Section: Pathology

Original Research Article

# ANALYZING THE GLEASON'S SCORE, KI-67 INDEX AND P53 EXPRESSION IN PROSTATE

**Shilpa Ruhela[1], Seema Chadha[2], Sonal Agarwal[3]**

[1]Senior Resident, Department of Pathology, Northern Railway Central Hospital, New Delhi, India.
[2]Additional Chief Health Director, Department of Pathology, Northern Railway Central Hospital, New Delhi, India.
[3]Senior Divisional Medical Officer, Department of Pathology, Northern Railway Central Hospital, New Delhi, India.

*Received* : 04/03/2025
*Received in revised form* : 22/04/2025
*Accepted* : 07/05/2025

*Keywords:*
*Prostate, Gleason's score, Ki-67 Index, p53, BPH, Acinar Adenocarcinoma.*

Corresponding Author:
**Dr. Pamelle Yadav,**
Email: pamelleraj@yahoo.co.in

DOI: 10.47009/jamp.2025.7.3.22

Source of Support: Nil,
Conflict of Interest: None declared

*Int J Acad Med Pharm*
2025; 7 (3); 110-113

## ABSTRACT

**Background: Aim**: To evaluate the expression of Ki-67 and P53 among various prostate lesions. **Introduction:** Prostate is the fourth leading cancer worldwide and third most common cause of death among males. Management of prostate cancer has been changed over the years and Gleason's score is widely used for grading the tumor but there is inter-observer variability. P53 and Ki-67 immunohistochemistry can be helpful both qualitatively and quantitatively in assessing the prognosis of prostate cancer. **Materials and Methods:** It is an observational analytical study performed in Northern Railway central hospital over a period of 2 years on 50 specimens received during this period. Histopathology examination and Gleason's scoring was done on cases diagnosed as prostate adenocarcinoma. Additionally, P53 and Ki-67 expression was studied in all the lesions and their intensity of expression was compared with Gleason's score in cases of prostate cancer. **Result:** Serum PSA and free PSA was raised in 36 and 12 cases respectively out of 50.72%cases were benign prostate hyperplasia and rest 28% were Acinar Adenocarcinoma. Out of 28% cases of adenocarcinoma,4+3,4+4,4+5,5+4 and 5+5 Gleason's score were seen in 8%,4%,4%,10% and 2%of them respectively. The co-relation between Ki-67 and Gleason's score showed 3+ and 4+index expression in high grade lesion. Similarly, 3+ index of P53 expression is seen in cases with 4+3 and 5+3 Gleason's score. **Conclusion:** The expression of both Ki-67 and P53 was found to be increased with increase Gleason's scoring. However, it was statistically significant in Ki-67 but not in P53.

## INTRODUCTION

Prostate cancer was first described in 1853.[1] It is the fourth leading cause of cancer worldwide with an incidence of 7.3% of all cases of cancer. The incidence in India is 10.7% and the mortality is 16.7%. It is the third most common cause of death from cancer in males, after lung and colorectal carcinoma.[2]

Due to the heterogenicity of prostate cancer, classical prognostic factors such as Serum Prostate Specific Antigen (PSA), Pathological staging, and Gleason's score are not sufficient to separate indolent from aggressive cancers. Therefore, new prognostic biomarkers can be essential tools in the clinical management of prostate carcinoma.[3]

The literature shows that some benign mimickers of prostate carcinoma, such as benign hyperplasia, prostatitis, atrophy, adenosis, atypical adenomatous hyperplasia, and nephrogenic adenoma, can make the diagnosis of prostate carcinoma challenging.[4] Several pathological parameters are required for its proper assessment. The Gleason grading and scoring is the most widely accepted method for providing information about the prognosis of prostate carcinoma.[5]

P53 is a tumor suppressor gene, and any mutation in p53 can result in uninhibited cellular growth, and therefore has been implicated in numerous malignancies. The increase expression of p53 is associated with a point mutation in one allele of P53 or loss of allele in other human cancers.[6] Thomas et al evaluated the expression of p53 in prostate cancer, and its utility as a prognostic indicator and they found that the p53 reactivity marks an aggressive subset of prostate cancer.[7]

Ki-67 is a DNA binding protein expressed in all cell cycle phases (S1, M, S2) but undetectable in the resting phases, i.e. G0 and G1. Ki 67 indicates the mitotic potential of any cell and is demonstrated by Immunohistochemistry (positive nuclei in IHC). A study had shown that the Ki-67 index was higher for carcinomas than for hyperplastic glands. Additionally, within the group of carcinomas, indices


ISSN (O): 2687-5365; ISSN (P): 2753-6556

were higher in patients with metastatic disease than in those without metastasis; so, a high Ki-67 index could define a group of patients with poor prognosis.[8]

The management of prostate cancer has changed drastically over the century with treatment ranging from classical radical prostatectomy to the latest High-intensity focused ultrasound (HIFU)therapy along with Hormonal treatment, chemotherapy, and radiotherapy.[9]

Even though Gleason's score helps to grade the any prostate lesion, it is subjected to inter-observer variability. The role of P53 and Ki-67, as quantitative and qualitative markers thus become important in order to assess the prognosis more clearly and therefore the patient can be given right treatment at the right time.

## MATERIALS AND METHODS

The study was an observational analytical study conducted in the Department of Pathology, Northern Railway Central Hospital, New Delhi over 2 years from July 2017 to June 2019. A total of 50 surgical samples of patients with prostate lesions and carcinoma were obtained from surgeries including Radical Prostatectomy, Transurethral resection of the prostate, and TRUS-guided biopsy. The biopsy tissues were grossed, representative sections were taken, and processed in an automatic tissue processor, and paraffin-embedded blocks were prepared. 4-micrometer thickness sections were taken and stained with conventional H &E stain and examined.

If the lesion was found to be carcinoma, Gleason grading and scoring were done in those cases. Microsections were also processed for immunohistochemistry using a monoclonal antibody against Ki-67 and p53. The intensity of expression of these markers was studied in all the lesions and their expressions were compared with the Gleason score in histologically proven prostate carcinoma cases.

The index for Ki-67 used are as follows.[10]

+1= index less than equal to 25%
+2=index between 26-50%
+3=index between 51-75%
+4=index between 76%-100%

Scoring of p53 was done taking into consideration two characteristics of the parameter, first was the percentage of the area stained and the second was staining intensity as shown below.[10]

| Percentage Positivity | Score | Staining Intensity | Score |
|---|---|---|---|
| <5% | 0 | Nil | 0 |
| 5-25% | 1 | Mild | 1 |
| 26-50% | 2 | Moderate | 2 |
| >50% | 3 | Severe | 3 |

Other significant data e.g. Serum PSA levels, clinical history, and age of the patients were also collected.

Results were analyzed with SPSS version 20.0 software. The continuous variables were presented as Mean+ SD and the categorical variables were expressed as frequencies and percentages. Pearson's chi-square test and chi-square test of association were used to determine if there is a relationship between any two categorical variables. P ≤0.05 was considered statistically significant.

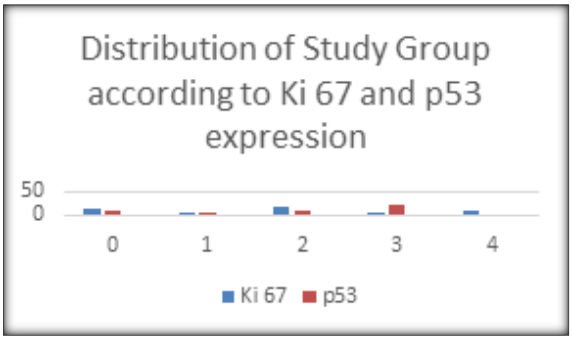
## RESULTS

Our study showed that about 86% of the patients were above 50 years of age.

The serum total PSA level was raised in 72% of the cases out of 50, which included both benign and malignant lesion of the prostate. The serum-free PSA level was normal in 76% of the cases and raised in 24% of the cases. [Table 1]

The Gleason score was evaluated in all the malignant cases, and found to be 4+3 in 8% of the cases,4+4 in 4% of the cases, 4+5 in 4% of the cases,5+4 in 10% of the cases, and 5+5 in 2% of the cases. [Table 2]

The Ki-67 staining intensity in the prostatic lesions was 1+ score in 7 (14%) cases, 2+score in 17(34%) cases, 3+ in 5(10%) of cases and 4+ in 9 (18%) of cases. The remaining 12 cases (24%) were negative (Graph 1)




The P53 staining intensity in the prostatic lesions scored 0 in 10 (20%) of cases, scored 1 in 6 (12%) of the cases of which all were benign, 2 in 11(22%) of cases and 3 in 23(50%) cases. [Graph 1]

Ki67 was assessed in all the 50 cases, however Gleasons score was done only for all the malignant cases, and. Results were analyzed, and the correlation between the two parameters showed the Ki67 index of 1+ and 2+ in benign lesions, and 3+ and 4+ index in high-grade (Gleason's score- 5+4,4+5,4+4 and 4+3) lesions. This difference is statistically significant(p=0.00), and shows that Ki 67 index increases with increasing Gleason's score. [Table 3]

All malignant lesions were negative for p53 scores of 0 and 1, 2 in 90.9% of the cases with benign lesions and 17.4% of lesions with Gleason score of 4+3 and 5+4 show scores 3 of p53. There is no statistically significant difference (p=0.246) in the staging of lesion according to p53 intensity and Gleason's score in our study.


ISSN (O): 2687-5365; ISSN (P): 2753-6556

**Table 1: The histopathological examination had shown acinar adenocarcinoma in 28% and Benign Prostate hyperplasia in 72% of the cases**

| Parameter | Categorization | Number of Patients (50) |
|---|---|---|
| Total Serum PSA | Normal | 14 |
| | Raised | 36 |
| Free PSA | Normal | 38 |
| | Raised | 12 |
| HPE | Acinar Adenocarcinoma | 14 |
| | BPH | 36 |

**Table 2**

| Gleason's score | No. of Cases | Percentage |
|---|---|---|
| 4+3 | 4 | 8% |
| 4+4 | 2 | 4% |
| 4+5 | 2 | 4% |
| 5+4 | 5 | 10% |
| 5+5 | 1 | 2% |
| NA | 36 | 72% |
| Total | 50 | 100% |

**Table 3**

| **Ki-67 Gleason's score** | **1+ n(%)** | **2+ n(%)** | **3+ n(%)** | **4+ n(%)** | **Negative n(%)** |
|---|---|---|---|---|---|
| 4+3 | 0 | 0 | 1(20) | 3(33.3) | 0 |
| 4+4 | 0 | 0 | 0 | 2(22.2) | 0 |
| 4+5 | 0 | 0 | 0 | 2(22.2) | 0 |
| 5+4 | 0 | 0 | 3(60) | 2(22.2) | 0 |
| 5+5 | 0 | 0 | 1(20) | 0 | 0 |
| NA (benign) | 7 (100) | 17 (100) | 0 | 0 | 12 (100) |
| Total | 7 (100) | 17 (100) | 5 (100) | 9 (100) | 12 (100) |

## DISCUSSION

Prostate cancer is one of the most prevalent cancers in males.[11] Management of prostate cancer has changed drastically over the centuries with treatment ranging from classical radical prostatectomy to the latest HIFU therapy along with Hormonal therapy, chemotherapy, and radiotherapy. Several markers for the diagnosis of the carcinoma of the prostate have been discovered but their prognostic value is obscure since research is scant.[9] Studies have shown that the presence and activity of p53 was greatly associated with the cell proliferation marker Ki-67, and the level of p53 activity was an important independent prognostic factor that was inversely associated with patient survival.[12]

In our study, about 80% of the cases were aged above 60 years. In a study by Madani et al, the mean age of patients was about 74.5 years ranging from 48 to 94 years.[13] Kaur et al had also observed similar results.[10]

Serum PSA level was raised in 72% of cases which included all histopathologically proven malignant cases. Similarly, Murti et al had shown that the majority of the malignant cases had an abnormal rise of serum PSA.[14]

The histopathological examination showed that the lesion was well differentiated in 14.2% of cases, moderately differentiated in 64.2% of cases and poorly differentiated in 21.04% of the cases. Similar results were obtained in a study conducted by Verma et al, the tumor differentiation was well differentiated in 8%, moderately differentiated in 62%, and poorly differentiated in 30%.[15]

The Ki-67 immunohistochemistry expression in the prostatic lesions showed that it was negative in 20% of the cases and positive in 80% of cases.

The p-53 intensity in prostate lesions was negative in 20% of the cases and positive in 80% of cases in our study. Kaur et al showed that the p53 was positive in 58% of the cases and negative in 42%.[10] Verma et al also observed similar results that 76% of cases of prostate cancer showed upregulation of p53 expression.[15]

The correlation between the Gleason's score and Ki-67 levels showed that a 5+4 score in lesions showed 3+ Ki-67 expression, and lesions with a 4+3 score showed 4+ expression. The relationship was statistically significant($p<0.00$) between the Gleason's grading and Ki-67 levels. Murti et al had shown the correlation of overexpression of Ki-67 with an increase in the Gleason's score.[14] Kaur et al showed an increase in positivity with an increase in grade, however, it was not statistically significant in their study.[10]

P53 expression was also found to be increased with a raised Gleason's score in our study; however, it was not statistically significant (P Value=0.246). Similarly, in a study conducted by Kaur et al, almost 16 cases had a Gleason's score of 5+4, of which 10 were positive and 6 were negative for p53, which was not statistically significant.[10]

## CONCLUSION

The present study found that with a rising Gleason's score, the expression of Ki-67 is increased, which is statistically significant. However, even though P53


ISSN (O): 2687-5365; ISSN (P): 2753-6556

expression was found to be increased with a raised Gleasons score, it was not found to be statistically significant.

**Limitations**

This study has certain limitations. The small study population necessitates further research with a larger sample size to validate the findings. Additionally, subjective interpretation of Gleason's score and IHC expression of p53 and Ki67 may influence results, highlighting the need to standardize assessment methods.

**Financial Support:** Nil

**Conflict of Interest:** Nil

## REFERENCES


1. Bray F, Laversanne M, Sung H, Ferlay J, Siegel RL, Soerjomataram I, et al. Global Cancer Statistics 2022: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries.CA: A Cancer Journal for Clinicians. April 2024;74(3):229-63.
2. van Leeuwen P, van den Bergh, Wolters T, Schroder F, Roobol M. Screening should more biopsies be taken in larger prostates? BJU Int. 2009; Oct: 104:7:919-24.
3. Mala R, Santos Gabriel Arantes D,ReisS,Vian N/ et al.Can we use Ki-67 expression to predict prostate Cancer aggresiveness? Rev Col Bras Cir e 2022300:1-7.
4. Srigley JR. Benign mimickers of prostatic adenocarcinoma. Mod Pathol. 2004; 17:328-48.
5. Humphrey PA. Gleason grading and prognostic factors in carcinoma of the prostate. Mod Pathol2004; 17:292-306.
6. Ozaki T,Nakagawara A. Role of p53 in cell Death and Human Cancers.Cancers(Basel).2011Mar3;3(1):994-1013.
7. Thomas DJ, Robinson M, King P, Hasan T, Charlton R, Martin J. P53 expression and clinical outcome in prostate cancer. Br J Urol. 1993; 72:778-81.
8. Rajeswari K, Meenakshisundaram K, Anushuya G, Rajalaxmi J. Ki 67 as a prognostic marker in comparison with Gleason's grading system in prostatic carcinoma. Ind J Pathol Oncol. 2016; 3:92-5.
9. Madu Co, Lu Y. Novel diagnostic biomarkers for prostate cancer. J Cancer. 2010; 1:150-77.
10. Kaur H, Paul M, Manjari M, et al. Ki-67 and p53 Immunohistochemical expression in prostate carcinoma: An experience from a tertiary care center of North India. Annals of Pathology and Laboratory Medicine. 2016;3(6):509-16.
11. Wei JT, Uzzo RG. Shared decision-making strategies for early prostate cancer. Semin Urol Oncol. 2002; Feb:20(1):74-8.
12. Borce M, Stausbat-Gron B, Overgaard J. P53 accumulation associated with bcl-2, the proliferation marker MIB-1 and survival in patients with prostate cancer subjected to watchful waiting. J Urol. 2000; 164:716-21.
13. Madani SH, Ameli S, Khazaei S, Kanani M, Izadi B. Frequency of Ki-67(MIB-1) and P%# expressions among patients with prostate cancer. Indian J PatholMicrobiol. 2011; 54:688-91.
14. Murti K, Warli SM, Lidya Imelda Laksmi. Relations between KI-67 immunohistochemistry expression with histopathology grading and prostate-specific antigen (PSA) values in adenocarcinoma prostate at Dr H. Adam Malik Hospital, Medan Indonesia. Bali Medical Journal 6(2): 289-293.
15. Verma R, Gupta V, Singh J, Verma M, et al. Significance of p53 and ki-67 expression in prostate cancer. Urol Ann. 2015;7(4):488–93.