VOLUME - 12, ISSUE - 05, MAY - 2023 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Pathology

ROLE OF EXPRESSION OF P63 AND CALPONIN IN PROSTATIC BIOPSIES

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ABSTRACT

Background: An increased number of mortality and morbidity in elderly men is caused due to prostatic diseases all over the world. An increase in mass screening programmes conducted with the help of Prostate Specific Antigen (PSA) blood test along with Digital rectal examination (DRE) and imaging studies has resulted in an upsurge in the diagnosis of prostatic cancer which is markedly noted in the recent decades. **Material And Methods:** A total 100 cases of formalin fixed paraffin embedded histological sections of various prostatic lesions including benign prostatic hyperplasia, prostatic intraepithelial lesion and prostate carcinoma were studied. Out of 100 cases, 55 cases were benign prostatic hyperplasia, 10 cases of prostatic intraepithelial lesion and 35 cases were of prostate adenocarcinoma. All the sections were stained with Hematoxylin and Eosin stain and then immunohistochemical staining of p63 and Calponin was performed on all the cases (figure 6- 12). The parameters used to analyse the expression of both p63 and calponin were - Pattern of staining, Percentage of stained cell, Intensity of staining reaction. **Results:** Total 100 cases included in this study, out of which 55 (55%) cases were benign prostatic hyperplasia, 10 (10%) cases of prostatic intraepithelial neoplasia, and 35 (35%) cases were prostatic adenocarcinoma, majority of specimens (78%) were TURP followed by trucut biopsy (20%), Suprapubic prostatectomy (2%). The proportion of Transurethral resection of prostate (TURP) was significantly higher as compared to the proportion of Trucut biopsy and supra pubic prostatectomy (SPP) ($p<.001$). Expression of calponin in various prostatic lesion. On analysing expression of proliferation marker calponin, in BPH it was expressed in only 52 cases out of 5 cases (94.5%) and 3 cases (8.6%) were negative. **Conclusion:** Our study concluded that the proportion of Benign prostatic hyperplasia was significantly higher as compared to the Prostatic intraepithelial neoplasia and Prostatic adenocarcinoma. Immunohistochemical staining by p63 is diagnostically reliable in identifying basal cells in prostatic needle biopsies and TURP specimens. p63 is a valuable tool with high sensitivity in differentiating BPH from prostatic carcinoma. The decreased or absent stromal staining of calponin which indicates a reactive stroma in malignancy can be used alone or in conjunction with p63 for confirmation of diagnosis of prostatic carcinoma

KEYWORDS :

INTRODUCTION

The adult prostate is the largest accessory gland of the male reproductive system. (1) It is a firm, rubbery, walnut sized gland located directly inferior to the urinary bladder and wraps the urethra's proximal surface circumferentially in the lower pelvis. It is enclosed by a fibrous capsule which is innervated by nerves and a plexus of arterial and venous vessels surrounded by a visceral layer of pelvic fascia. (2) It weighs 11 grams (around 7- 16 grams on average). (3) It is a compound tubular-alveolar gland which acts a muscle-driven mechanical switch between ejaculation and urination.(4) Embryologically, due to epithelial evaginations from the prostatic urethra, the prostate develops during the third month of pregnancy. Simple peri- urethral glands (Alberian cervical glands) are produced by evaginations from the proximal prostatic urethra. (5)

The central zone located posterior to the transition zone surrounds the ejaculatory duct makes up the entire base of the prostate gland. Both inflammation and cancer are resistant to this region. Benign Prostatic Hyperplasia (figure 1) and Atypical Adenomatous Hyperplasia are most frequently found in the transition zone, which has the smallest surface area in the prostate gland. (5).

An increased number of mortality and morbidity in elderly men is caused due to prostatic diseases all over the world. Prostatic cancer has become a major health threat in industrialized world during the recent years of the 21st century. At least three fourth of the registered cases all over the globe has been contributed by prostatic cancer. (6) Prostate cancer is considered as the sixth commonest cancer all over the world. It is accounted to be the second most commonly occurring malignancy worldwide, being preceded by lung cancer in men. Prostatic cancer is considered as the fifth leading cause of mortality associated to cancer amongst men. (7–9)

As of 2018, one in nine men was estimated to be at risk of developing prostate cancer during their lifetime. (10) Prostate cancer accounts for 1,276,000 new cases causing 359,000 deaths (3.8% of total number of deaths caused by cancer among men) in 2018. (11,12) The global burden of prostatic cancer, by the year is estimated to rise to 1,700,000 novel cases and 499,000 deaths owing to ageing and the exponential growth of the population all over the world. (13) An increase in mass screening programmes conducted with the help of Prostate Specific Antigen (PSA) blood test along with Digital rectal examination (DRE) and imaging studies has resulted in an upsurge in the diagnosis of prostatic cancer which is markedly noted in the recent decades. (14–16) The screening for prostate cancer at any form aims to reduce the disease-

specific overall mortality which in turn shall improve the quality of life of the individual. Successful treatment can be achieved definitely in a shorter span of time, since the screening identifies cancers at an early and treatable stage. (17)

Biopsies' including needle core and Transurethral Resection of the Prostate (TURP) requires interpretations which are accurate for early diagnosis. This is very challenging in the presence of benign mimickers and assessment of biopsies small volume. Prostatic epithelium typically contains the basal cell nuclear marker p63. It is considered to be a associated with the p53 family. p63/ TP63 (Transformation Related Protein 63) is a nuclear transcription factor that is restricted to the basal cells of the prostate, sweat glands, salivary glands, breast, and squamous epithelia. It is possible to identify benign imitators by using this negative immuno staining in cancer. A recent study demonstrated that using a cocktail of antibodies boosts the sensitivity of detection.

The three isoforms of Calponin are h1, h2, and h3. These are actin filament related regulatory cytoplasmic proteins. The basic isoform h1 is found to be only smooth muscles. Numerous studies demonstrate that smooth muscle cells strongly express Calponin in the normal prostate gland. Calponin expression with stromal cells varies in pre-neoplastic situations such high grade PIN. Because the reactive stroma has replaced fibro-muscular stroma in prostatic cancer, the expression of Calponin varies from zero to very scanty. (18) On the basis of this idea, we shall be analysing the expression of p63, a diagnostic marker, and Calponin on different pathological lesions of the prostate in prostatic biopsies, including both transurethral resection of prostate and needle core biopsy.

METHODOLOGY:

This prospective and observational study was conducted in the department of Pathology, B R D Medical College, Gorakhpur, U.P over a period of 1 year (July 2021 to June 2022). This study was carried out on the 100 patients of prostatic lesions attending surgery opd , whose biopsy samples had been received for histopathological examination from department of surgery. Formalin fixed paraffin embedded blocks and haematoxylin eosin stained sections of 100 prostatic biopsies which included both TURP and needle core are taken up for the study. Based on histopathological examination, they were categorized into Benign prostatic hyperplasia, Prostatic intraepithelial neoplasia, Prostatic adenocarcinoma.

Prostatic adenocarcinoma was assigned Gleason grade ranging from grade 1 to grade 5(figure 2-5) according to modified Gleason grading system. Immunohistochemistry will be performed on the tissue sections taken from the blocks along with positive and negative control.

A total 100 cases of formalin fixed paraffin embedded histological sections of various prostatic lesions including benign prostatic hyperplasia, prostatic intraepithelial lesion and prostate carcinoma were studied. Out of 100 cases, 55 cases were benign prostatic hyperplasia, 10 cases of prostatic intraepithelial lesion and 35 cases were of prostate adenocarcinoma. All the sections were stained with Hematoxylin and Eosin stain and then immunohistochemical staining of p63 and Calponin was performed on all the cases (figure 6- 12) . The parameters used to analyse the expression of both p63 and calponin were - Pattern of staining, Percentage of stained cell, Intensity of staining reaction.

All relevant data were collected and appropriate statistical tools were applied to analyses the data. Analysis was done by data sorting method, classified by tabulation and presentation by pie charts and histograms. Statistical analysis was done using chi square test. A P value < 0.05 were taken as significant.

RESULTS:

Total 100 cases included in this study, out of which 55 (55%) cases were benign prostatic hyperplasia, 10 (10%) cases of prostatic intraepithelial neoplasia, and 35 (35%) cases were prostatic adenocarcinoma. The proportion of benign prostatic hyperplasia was significantly higher as compared to the prostatic intraepithelial neoplasia and prostatic adenocarcinoma. (TABLE 1) The age of patients was ranged from 35 years to 82 years with mean age of 66.78 ± 9.0 years.(TABLE 2) Out of 10 Prostatic intraepithelial Neoplasia, maximum number 5 (50%) were observed in the age group of 70-79 years followed by 3 cases 30% in the age group 60-69 (30%). (TABLE 3)

Out of 100 prostatic specimens received for histopathological examination, majority of specimens (78%) were TURP followed by trucut biopsy (20%), Suprapubic prostatectomy (2%). The proportion of Transurethral resection of prostate (TURP) was significantly higher as compared to the proportion of Trucut biopsy and supra pubic prostatectomy (SPP) ($p<.001$) (TABLE 4). In most of the malignant lesions (68.6%), serum PSA level was more than 20ng/ml. PSA level was in range of 11-20 ng/ml in 20.0% of cases and PSA levels were in between 4-10 ng/ml in 4 cases (11.4%). In prostatic intraepithelial lesion, 4 cases (40%) PSA level was less than 4 ng/ml and in 2 cases (20%), it was mildly increased. In 4 cases of High-grade PIN, level was above 20 ng/ml in 3 cases (30%) and it was between 11-20 ng/ml in 1 case. Serum PSA level of 0-4 ng/ml was observed in majority of benign lesions,40 cases (72.7%). Mild increase in PSA level was seen in 27.3% cases. PSA level (ng/ml) was significantly associated with the various prostatic lesions ($p<.05$). (TABLE 4)

Gleason score 7 was the commonest pattern observed in 21 cases (60%), followed by Gleason score 8 in 9 cases (25.7%). Gleason score of 9 was observed in 2 cases (5.7%). Gleason score of less than or equal to 6 was observed in 3 cases (8.6%). Our analysis indicates no significant association between PSA level and Gleason's score ($p>.05$)

Based on tumor differentiation, 6 cases (17.1%) were well differentiated prostatic adenocarcinoma. 21 cases (60%) were moderately differentiated adenocarcinoma and 8 cases (22.9%) were poorly differentiated adenocarcinoma. The proportion of moderately differentiated adenocarcinoma is significantly higher as compared to the Well differentiated adenocarcinoma and poorly differentiated adenocarcinoma ($p<.01$) (table 5)

Expression of calponin in various prostatic lesion. On analysing expression of proliferation marker calponin, in BPH it was expressed in only 52 cases out of 5 cases (94.5%) and 3 cases (8.6%) were negative whereas while Among PIN cases, out of 10 cases, the calponin was expressed in7 (70%) cases and it was negative in 3 (30%) cases. In malignant lesion, calponin was expressed in 5 out of 35 cases (9.1%), and negative in 30 cases (85.7%). The association of expression of calponin between benign prostatic hyperplasia and carcinoma prostate was found to be highly significant (P value is <0.0001). (table 6)

Out of total 3 cases of well differentiated adenocarcinoma, 2 cases (40%) were both p63 and calponin negative, 1 case (20%) was p63 positive and Ki67 negative. Of total 21 cases of moderately differentiated adenocarcinoma, 2 cases (5.6%) were both p63 and Calponin negative, 5 cases (13.9%) were p63 negative and calponin positive, 6 cases (16.7%) were p63 positive and Calponin negative, 8 cases (22.2%) were both p63 and Calponin positive. Total 11 cases of poorly

differentiated adenocarcinoma, 1 case (5.3%) was both p63 and Calponin negative, 3 cases (21.0%) were p63 negative and Calponin positive, 4 case (26.3%) were p63 positive and Calponin negative, 3 cases (26.3%) were both p63 positive and calponin positive. A statistically significant association was observed between calponin positivity and p63expression (%). (p = 0<.05).(TABLE 7)

DISCUSSION

In our study, out of total 100 cases of prostatic lesions included in our study, the proportion of BPH(55%) was significantly higher as compared to the Prostatic intraepithelial neoplasia (PIN) (10%) and Prostatic adenocarcinoma (35%).In both industrialised and developing nations, prostate cancer is quickly becoming one of the main causes of cancer. 8 per 100,000 people are thought to be affected by prostate cancer in India. According to a study by **Quatani FA et al.**(19) the majority of cases are in the 70–90 age range. Our study supports this finding. Majority of the lesions belonged to the age group of 60-79 years. 45.5%, 30% and 5.7% cases of benign lesions, PIN and Prostatic adenocarcinoma respectively belonged to the age group of60-69 years. Similarly25.5%, 50% and 45.7% cases of benign lesions, PIN and Prostatic adenocarcinoma respectively belonged to the age group of 70-79 years. The mean age for benign prostatic lesions was 66.78 ± 9.0 years while that for PIN was 67.25 ± 8.6 years and for prostatic malignant lesions it was 73.63 ± 8.3 years.

Also,in our study maximum specimen of prostatic lesion were of Transurethral resection of prostate (TURP) in 78 cases (78%) followed by trucut biopsy in 20% and suprapubic prostactomy in 2%. **Puttaswamy K et al** (20) **2016** have similar finding however in **Sharma et al 2017** (21)study only specimen were of Transurethral resection of prostate (TURP).

We observed in the present study, benign prostatic hyperplasia, out of 55 cases, p63 was expressed in 44 (80%) and in 11 (20%) cases it was negative. Total 10 cases of prostatic intraepithelial neoplasia, in 8 (80%) cases, p63 was expressed 2 cases (20.0%) were negative. On analysing the expression of p63 in various prostatic lesions, in malignant lesion it was positive in 8(22.9%) out of 35 cases and negative in 27 cases (77.1%), while in PIN lesion p63 was expressed in only 8 cases (80.0%) and 2 cases (20%) were negative. In Quatani FA (19) et al. study in out of 50 cases of BPH 49 cases (89%) expressed p63 and 1 cases (2%) not expressed p63. In Shiran MS et al (22) study in out of 43 cases of BPH 38 cases (88%) expressed p63 and 5 cases (12%) not expressed p63. In Ng VW et al study in out of 138 cases of BPH 128 cases (93%) expressed p63 and 10 cases (7%) not expressed p63.

For the histological grading of prostate cancer, numerous grading schemes have been developed. The prostate biopsy Gleason score is correlated with tumour volume, tumour aggressiveness, serum PSA levels, prognosis, and treatment strategy. The Gleason score is frequently used to evaluate clinical trial eligibility, including for watchful waiting trials. Carcinoma prostate were categorized according to Gleason's score. Gleason score 7 was the commonest pattern observed in 21 cases (60%), followed by Gleason score 8 in 9 cases (25.7%). Gleason score of 9 was observed in 2 cases (5.7%). Gleason score of less than or equal to 6 was observed in 3 cases (8.6%). Similar results were obtained in a study by **Josephine** (24) with 35% cases showing Gleason score 7. In the current study, the anlaysis indicates that there is no significant association between PSA level and Gleason's score (p>.05).

Total 41.7% cases exhibited positivity for both p63 and calponin marker. Out of total 3 cases of well differentiated adenocarcinoma cases, 2 cases were both p63 and calponin negative, 1 case (20%) was p63 positive and calponin negative. Of total 21 cases of moderately differentiated adenocarcinoma, 2 cases were both p63 and Calponin negative, 5 cases were p63 negative and ki-16 positive, 6 cases were p63 positive and Calponin negative, 8 cases were both p63 and Calponin positive. Of the total 11 cases of poorly differentiated adenocarcinoma, 1 case was both p63 and Calponin negative, 3 cases were p63 negative and Calponin positive, 4 cases were p63 positive and Calponin negative, 3 cases were both p63 positive and calponin positive. A statistically significant association was observed between calponin positivity and p63 expression (%). (p = 0<.05)

CONCLUSION

Our study concluded that the proportion of Benign prostatic hyperplasia was significantly higher as compared to the Prostatic intraepithelial neoplasia and Prostatic adenocarcinoma. Maximum number of benign lesions (25, 45.5%) were observed in the age group 60-69 years followed by the 14 (25.5%) in the age group 70-79 years. Immuno histochemical staining by p63 is diagnostically reliable in identifying basal cells in prostatic needle biopsies and TURP specimens. p63 is a valuable tool with high sensitivity in differentiating BPH from prostatic carcinoma. The decreased or absent stromal staining of calponin which indicates a reactive stroma in malignancy can be used alone or in conjunction with p63 for confirmation of diagnosis of prostatic carcinoma. In future, specific studies will be directed towards identifying specific markers of reactive stroma which will aid in predicting the rate of cancer progression and possibility of recurrence. The future holds promise for novel therapeutic drugs targeting specific components of reactive stroma.

Table 1. Distribution of prostatic lesion

Nature of lesions	Number of cases	Percentage (%)
Benign prostatic hyperplasia	55	55.0%
Prostatic intraepithelial neoplasia	10	10.0%
Prostatic adenocarcinoma	35	35.0%
Total	100	100.0%

Table 2. Age wise distribution of benign prostatic lesions

Age (years)	Benign lesions (Number)	Percentage (%)
30-39	2	3.6%
40-49	6	10.9%
50-59	6	10.9%
60-69	25	45.5%
70-79	14	25.5%
>=80	2	3.6%
Total	55	100.0%

Table 3. Age wise distribution of prostatic intraepithelial neoplasia

Age (years)	Prostatic intraepithelial neoplasia (Number)	Percentage (%)
30-39	0	0.0%
40-49	0	0.0%
50-59	1	10.0%
60-69	3	30.0%
70-79	5	50.0%
>=80	1	10.0%
Total	10	100.0%

Table 4. Serum PSA level in various prostatic lesions

PSA level (ng/ml)	Benign lesions		Prostatic intraepithelial neoplasia		Malignant lesions	
	Number	Percentage (%)	Number	Percentage (%)	Number	Percentage (%)
0-4	40	72.7%	4	40.0%	0	0.0%
4-10	15	27.3%	2	20.0%	4	11.4%
11-20	0	0.0%	1	10.0%	7	20.0%
>20	0	0.0%	3	30.0%	24	68.6%
Total	55	100.0%	10	100.0%	35	100.0%

Table 5. Histological differentiation of prostatic adenocarcinoma cases		
Histological differentiation	Number of cases	Percentage (%)
Well differentiated adenocarcinoma	6	17.1%
Moderately differentiated adenocarcinoma	21	60.0%
Poorly differentiated adenocarcinoma	8	22.9%
Total	35	100.0%

Table 6.Expression of calponin in various prostatic lesion						
Prostatic lesion	Number of cases	calponin negative		calponin positive		p-value
		n	%	n	%	
Benign prostatic hyperplasia	55	3	8.6%	52	94.5%	<.01**
Prostatic intraepithelial lesion	10	3	30.0%	7	70.0%	<.01**
Malignant prostatic lesion	35	30	85.7%	5	9.1%	<.01**
Total	100	45	100.0%	55	100.0%	

Table 7. Correlation with both p63 and Calponin expression								
Histological grade	P63 negative and Calponin negative		P63 negative and Calponin negative		P63 negative and Calponin Positive		P63 positive and Calponin Negative	
	n	%	n	%	n	%	n	%
Well differentiated adenocarcinoma	2	40.0%	0	0.0%	1	20.0%	0	0.0%
Moderately differentiated adenocarcinoma	2	5.6%	5	13.9%	6	16.7%	8	22.2%
Poorly differentiated adenocarcinoma	1	5.3%	3	21.0%	4	26.3%	3	26.3%
Total (n=60)	5	14.29%	8	22.86%	11	31.43%	11	31.43%
P<.001, significant association								

Figure 1 **Benign Prostatic Hyperplasia H&E (10x)**

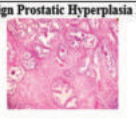

figure 2**Gleason pattern 3 H&E (10x)**

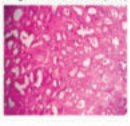

figure 3 **Gleason pattern 5-H&E (40x)**

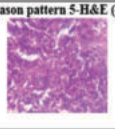

Figure 4 p63 strong basal nuclear positivity (10X)

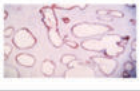

Figure 5 **p63 positive in basal cells(40x)**

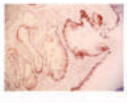

Figure 6: **p63 negative staining(40x)**

Figure 7 **Calponin high index of staining(40x)**

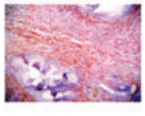

Figure 8: Calponin moderate staining (10x)

REFERENCES

1. Christine H. Lee, Oluyemi Akin-Olugbade, Alexander Kirschenbaum. Overview of Prostate Anatomy, Histology, and Pathology. 2011;40(3):p565-575.
2. Singh O, Bolla SR. Anatomy, Abdomen and Pelvis, Prostate. In: StatPearls [Internet]. 2022.
3. Leissner KH, Tisell LE. The weight of the human prostate. Scand J Urol Nephrol. 1979;13(2):137–42.
4. Prokar Dasgupta. ABC of Prostate Cancer. 2012.
5. Kajdacsy-Balla A. Urologic PathologyPetersenR.O., SesterhennI.A. and DavisC.J.: Urologic Pathology. Philadelphia: Lippincott Williams & Wilkins2009. 636 pages. J Urol. 2010 May;183(5):2103–2103.
6. Perin N.N. Global variation in cancer incidence and mortality. Curr Sci. 2001;81:465–74.
7. Rawla P. Epidemiology of Prostate Cancer. World J Oncol. 2019;10(2):63–89.
8. Baig MK, Hassan U, Mansoor S. Role of p63 in differentiating morphologically ambiguous lesions of prostate. J Coll Physicians Surg Pak. 2012 Dec;22(12):773-7.
9. Grisanzio C, Signoretti S. p63 in prostate biology and pathology. J Cell Biochem. 2008 Apr;103(5):1354-68.
10. Sanda MG, Cadeddu JA, Kirkby E. Clinically localized prostate cancer:AUA/ASTRO/SUO Guideline. Part II: Recommended approaches and details of specific care options. J Urol. 2018;199:990–7.
11. Bray F, Ferlay J, Soerjomataram I, Siegel RL. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394–424.
12. Ferlay J EM, Lam F, Colombet M, Mery L. Global cancer observatory: cancer today. Lyon, France: International Agency for Research on Cancer. [cited 2019 Feb 2]; Available from: https://gco.iarc.fr/today
13. Ferlay J, Shin HR, Bray F. Cancer incidence and mortality worldwide: IARC, Cancer Base No. 10. Lyon France. Int Agency Res Cancer GLOBOCON 2008.2010;
14. Humphrey PA. Histological variants of prostatic carcinoma and their significance. Histopathology. 2012 Jan;60(1):59–74.
15. Humphrey, P A. Diagnosis of adenocarcinoma in prostate needle biopsy tissue. J Clin Pathol. 2007;60(1):35–42.
16. Epstein JI, Walsh PC, Carmichael M, Brendler CB. Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA. 1994 Feb 2;271(5):368–74.
17. Ilic D, Neuberger MM, Djulbegovic M, Dahm P. Screening for prostate cancer. Cochrane Database Syst Rev. 2013 Jan 31;2013(1):CD004720.
18. Billis A, Meirelles L, Freitas LLL, Polidoro AS, Fernandes HA, Padilha MM. Adenocarcinoma on needle prostatic biopsies: Does reactive stroma predicts biochemical recurrence in patients following radical prostatectomy? Int Braz J Urol. 2013 Jun;39(3):320–7.
19. Quatani FA, Atta IS, Mady EA. p63 and cyclin D1 expression in benign prostatic hyperplasia versus prostatic adenocarcinoma: a clinicopathologic, radiological and immunohistochemical study. ijhs. 2014:2:305-20.
20. Puttaswamy K, Parthiban R, Shariff S. Histopathological study of prostatic biopsies in men with prostatism. J Med Sci. 2016;2(1):12.
21. Sharma A, Sharma M, Gandhi S, Khajuria A, Goswami KC. Histomorphological spectrum of prostatic lesion: a retrospective analysis of transurethral resection of prostate specimens. Int J Res Med Sci 2017:5:2373-2378.
22. Shiran MS, Tan GC, Sabariah AR, Rampal L, Phang KS. p63 as a complimentary basal cell specific marker to high molecular weight-cytokeratin in distinguishing prostatic carcinoma from benign prostatic lesions. Med J Malaysia. 2007;62(1):36–9.
23. Montironi R, Mazzuccheli R, Scarpelli M, Lopez-Beltran A, Fellegara G, Algaba F. Gleason grading of prostate cancer in needle biopsies or radical prostatectomy specimens: contemporary approach, current clinical significance and sources of pathology discrepancies. BJU Int. 2005 Jun;95(8):1146–52.
24. Josephine A. Clinicopathological Study of Prostatic Biopsies. J Clin Diagn Res JCDR. 2014 Sep;8(9):FC04–6.