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Histopathology

The Clinicopathologic Pattern of Prostate Cancer at a Tertiary Care Teaching Hospital in Bangladesh

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Abstract

Original Research Article

Objectives: The objective of this study was to determine the clinicopathologic pattern of prostatic diseases. To determine the Gleason grading and scoring of prostate cancer in Bangladesh. ***Methods:*** The records of patients who underwent histopathological examinations of prostatic biopsy specimens were reviewed retrospectively at National Institute of Kidney Diseases and Urology in Bangladesh during the period of January 2022 to December 2023. The histological diagnosis prostatic diseases and Gleason grading and scoring of the biopsy specimens of prostate cancer patients were studied. ***Results:*** A total of 220 patients were included in this study. The age ranged from 45-100 years (median age: 58 years). One hundred and sixty cases of transurethral resection of the prostate (TURP), 40 cases of digital guided transrectal core biopsy specimens, 10 cases of transrectal ultrasound (TRUS) guided core biopsy specimens, 08 cases of simple prostatectomies and 02 cases of radical prostatectomies were studied. The most frequent disease of this study group were benign hyperplasia prostate (67.27%, n=220) followed by adenocarcinoma of prostate in 60 cases (27.27%, n=220). Out of 220 total cases of prostatic biopsy, 160 (72.27%, n=220) cases were prostatic diseases and rest 60 (27.27%, n=220) prostate cancer. Diagnostic sensitivity of TRUS guided biopsy specimens (80%, n=10) were more than digital guided core biopsy specimens (62.5%, n=40). Fourteen cases (8.75%, n=148) of TURP obtained biopsy showed prostate cancer. Out of 8 cases of total prostatectomy obtained biopsy, 07(87.5%) cases were. Rest one (12.5%) was benign hyperplasia prostate. All of the two radical prostatectomy specimens obtained prostatic tissue showed poorly differentiated adenocarcinoma prostate. Out of 8 cases of total prostatectomy obtained biopsy, 07(87.5%) cases were adenocarcinoma prostate. Rest one (12.5%) was benign hyperplasia prostate. All radical prostatectomy obtained prostatic tissue showed poorly differentiated adenocarcinoma prostate. Of adenocarcinoma prostate in 60 cases, 59 cases (98.33%) showed high serum PSA and rest one case (1.67%) was decreased serum PSA because of poorly differentiated carcinoma with extensive areas of necrosis. Among total 160 cases (72.27%, n=220) of prostatic diseases, only 10 cases (6.25%, n=160) cases showed high serum PSA. Out of 148 cases (72.27%, n=220) of BEP, only 7 cases (4.72%, n=148) showed serum PSA high. The most frequent Gleason score among prostatic carcinoma were group 3 and 4 and Gleason score 7 (45%, n=60) followed by group-4- 5 and Gleason score 8-10 (33.33%, n=60) in this study group. Only (21.67%, n=60) of prostatic carcinoma were Gleason score 6 (well differentiated adenocarcinoma). ***Conclusions:*** The Pattern of prostate cancer can be easily diagnosed by histopathology of TURP obtained prostatic tissue biopsy and digital or ultrasound guided core biopsy. Gleason Grading and scoring of prostate cancer is of great prognostic and therapeutic value. Further future studies addressing this issue needed to confirm the potential rising trend, and its possible etiology.

Keywords: TURP, TRUS, DRE, Prostate cancer (PCa), Benign Enlargement Prostate (BEP) Prostate specific antigen (PSA).

INTRODUCTION

Prostate cancer is one of the most commonly diagnosed cancers in men. Worldwide, it is the second most common male malignancy (lung cancer is first). In 2018, more than 1.6 million men were diagnosed with prostate cancer globally and over 366,000 died from it [1]. Prostate cancer is often clinically indolent, sometimes, no intervention is required. The diagnosis of prostate cancer is suspected when individuals have a hard, irregular enlarged prostate or nodule on physical examination as well as an elevated prostate-specific antigen (PSA) level on laboratory analysis. Now a days, wide spread use of prostate specific antigen (PSA) and transrectal biopsy core with or without ultrasound make prostate cancer diagnosis becoming easy. The diagnosis is confirmed with a biopsy and histopathologic assessment. The Gleason score is the primary initial histologic assessment tool used to grade prostate malignancies and has proven to have significant prognostic value [2]. The Gleason grade is primarily based on the architecture or arrangement of the malignant cells within the tumor and the degree of differentiation. Since the prostate is a gland, the less glandular the microscopic appearance, the higher the Gleason grade, ranging from 1 to a maximum of 5. A Gleason grade of 1 would appear almost normal while a Gleason grade of 5 would not show any glandular features at all; just sheets of abnormal cells [3].

Gleason grade is an established prognostic indicator in Ca prostate. This grading system is based entirely on the histologic pattern of arrangement of prostatic carcinoma cells in H&E-stained sections. Five basic grade patterns are used to generate a histologic score, which can range from 2 to 10. Increasing Gleason grade or score is directly related to the poor prognostic value.

In the light of above context, a study was performed at a tertiary teaching hospital, Dhaka to determine clinicpathologic pattern followed by Gleason grading and scoring of prostate cancer.

MATERIALS AND METHODS

This was a retrospective study. 'National Institute of Kidney Diseases and Urology' (NIKDU) is the only national and tertiary care hospital representing whole Bangladesh regarding kidney and urology related diseases located at Sher-E-Bangla Nagar, Dhaka. Hence, the data presented here represents to a major part of the Bangladeshi population.

The medical records of patients who underwent histopathological examinations of prostatic specimens taken by the technique of Transurethral resection of prostate (TURP), digital transrectal and Transrectal ultrasound (TRUS) core biopsy specimens were reviewed at National Institute of Kidney Diseases and Urology during the period of January 2022 to December 2023. The clinical information, age, PSA value, digital rectal examination (DRE) findings, indications for biopsy, histological diagnosis and histological grading of cancer patients were studied thoroughly. The Transurethral resection of prostate (TURP) and digiital guided transrectal specimens were collected by experienced Urologist and Transrectal ultrasound (TRUS) guided prostatic biopsy cores by Urologist with the help of Sonologist. Written informed consent was obtained for each patient prior to digital and TRUS guided biopsies. The inclusion criteria were TURP indicated operated specimens, digital guided transrectal and TRUS guided biopsy specimens. The repeat biopsies were excluded from the study. The cutoff value for prostate cancer was fixed serum PSA 4ng/ml.

TURP operation were done with or without suspicion of cancer. Moreover, it was done as the treatment of mostly due to benign enlargement of prostate. TRUS core biopsy or digital guided transrectal core biopsy were done due to highly suspicious of malignancy. The histological diagnosis and Gleason's grading and scoring of the biopsy specimens of prostatic cancer patients were studied. Digital guided transrectal or Transrectal ultrasound guided biopsy cores were taken from various sites in the prostate according to the standard technique. Microscopic results were stratified according to pathological findings such as adenocarcinoma, benign prostatic hyperplasia (BPH) alone, BPH with inflammation and inflammation alone. Prostate cancers were graded and scored according to the Gleason system. Gleason's grading or scoring were not perform other than prostate cancer such as urothelial carcinoma. Transrectal biopsy core were studied by observing total number of biopsy core sent for histopathology, the number and percentage of biopsy cores that contain cancer in each of the core and Gleason's grading, grouping and scoring.

Method of Gleason scoring done in this study group:

Gleason pattern-1 means that the cells look almost like normal prostate cells and gland. Gleason pattern -2 with more spaces between glands, Gleason pattern 3 describes well-formed, separated glands, variable in size. Gleason pattern 4 includes fused glands, cribriform and glomeruloid structures and poorly formed glands. Gleason pattern 5 involves poorly differentiated individual cells, sheets of tumour, solid nests, cords and linear arrays as well as comedo necrosis. Despite several changes in clinical diagnosis of prostate cancer, the histological Gleason scoring system is still the most powerful prognostic tool [4]. The final Gleason score is reported as the sum of the two most predominant patterns present in the histological specimen, and in current clinical practice the lowest Gleason score assigned is Gleason 6 (3 + 3) [5].

The Gleason grade or group was based on how abnormal the cells appear. Group-3 with infiltration of cells from glands at margin, group-4 with irregular masses of cells, glands and group-5 with lack of glands and sheets of cells. The cells look very different from normal prostate cells. The Gleason grade or Gleason pattern ranged from 1 to 5 with 5 having the worst prognosis. Most prostate cancers contain cells that are different grades. So the two most common grades were used. Higher numbers indicated a faster growing cancer that is more likely to spread.

The Gleason Score is always a sum of two numbers. These two numbers represent the Gleason grade of the predominant pattern added to the grade of the next most common pattern. If only one Gleason grade is present, then this is doubled. The Gleason score (GS) ranged from 2 to 10 with 10 having the worst prognosis. If the highest grade takes up most (95% or more) of the biopsy, the grade for that area was counted twice as the Gleason score. Primary grade was regarded as the most predominant and secondary grade was the next most predominant pattern. A Gleason Score of less than 6 usually indicates indolent cancer that is less likely to be clinically significant and cannot be diagnosed only by light microscope. A Gleason score of 6 (3+3) was regarded as low grade or well differentiated adenocarcinoma of prostate. A Gleason score of 7 (3+4 or 4+3) was intermediate grade or moderately differentiated adenocarcinoma and a Gleason score of 8 to 10 was high grade or poorly differentiated adenocarcinoma.

RESULTS

A total of 220 patients were included in this study. The age ranged from 50-100 years with median age 58years. One hundred and sixty cases of transurethral resection of the prostate (TURP), 40 cases of digital guided transrectal and 10 transrectal ultrasound guided biopsy cores (TRUS), 08 cases of simple prostatectomies and 02 cases of radical prostatectomies were studied.

Table-1: Distribution of prostatic cancer and other prostatic diseases in this study

Diagnosis	Individual total number of cases	Percentage
Adenocarcinoma	60	27.27
Benign hyperplasia prostate	148	67.27
Benign hyperplasia prostate with prostatitis	07	3.18
Chronic Prostatitis only	05	2.27
Total	**220**	**100**

Table-1 shows most frequent disease of this study group were benign hyperplasia prostate (67.27%) followed by adenocarcinoma of prostatic in 60 cases (27.27%). Out of 220 total cases of prostatic biopsy, 160 (72.27%) cases were prostatic diseases and rest 60 (27.27%) prostatic carcinoma.

Table-2: Two hundred twenty two prostatic biopsy cases in different techniques of biopsy with prostate cancer

Prostatic tissue	Total number of biopsy	Prostate cancer patients with percentage	Prostate cancer negative patients with percentage
TURP biopsy cases	160	14 (8.75%)	146 (91.25%)
Digital guided core biopsy	40	25 (62.5%)	15 (37.5%)
TRUS core biopsy cases	10	8 (80%)	02 (20%)
Total prostatectomy	08	07 (87.5%)	01 (12.5%)
Radical prostatectomy	02	02 (100%)	00
Total	**220**	**60**	**160**

Table-2 shows that the diagnostic sensitivity of TRUS guided biopsy specimens (80%) were more than digital guided biopsy specimens (62.5%). Fourteen cases (8.75%) of TURP obtained biopsy showed prostate cancer. Out of 8 cases of total prostatectomy obtained biopsy, 07(87.5%) cases were. Rest one (12.5%) was benign hyperplasia prostate. All radical prostatectomy obtained prostatic tissue showed poorly differentiated adenocarcinoma prostate.

Table-3: Distribution of Sixty prostate cancer positive patients in PSA and DRE (N=60)

Indications	N	(%)
Elevated PSA	58	(96.66)
Abnormal DRE+	1	(1.67)
Elevated PSA+abnormal DRE	1	(1.67)

PSA-prostate specific antigen, TRUS-Transrectal ultrasound, DRE: Digital Rectal Examination

Table-3 shows that 58 cases (96.66%) of prostate cancer were previous indication of cancer by elevated serum PSA. In one case, there were both DRE abnormality and elevated PSA. In another case, there was abnormal DRE findings only.

Table-4: Prostate specific antigen (PSA) values among patients with prostatic diseases (N=70)

Disease	Total number	PSA values (ng/ml)	Number of high values	Percentage (%)
Adenocarcinoma	60	4-1540	59	98.33
		3 ng/ml	01	1.67
BEP	148	4-8	07	4.72
BEP with chronic prostatitis	07	4-10	02	28.57
Chronic prostatitis only	05	08	01	20
Total	**220**	-	**70**	

Table-4 shows correlation between serum elevation of PSA with prostatic carcinoma and other diseases in this study. Of adenocarcinoma prostate in 60 cases, 59 cases (98.33%) showed high serum PSA and rest one case (1.67%) was decreased serum PSA because of poorly differentiated carcinoma with extensive areas of necrosis. Among total 160 cases (72.27%, n=220) of prostatic diseases, only 10 cases (6.25%, n=160) cases showed high serum PSA. Out of 148 cases (72.27%, n=220) of BEP, only 7 cases (4.72%, n=148) showed serum PSA high. However, In case of prostatic disease, serum high PSA range were 4-10 ng/ml only.

Prostate specific antigen values ranged widely between 0.04-1550ng/ml. A total 70 cases (31.82%, n=220) showed high serum PSA values. Among 160 non-cancer cases (72.73%, n=220) of prostatic tissue, only 11 patients (6.85%, n=160) revealed PSA values high ranged 6-10 ng/ml. Among the cancer patients, PSA values were high in 59 cases (98.33%) patients. Only one prostate cancer patient showed PSA low values.

Table-5: Gleason grading and scoring of Prostatic carcinoma in this study group (n=60)

Gleason grade group	Gleason scoring	Number with percentage	Prognostic value
Group-1	3+3=6	13 (21.67)	Well differentiated adenocarcinoma
Group-2	3+4=7	17 (28.33)	Moderately differentiated adenocarcinoma
Group-3	4+3=7	10 (16.67)	Moderately differentiated adenocarcinoma
Group-4	4+4	18 (30)	Poorly differentiated adenocarcinoma
Group-5	(4+5)=9; (5+4)=9 Or (5+5)=10	02 (3.33)	Poorly differentiated adenocarcinoma

Table-5 shows that most frequent Gleason score among prostatic carcinoma were group 3 and 4 and Gleason score 7 (45%, n=60) followed by group-4- 5 and Gleason score 8-10 (33.33%, n=60) in this study group. Only 13 cases (21.67%, n=60) of prostatic carcinoma were Gleason score 6 (well differentiated adenocarcinoma).

DISCUSSION

The diagnosis of prostate cancer (PCa) mostly relies on clinical assessment with digital rectal or transrectal ultrasound guided core biopsy examination, serum PSA and histological examination.

A total of 220 cases of prostatic biopsy specimens obtained by TURP, digital guided transrectal or TRUS technique were studied. The primary objective of this retrospective study is to determine the clinicopathologic patterns of prostatic diseases and gleason grading-scoring of prostate cancers in Bangladeshi patients. The incidence of prostate cancer (PCa) has been reported to be low in Southeast Asia and Middle east [9]. Prostate cancer is the third most common cancer in men in the world, with 543,000 new cases each year according to the World Cancer Report 2003 [10]. During1994, there were 137 new cases of PCa among Saudis, accounting for 2.7% of all newly diagnosed cases. Prostate cancer ranked sixth for males with a crude incidence rate of 2.1 per 100,000 for that year [11, 12].

This was very low compared to the western countries [5]. Two reports of two different prostatic biopsy specimens study group from Saudi Arabia showed the incidence of prostate cancer were 27.5% and 28.7% respectively when combined PSA, DRE, and TRUS were used [13, 14].

The current study shows an overall incidence of 27.27% of prostatic carcinoma among all prostatic specimens confirming the similar low incidence of prostatic carcinoma in the Middle East and Southeast Asian region. Still the western cancer detection rate is higher in the range of 65-80% [8, 9]. Our study showed 76% incidence of PCa in TRUS biopsies but 34.3% were shown in another study of Taha and Kamal *et al.*, in 2005 [10]. The incidence regarding prostate cancer were reported as 15%, compared to a 7.2% incidence reported 12 years ago [15].

There was a difference regarding prostatic cancer positivity of TURP obtained biopsy (8.75%) and TRUS obtained biopsy (74%) in this study group. It was due to TURP operation was performed mostly due to therapeutic purpose, on clinical impression of benign enlargement of the prostate and histopathological examination was the obligatory consequences. On the other hand, TRUS technique was to perform for diagnostic purpose and operation was the after diagnostic impact.

One of the prostate cancer in our study revealed lower serum PSA value (3ng/ml). Very recently, many authors have recommended lowering the total serum PSA cutoff for prostate biopsy from 4-2.5 ng/ml. They found, up to 17% of men with a PSA level below the prostate biopsy cutoff of 2.5 ng/ml may have prostate cancer [16].

In 2009, Jones *et al.*, [17] reported on the probability of finding incidental PCa during TURP in the PSA era. In their study, ninety-five of their patients were biopsied before TURP. Elevated PSA (using the cutoff of 4.0 ng/ml) was observed in 90 patients and was the most common indication for biopsy. Of the 95 patients, 5 (5.3%) were found to have unrecognized cancer in the TURP specimen, highlighting the need to lower the PSA cutoff.20 Our findings support the recommendations to do the cutoff value for prostatic biopsy to 2.5 rather than 4 ng/ ml. Using 4 ng/ml as a cutoff could miss up to 13.6% of our cancer patients.

Prostate cancer is the second leading cause of cancer death in men [18] Prostatic carcinomas are graded according to the Gleason scoring system which was first established by Donald Gleason in 1966 [19]. The Gleason scoring system is acknowledged by the World Health Organization (WHO) and has been modified and revised in 2005 and 2014 by the International Society of Urological Pathology (ISUP) [20].

Prostate cancer is diagnosed after a biopsy. One or more tissue samples are taken from the prostate and examined under the microscope. The Gleason grading system refers to how abnormal the prostate cancer cells look and how likely the cancer is to advance and spread. A lower Gleason grade means that the cancer is slower growing and is less aggressive.

Gleason grade is an established prognostic indicator in Ca prostate. This grading system is based entirely on the histologic pattern of arrangement of prostatic carcinoma cells in H&E-stained sections. Five basic grade patterns are used to generate a histologic score, which can range from 2 to 10. Increasing Gleason grade or score is directly related to the poor prognostic value.

CONCLUSION

Pattern of prostate cancer can be determined by TURP and digital or ultrasound guided core biopsy of prostate. Gleason grading and Scoring of prostate cancer is a gold standard diagnostic and prognostic tool in Bangladesh. The Gleason score also helps to treatment options. However, the rate of incidental prostate cancer detected in surgical specimens removed from clinically presumed benign disease appears to be rising.

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