade, several extended and saturation biopsy schemes have been used.⁵ Trans rectal ultrasound guidance of biopsies allows multiple prostate cores to be obtained safely, with reduced sampling error and increased accuracy in diagnosing prostate cancer in men with palpable prostate abnormalities.⁶ Trans rectal ultrasound (TRUS)-guided, systematic needle biopsy is the most reliable method to detect cancer of prostate on the basis of clinical suspicion due to raised PSA and abnormal DRE.⁷ Numerous techniques have been devised and implemented for detection of prostate cancer with biopsy. In 1989, Hodge et al recommended systematic sextant biopsies which were taken in parasagittal plane halfway between the lateral border and midline of the prostate on the right and left sides from the base, mid gland and apex of prostate.^{6,8} Stamey et al. recommended shifting of the biopsy more laterally to adequately sample the anterior horn of the peripheral zone.⁹ In 2000, Presti et al determined that six

systematic biopsies of the peripheral zone were not sufficient; minimum 8 core biopsies including the apex, mid-lobar area, mid-gland area, lateral mid-gland area and lateral base should be done.¹⁰ Extended 10-12 core biopsies are now a part of contemporary pathology practice and ensure greater sensitivity for prostate cancer detection.¹¹ In 1966 Donald Gleason presented a score as a prognostic predictor for prostate cancer according to which Gleason grade is the sum of primary and secondary architectural patterns seen in histopathology specimens.¹² International Society of Urological Pathology (ISUP) arranged consensus conferences in 2005 in San Antonio, Texas (USA) and subsequently in 2014 in Chicago (USA) which led to the development of prognostic grade groups (I-V).¹³ Due to increased patient influx in our hospital and lack of sufficient equipment, specimens obtained from TURP (Transurethral Resection of Prostate) are also used to study histopathological pattern of prostate lesions. This study aims to determine the frequency of prostate adenocarcinoma in TRUS-guided needle biopsies and TURP specimen along with grading them according to the modified Gleason grading system.

Materials And Methods

This was a descriptive cross-sectional study carried out at the department of Histopathology, Benazir Bhutto Hospital, Rawalpindi from January 2014 to January 2017 for all the consecutive cases of TRUS needle biopsies and TURP specimens. Standard tissue sections were made from the specimens and stained by Hematoxylin and Eosin. Lab request forms and histopathology reports were retrieved and reviewed. New grade groups were assigned to all the cases and arranged in parallel to the previously assigned Gleason scores. Data was entered in IBM SPSS, version 23 and descriptive statistics were calculated. Cross-tabulations were made for the variables of age-groups according to the Gleason grade seen in all cases of Prostatic adenocarcinoma. Numbers (percentages) were calculated for categorical data such as the frequency of adenocarcinoma observed in TRUS-guided biopsies and TURP specimens.

Results

178 specimens were collected from trans rectal needle biopsies and prostatic chips obtained by TURP. 43 cases out of 178 specimens (24.2%) of prostatic adenocarcinoma were detected. (Table I and II) The rest 133 cases (74.7%) were that of benign prostatic hyperplasia. 2 cases of squamous metaplasia were also observed. The mean age of all the patients was 65.86 ± 9.02 years; ranging from 47 to 90 (Range=43) with the median of 65 years and mode of 70 years.

Majority of the patients (38.8%) were of the age group 61-70 years. (Table III and IV)



Figure I. Prostate Chips Obtained by Transurethral Resection of Prostate

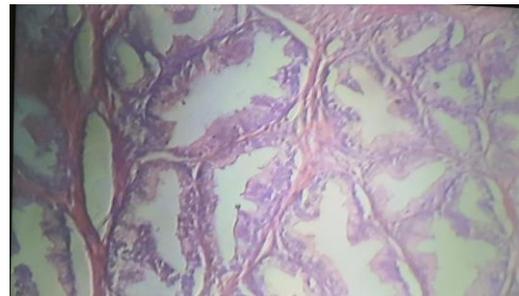


Figure II. Benign Prostatic Hyperplasia

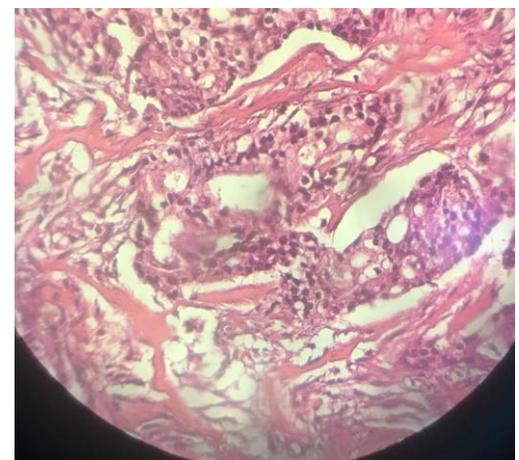


Figure III. Gleason grade V prostate cancer

The tagging of the 43 cases of prostatic adenocarcinoma on the basis of Gleason score disclosed that 17 cases (39.5%) had Gleason grade pattern IV followed by 13 cases of Gleason grade pattern III (30.2%) and 8 cases of Gleason grade pattern II (18.6%). 5 cases (11.7%) of grade pattern V were also seen. No case of grade pattern I was seen. According to old Gleason score 17 cases had Gleason score 8 while 21 cases of Gleason score 7 were seen. Out of the 21 cases with Gleason score 7, 8 cases were

placed in Grade pattern II according to ISUP system 2014 after microscopic evaluation and 13 were placed in grade pattern III. All the 5 cases of Gleason score 9 were assigned Grade V. (Table V)

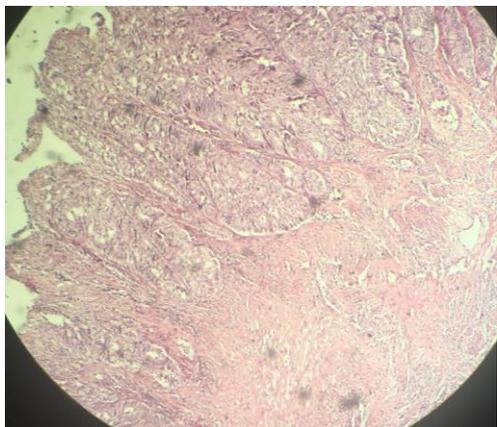


Figure IV. Grade V Gleason Grade Prostate cancer

Table I: Table showing old Gleason scoring system and New Grade Groups as per ISUP 2014

Gleason Scoring System based on primary and secondary architectural patterns	New Grade Groups (ISUP 2014)
Gleason score 3+3=6	Gleason Grade I
Gleason score 3+4=7	Gleason Grade II
Gleason score 4+3=7	Gleason Grade III
Gleason score 4+4=8	Gleason Grade IV
Gleason score 9,10	Gleason Grade V

Table II: Types of Prostatic Lesions seen in sample

Prostatic Lesion	Frequency	Percentage
Benign prostatic hyperplasia	133	74.7
Adenocarcinoma	43	24.2
Squamous metaplasia	2	1.1
Total	178	100.0

Table III: Age wise distribution of patients undergoing trans rectal needle biopsy

Age	Frequency	Percentage
40 to 50 years	4	2.2
51 to 60 years	59	33.1
61 to 70 years	69	38.8
above 70 years	46	25.8
Total	178	100.0

Table IV: Age groups of patients classified according to modified Gleason grading for prostatic adenocarcinoma

		Grade				Total
		2.00	3.00	4.00	5.00	
Age groups of patients	51 to 60 years	3	5	2	1	11
	61 to 70 years	3	6	9	1	19
	above 70 years	2	2	6	3	13
Total		8	13	17	5	43

Table V: Classification of different Gleason scores in Grade groups

GRADE	SCORE			Total
	7.00	8.00	9.00	
2.00	8	0	0	8
3.00	13	1	0	13
4.00	0	17	0	17
5.00	0	0	5	5
TOTAL	21	17	5	43

Discussion

Trans rectal ultrasound-guided needed biopsy is now a well-recognized technique with respect to its accuracy in prostate cancer diagnosis.¹⁴ In our study we focused on the detection of prostatic adenocarcinoma in the prostatic chips as well as biopsy specimen over a period of three years in order to prolong the duration of our study as well as to include the adequate number of patients in the sample.¹⁵

The cancer detection rate in our study was 24.2% while in the recent studies conducted in Pakistan, the detection of prostate cancer was much higher.^{3,16,17} The difference between the detection rates can be due to sample size variation and availability and utility of TRUS in different clinical settings. Similar variation of our result was seen with international studies as well. These differences, in addition to study population and duration can also be attributed to the fact that all the patients in those studies had raised PSA with or without prostatism.¹⁸⁻²²

The mean age of our cases of prostate cancer were found in concordance to all the mentioned researches. Gleason score was first proposed in 1966.¹¹ After the changes made in 2014 by ISUP modified grade pattern

for prostatic adenocarcinoma has gained immense acceptability among urologists and pathologists.¹³ Gleason score continues to be a very important predictor of prognosis of prostate cancer as well as for clinical management.²³ There is a lot of difference between the present Gleason grading system practice and the original one. On needle core biopsy, Gleason grade patterns I and II are not assigned any longer due to two main reasons; bad reproducibility and because poor correlation was seen with radical prostatectomy.^{24,25} Many studies show that a tertiary pattern might also be seen which worsens the prognosis, but does not make it worse than the next higher score still.²⁶⁻²⁹ There have been numerous changes in studying the oncology of prostate as well as grading methods. The ultimate goal of these grading patterns is better prognosis and good clinical management. At present the modified grading pattern is a translation of the old Gleason scoring system e.g. 4+3=7 is Grade Group III. But with the passage of time histopathologists will learn to classify grades of prostate cancer directly on the basis of histological pattern seen under the microscope e.g. in grade III distinctly infiltrative margins are seen.³⁰ There are some limitations in the present study. Firstly, the data was collected from a single centre. Some of the patients were excluded from the study because of missing data. Finally, lymph node dissections were not done, so the Gleason pattern could not be correlated with the degree of spread. PSA screening is not done routinely in the current setting so this also reduces the detection rate of prostate cancer. Large scale multicentre studies are needed to overcome these limitations along with PSA screening which would help greatly in the early detection of prostatic adenocarcinoma.

Conclusion

24.2% of our patients undergoing biopsy for prostatic carcinoma were diagnosed adenocarcinoma histopathologically. Grade IV and II Gleason grade was noted in majority of these patients.

References

1. Bashir MN. Epidemiology of Prostate Cancer. *Asian Pac J Cancer Prev* 2015;16(13):5137-5141.
2. Seigel RL, Miller KD, Jemal A. Cancer statistics. *CA Cancer J Clin* 2016;7-30.
3. Barakzai MA, Mubarak M, Kazi JI. Histopathological lesions in transrectal ultrasound guided biopsies of prostate with raised serum prostate specific antigen. *Nephro-Urol Mon* 2011;3(3):186-90.
4. Aziz Z, Sana S, Saeed S, Akram M. Institution based tumor registry from Punjab. Five year data based analysis. *J Pak Med Assoc* 2003;53(8):350-3.
5. Kanao K, Eastham JA, Scardino PT, Reuter VE, Fine SW. Can transrectal needle biopsy be optimised to detect nearly all

- prostate cancer with a volume of ≥ 0.5 mL? A three-dimensional analysis. *BJU Int* 2013; 112: 898-904.
6. Hodge KK, McNeal JE, Stamey TA. Ultrasound guided transrectal core biopsies of the palpable abnormal prostate. *J Urol* 1989; 142(1):66-70.
7. Shariat SF, Roehrborn CG. Using biopsy to detect prostate cancer. *Rev Urol* 2008;10(4):262-80.
8. 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):71-5.
9. Stamey TA. Making the most out of six systematic sextant biopsies. *Urology* 1995; 45(1):2-12.
10. Presti JC, 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):166-7.
11. Presti JC Jr, O'Dowd GJ, Miller MC, Mattu R, Veltri RW. Extended peripheral zone biopsy schemes increase cancer detection rates and minimize variance in prostate specific antigen and age related cancer rates. Results of a community multi-practice study. *J Urol* 2003;169(1):125-9.
12. Pierorazio PM, Walsh PC, Partin AW, Epstein JI. Prognostic Gleason grade grouping: data based on the modified Gleason scoring system. *BJU Int* 2013; 111(5): 753-60.
13. Chen N and Zhou Q. The evolving Gleason grading system. *Chin J Cancer Res* 2016; 28(1):58-64.
14. Applewhite JC, Matlaga BR, McCullough DL. Results of the 5 region prostate biopsy method: the repeat biopsy population. *J Urol* 2002; 168:500-503.
15. Hingrajia NM, Desai H, Goswami HM, et al. Histopathological study of transrectal ultrasound guided biopsies of prostate in patients with raised serum prostate specific antigen. *NHL Journal of Medical Science* 2015; 4(1):70-4.
16. Rashid R, Mubarak M, Kazi JI. Frequency of Adenocarcinoma in Transrectal Ultrasound-guided Prostate Needle Biopsies in Men with Clinical Suspicion of Prostate Cancer and Raised Serum Prostate Specific Antigen Rahma. *Middle East Journal of Cancer* 2013; 4(2): 73-78.
17. Sohail SK, Sarfraz R, Imran M, Khan NA, Yusuf NW. Power doppler ultrasonography guided and random prostate biopsy in prostate cancer diagnosis - a comparative study *J Pak Med Assoc* 2015 Jan; 65(1):65-8.
18. 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.
19. 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.
20. 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.
21. Ravery V, Goldblatt L, Royer B, Blanc E, Toubanc M, Boccon-Gibod L. Extensive biopsy protocol improves the detection rate of prostate cancer. *J Urol* 2000; 164(2):393-6.
22. Babaian RJ. Extended field prostate biopsy enhances cancer detection. *Urology* 2000; 55(4):453-6.
23. Gordetsky J and Epstein J. Grading of prostatic adenocarcinoma: current state and prognostic implications. *Diagnostic Pathology* 2016; 11(25): 1-8.
24. Epstein JI. Gleason score 2-4 adenocarcinoma of the prostate on needle biopsy: a diagnosis that should not be made. *Am J SurgPathol* 2000; 24(4):477-8.

25. Cury J, Coelho RF, Srougi M. Well-differentiated prostate cancer in core biopsy specimens may be associated with extraprostatic disease. *Sao Paulo Med J* 2008; 126(2):119-22.
26. Pan CC, Potter SR, Partin AW, Epstein JI. The prognostic significance of tertiary Gleason patterns of higher grade in radical prostatectomy specimens: a proposal to modify the Gleason grading system. *Am J SurgPathol* 2000; 24(4): 563-569.
27. vanOort IM, Schout BM, Kiemeny LA, Hulsbergen CA, Witjes JA. Does the tertiary Gleason pattern influence the PSA progression-free interval after retropubic radical prostatectomy for organ-confined prostate cancer? *Eur Urol* 2005; 48(4):572-576.
28. Hattab EM, Koch MO, Eble JN, Lin H, Cheng L. Tertiary Gleason pattern 5 is a powerful predictor of biochemical relapse in patients with Gleason score 7 prostatic adenocarcinoma. *J Urol* 2006; 175(5):1695-1699.
29. Trock BJ, Guo CC, Gonzalgo ML, Magheli A, Loeb S, Epstein JI. Tertiary Gleason patterns and biochemical recurrence after prostatectomy: proposal for a modified Gleason scoring system. *J Urol* 2009; 182(4):1364-1370.
30. Kryvenko ON and Epstein JI. Prostate Cancer Grading A Decade After the 2005 Modified Gleason Grading System. *Arch Pathol Lab Med* 2016; 140: 1140-52.