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Original Research Article

Correlation of p53 Immunohistochemistry with Gleason Grading in Prostate Carcinoma - A Cross-Sectional Study from a Tertiary Care Centre

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Abstract: ***Background:*** Prostate carcinoma is one of the most common malignancies affecting elderly men and shows wide variability in biological behaviour. Gleason grading remains the cornerstone for prognostication; however, additional molecular markers may improve risk stratification. The tumor suppressor gene p53 is frequently altered in advanced malignancies, and its IHC (immunohistochemical) expression has been proposed as a potential prognostic indicator in prostate cancer. This study evaluates the relationship between p53 expression and Gleason grading in prostate carcinoma. ***Methods*** This cross-sectional study included 50 histopathologically confirmed cases of prostate carcinoma received over a two-year period at a tertiary care center. Specimens comprised TURP chips and TRU-CUT biopsies. Routine hematoxylin and eosin staining was performed, and tumors were graded using the Gleason grading system and categorized into risk groups. Immunohistochemical staining for p53 was carried out using a monoclonal antibody, and nuclear staining intensity was graded as negative (0), weak (1+), intermediate (2+), or strong (3+). Statistical analysis was performed using the chi-square test to assess correlation between p53 expression and Gleason grading. ***Results*** The mean age of patients was 68.12 ± 9.06 years, with most cases occurring between 61 and 80 years. Acinar adenocarcinoma was the predominant histological subtype (88%). High/very high Gleason risk group constituted 56% of cases, followed by the intermediate group (42%). Strong p53 expression (3+) was observed in 38% of cases, intermediate expression in 26%, weak expression in 12%, and negative expression in 24%. Although higher Gleason grades showed a trend toward increased p53 expression, the correlation was not statistically significant ($\chi^2 = 4.26$, $p = 0.107$). ***Conclusions*** p53 overexpression is frequently observed in high-grade prostate carcinomas; however, its expression does not show a statistically significant correlation with Gleason grading. The presence of p53-negative cases among high-grade tumors suggests molecular heterogeneity in prostate carcinoma. p53 may serve as an adjunct marker but should be interpreted alongside histopathological findings.

Keywords: Prostate Carcinoma, Gleason Grading, p53 Immunohistochemistry, Adenocarcinoma, Prognostic Markers.

INTRODUCTION

The prostate is the largest accessory gland of the male reproductive system. It is a walnut-sized, firm, fibromuscular gland that circumferentially surrounds the proximal urethra in the lower pelvis and lies immediately inferior to the urinary bladder. It is enclosed by a fibrous capsule covered by visceral pelvic fascia and supplied by a rich neurovascular plexus. The normal adult prostate weighs approximately 11 g, with a reported range of 7–16 g. Functionally, it serves as a complex fibromuscular organ facilitating both urinary continence and ejaculation. [1-3]

Embryologically, the prostate develops during the third month of intrauterine life from epithelial evaginations of the prostatic urethra, forming periurethral (Alberian cervical) glands.[2] Anatomically, the gland is divided into zones, of which the central zone surrounds the ejaculatory ducts and is relatively resistant to inflammation and malignancy. In contrast, the transition zone is commonly involved in benign prostatic hyperplasia and atypical adenomatous hyperplasia.[4]

Prostate cancer has emerged as a major global health concern in recent decades. It accounts for a substantial proportion of male malignancies worldwide and is ranked as the sixth most common cancer globally.[5] In India, prostate cancer is the second leading cause of cancer-related mortality among men, following oral cancer, as reported by ICMR and GLOBOCAN 2012.[6-8] The incidence of prostate cancer is expected to increase markedly, particularly among men over 65 years of age, with projections suggesting a fourfold rise between 2020 and 2050.[8]

Histopathological diagnosis of prostatic carcinoma relies on characteristic morphological features such as infiltrative glandular architecture, absence of basal cells, nuclear atypia, and hyperchromasia.[9] While most prostate cancers demonstrate indolent growth, a subset behaves aggressively with metastasis to lymph nodes, lungs, and bones.[8] Immunohistochemical markers such as AMACR and p63 aid in differentiating benign from malignant lesions, with loss of basal cell markers supporting malignancy.[10-12]

Recent studies have highlighted genetic alterations, including mutations in TP53, SPOP, and FOXA1, particularly in high-grade and invasive prostatic carcinomas.[4,13]

AIMS AND OBJECTIVES

The present study aims to correlate p53 immunohistochemical expression with Gleason grading in prostate carcinoma in a tertiary care centre. The objectives of the study are to evaluate the histomorphological patterns of prostate carcinoma, to assess the expression of p53 in prostate carcinoma using immunohistochemistry, and to determine the relationship between Gleason grade and p53 expression in order to better understand their diagnostic and prognostic relevance.

MATERIALS AND METHODS

Study Design

The present study was designed as a cross-sectional study conducted over a period of two years at Rangaraya Medical College, in collaboration with the Department of Urology. A total of 50 prostatic biopsy specimens, including TURP chips and TRU-CUT biopsies, received in the Department of Pathology were included. All specimens were fixed in 10% neutral buffered formalin, processed into paraffin-embedded blocks, and sectioned at 4-micron thickness. Routine hematoxylin and eosin staining was performed for histopathological evaluation, and immunohistochemistry was carried out on selected sections.

Inclusion and Exclusion Criteria

The study included fifty biopsy-proven cases of prostate carcinoma. Cases with non-neoplastic prostatic lesions were excluded from the study. In addition, specimens that were inappropriately fixed or unsuitable for proper histopathological and immunohistochemical evaluation were excluded, as were patients who were unwilling to participate in the study.

Data Collection Procedure

Data collection was performed using histopathological and immunohistochemical evaluation of prostatic tissue sections. Formalin-fixed, paraffin-embedded tissue sections were routinely stained with hematoxylin and eosin (H&E) to assess histomorphological features, wherein nuclei stained blue and cytoplasm and connective tissue appeared in varying shades of pink. Selected sections were further subjected to p53 immunohistochemistry using the peroxidase–antiperoxidase method. Antigen retrieval was carried out using sodium citrate buffer (pH 6.0), followed by blocking of endogenous peroxidase activity and nonspecific binding. Sections were incubated with a rabbit monoclonal anti-p53 antibody (clone ZR153), followed by secondary antibody, HRP polymer, and visualization with DAB chromogen. Slides were counterstained with hematoxylin, mounted, and evaluated for nuclear p53 expression, which was graded based on staining intensity as negative, weak, moderate, or strong.

RESULTS

Age Group	No. of Cases	Percentage
51-60	13	26%
61-70	16	32%
71-80	19	38%
>81	2	4%
Total	**50**	**100%**

Table 1: Age Wise Distribution (n=50)

Table 1 illustrates the age-wise distribution of prostate carcinoma cases, showing that the majority of patients belonged to the age group of 71 to 80 years (38%), followed by 61 to 70 years (32%). This highlights the predominance of prostate carcinoma in elderly individuals.

Age Category	Low/Very Low	Intermediate	High/Very High	Total
51–60 years	0 (0.0%)	5 (38.5%)	8 (61.5%)	13 (100.0%)
61–70 years	0 (0.0%)	8 (50.0%)	8 (50.0%)	16 (100.0%)
71–80 years	1 (5.3%)	7 (36.8%)	11 (57.9%)	19 (100.0%)
>81 years	0 (0.0%)	1 (50.0%)	1 (50.0%)	2 (100.0%)
Total	1 (2.0%)	21 (42.0%)	**28 (56.0%)**	50 (100.0%)
Chi-Square Test: $\chi^2(6) = 2.264$, $p = .894$ → Not significant				

Table 2: Age Category × Risk Group (n=50)

Table 2 shows the distribution of Gleason risk groups across different age categories. Although the high/very high risk group predominated across all age groups, no statistically significant association was observed between age category and risk group (p = 0.894).

Diagnosis Type	No. of Cases	Percentage
Acinar adenocarcinoma	44	88.0%
Acinar adenocarcinoma (Foamy)	3	6.0%
Acinar adenocarcinoma (Neuroendocrine differention)	2	4.0%
Acinar adenocarcinoma (Sarcomatoid)	1	2.0%
Total	**50**	**100.0%**

Table 3: Histomorphology Patterns of Prostate Carcinoma (n=50)

Table 3 observes the histomorphological patterns of prostate carcinoma in the study population. Conventional acinar adenocarcinoma was the most common subtype (88%), while variant morphologies such as foamy, neuroendocrine, and sarcomatoid differentiation were infrequent.

Gleason Score	No. of Cases (n=50)	Percentage
3+2	1	2.0%
3+4	15	30.0%
3+5	3	6.0%
4+3	6	12.0%
4+4	1	2.0%
4+5	6	12.0%
5+4	15	30.0%
5+5	3	6.0%
Total	**50**	**100.0%**

Table 4: Gleason Score (n=50)

Table 4 depicts the distribution of individual Gleason scores among the cases studied. Higher Gleason scores, particularly 3+4 and 5+4, were most frequently observed, indicating a predominance of aggressive tumor patterns.

Grading Category	No. of Cases	Percentage
Low/Very Low	1	2.0%
Intermediate	21	42.0%
High/Very High	**28**	**56.0%**

Table 5: Gleason Grading Risk Group (n=50)

Table 5 demonstrates the distribution of cases according to Gleason grading risk groups. More than half of the cases (56%) belonged to the high/very high risk category, suggesting that a significant proportion of patients presented with advanced disease.

Gleason Grade	Frequency	Percentage
Grade 1	1	2.0%
Grade 2	15	30.0%

Grade 3	6	12.0%
Grade 4	4	8.0%
Grade 5	24	48.0%
Total	**50**	**100.0%**

Table 6: Gleason Grading (n=50)

Table 6 presents the frequency distribution of Gleason grades in prostate carcinoma. Gleason Grade 5 was the most common (48%), reflecting a higher burden of poorly differentiated tumors in the study cohort.

p53 Expression	Frequency	Percentage
Negative (0)	12	24%
Weak (1+)	6	12%
Intermediate (2+)	13	26%
Strong (3+)	19	38%
Total	**50**	**100%**

Table 7: p53 Expression (n=50)

Table 7 summarizes the pattern of p53 immunohistochemical expression among the cases. Strong p53 expression (3+) was the most frequent finding (38%), followed by intermediate expression, while 24% of cases showed negative p53 staining.

Risk Groups	Gleason Grade Group	p53 Negative (0) n =12	p53 1+n =6	p53 2+n =13	p53 3+n =19
Low/Very Low	1	0 (0.0%)	0 (0.0%)	1 (2.0%)	0 (0.0%)
Intermediate	2	7 (14.0%)	2 (4.0%)	3 (6.0%)	3 (6.0%)
	3	2 (4.0%)	0 (0.0%)	1 (2.0%)	3 (6.0%)
High/Very High	4	1 (2.0%)	0 (0.0%)	1 (2.0%)	2 (4.0%)
	5	2 (4.0%)	4 (8.0%)	7 (14.0%)	11 (22.0%)

Table 8: Gleason Grading × p53 Expression (n=50)

Table 8 correlates Gleason grading with p53 expression levels. Although higher Gleason grades tended to show increased p53 expression, the association was not statistically significant, indicating heterogeneous p53 expression across different tumor grades.

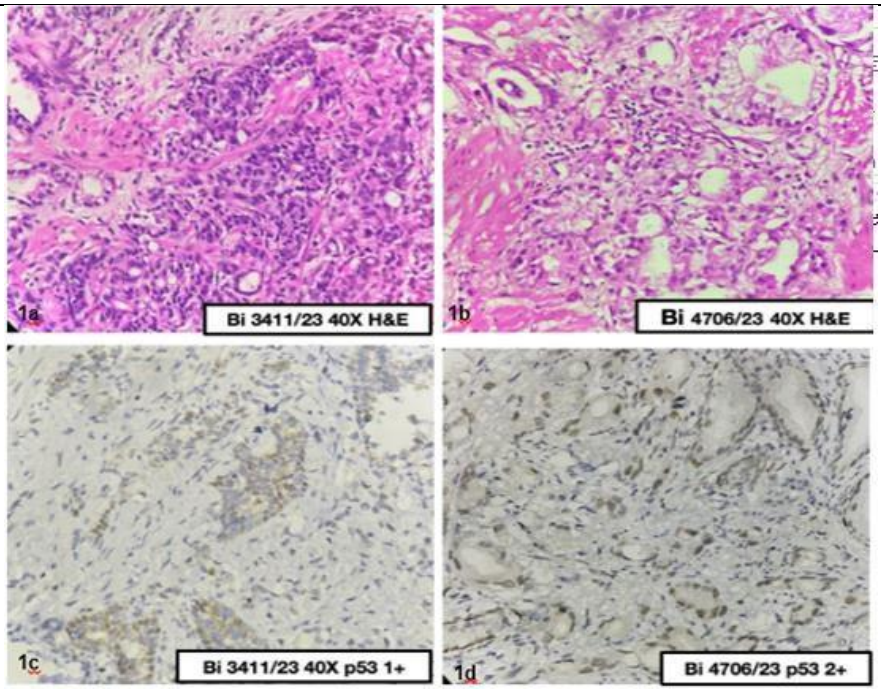

Figure 1a, 1b, Acinar adenocarcinoma. Fig 1c IHC 1+ intensity, 1d IHC 2+ intensity

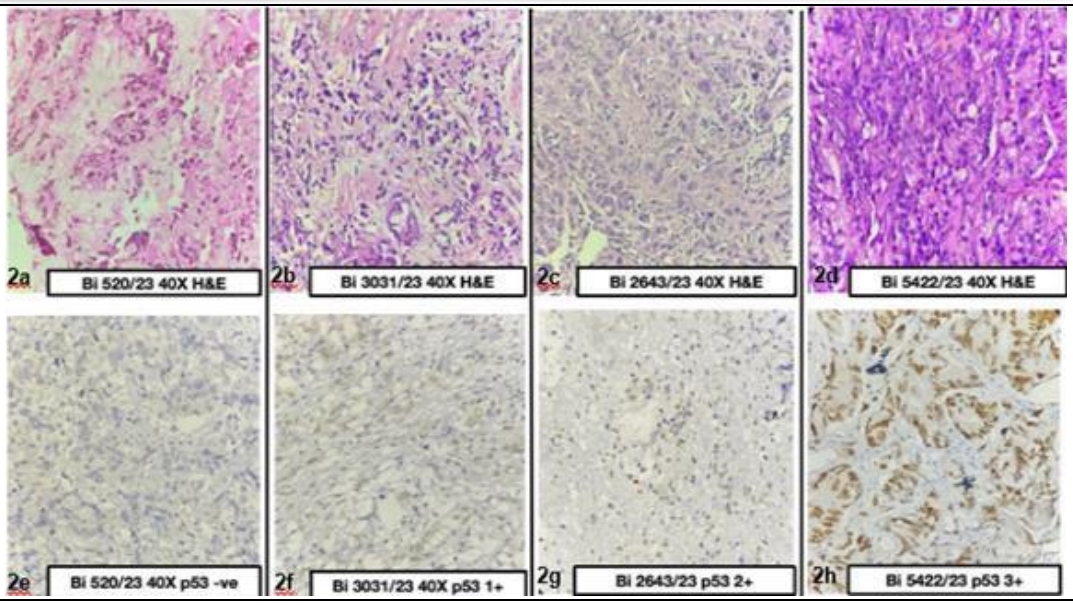

Figure 2a, 2b, 2c, 2d Acinar adenocarcinoma. Figure 2e IHC 0 intensity, 2f IHC 1+ intensity, 2g IHC 2+ intensity 2h IHC 3+intensity

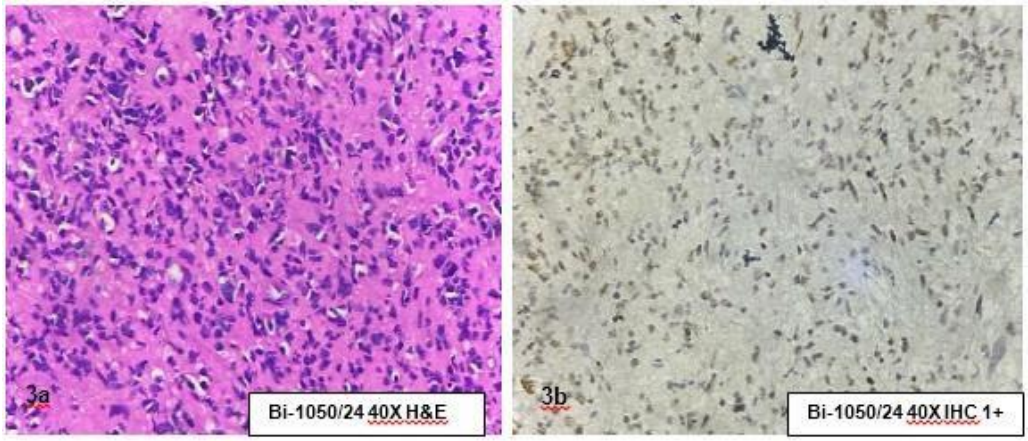

Figure 3a, Acinar adenocarcinoma (Sarcomatoid) Figure 3b IHC 1+ intensity

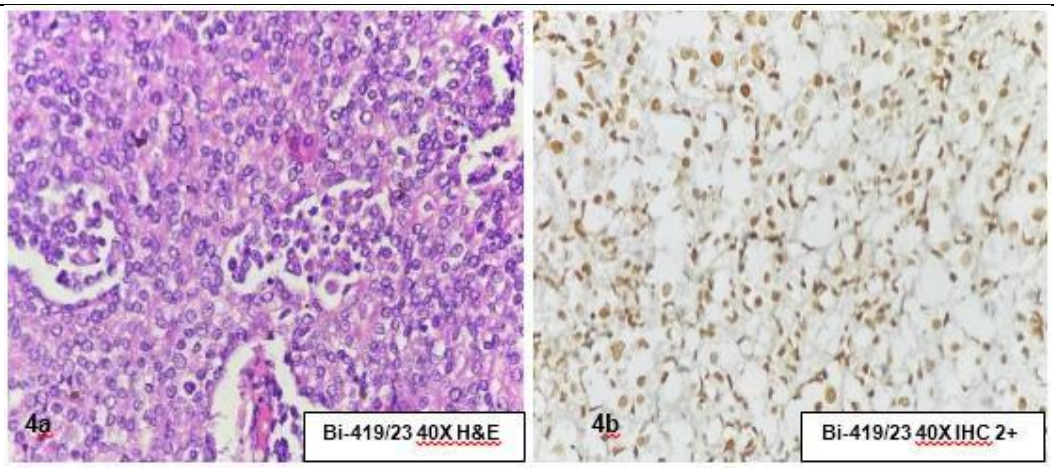

Figure 4a, Acinar adenocarcinoma (Neuroendocrine differentiation) Figure 4b IHC 2+ intensity

DISCUSSION

Prostate carcinoma is predominantly a disease of elderly men and continues to present a major clinical challenge due to its heterogeneous biological behaviour. The present study was undertaken to analyze the histomorphological spectrum of prostate

carcinoma, assess Gleason grading, and evaluate the expression of p53 immunohistochemistry in relation to tumor grade, thereby exploring its potential diagnostic and prognostic significance.

In the current study, the majority of patients belonged to the sixth to eighth decades of life, with a mean age of 68.12 years. This age distribution is consistent with previous studies by Castillejos-Molina and others, which also reported a predominance of prostate carcinoma in elderly males.[6,14] The increasing incidence of prostate cancer with advancing age may be attributed to hormonal changes, genetic alterations, and prolonged exposure to environmental risk factors. Histomorphological evaluation revealed that conventional acinar adenocarcinoma was the most common subtype, accounting for 88% of cases. Variant morphologies such as foamy gland carcinoma, neuroendocrine differentiation, and sarcomatoid carcinoma were observed in a small proportion of cases. These findings are in concordance with multiple earlier studies, including those by Nelson RS, Dhom G. Ravikanth et al., and Preethi et al., all of whom reported acinar adenocarcinoma as the predominant histological pattern.[15-20] Recognition of these variants is important, as some are associated with aggressive behaviour and altered therapeutic response.

Gleason grading remains the most reliable histopathological prognostic indicator in prostate carcinoma. In the present study, more than half of the cases (56%) were classified under the High/Very High Gleason risk group, with Gleason grades 4 and 5 being most frequent. Similar findings have been reported by Wahid et al., Urs et al., Madani et al., and others, who also documented a predominance of poorly differentiated tumors.[14] This suggests that a significant number of patients present with advanced disease at diagnosis, particularly in developing regions where early screening may be limited.

The tumor suppressor gene p53 plays a critical role in regulating cell cycle arrest, DNA repair, and apoptosis. Mutations in TP53 are considered late events in prostate carcinogenesis and are often associated with tumor progression and treatment resistance. In the present study, strong p53 expression was observed in 38% of cases, while intermediate and weak expression were seen in 26% and 12% of cases, respectively. Notably, 24% of cases demonstrated negative p53 expression. Similar patterns of p53 expression have been reported by Sasor et al. and Zakia et al., whereas studies by Kaur et al. and Ganraj et al. demonstrated a statistically significant association between p53 overexpression and higher Gleason grades.[6,17]

Although a trend toward increased p53 expression with increasing Gleason grade was observed in this study, the association was not statistically significant ($p = 0.107$). This finding is in agreement with studies by Sasor et al. and Yaman et al., which also failed to demonstrate a significant correlation between p53 expression and tumor grade. The presence of p53-negative cases among high-grade tumors suggests molecular heterogeneity and indicates that alternative oncogenic pathways may contribute to tumor aggressiveness in such cases.[6,17,21]

Immunohistochemistry plays a crucial adjunctive role in the evaluation of diagnostically challenging prostatic lesions, particularly in small biopsies and TURP specimens. While markers such as p63 and high-molecular-weight cytokeratin aid in identifying basal cells, p53 staining provides valuable information regarding tumor progression and aggressiveness. However, none of these markers should be interpreted in isolation, and correlation with histomorphological findings remains essential.[22,23]

The findings of the present study emphasize that p53 overexpression is commonly associated with higher-grade prostate carcinomas, but its absence does not exclude aggressive disease. The variable expression of p53 highlights the complex molecular landscape of prostate carcinoma and underscores the need for integrated histopathological and molecular assessment for accurate prognostication.

Limitations

The present study is limited by its relatively small sample size and restricted study period, as it was conducted in a single geographic region. Diagnostic evaluation of prostate adenocarcinoma is inherently challenging due to the presence of close benign and malignant mimickers, and p53 expression may also be observed in certain benign conditions; therefore, its interpretation requires correlation with histopathological features and immunohistochemistry. Additionally, the cross-sectional design, difficulty in obtaining consistent follow-up, and cautious approach to surgical intervention in elderly patients with limited life expectancy further limit long-term outcome assessment.

CONCLUSION

The present study demonstrates an association between p53 expression and higher Gleason grades in prostate adenocarcinoma, suggesting that p53 may serve as a useful adjunct predictive and prognostic marker for identifying high-grade tumors. The frequent p53 expression observed in advanced-grade carcinomas supports the concept that p53 mutation is a late event in prostate carcinogenesis, in agreement with previous studies by Kaur et al. Notably, the presence of p53-negative cases among high-grade tumors indicates biological heterogeneity and may be associated with a relatively better prognosis. Further

large-scale studies, including correlation with DNA aneuploidy and other molecular markers, are warranted to validate these findings and enhance prognostic stratification.

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