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Research Article

CLINICOPATHOLOGICAL CORRELATION OF P53 EXPRESSION IN BENIGN PROSTATIC HYPERPLASIA AND PROSTATE ADENOCARCINOMA

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ABSTRACT

Objective: The objective of the study is to assess clinicopathological parameters in patients with benign prostatic hyperplasia (BPH) and prostate adenocarcinoma and evaluate their correlation with p53 overexpression in these prostatic conditions.

Methods: The present ambispective study was conducted in the Department of Pathology in a tertiary care hospital in Northern India from 2022 to 2024. This study included prostatic trucut biopsies, transurethral prostatic resection (TURP) chips, and radical prostatectomy specimens from patients with BPH or prostatic adenocarcinoma. Tissue samples were processed, embedded in paraffin, sectioned, and stained with hematoxylin and eosin (H&E) for histopathological evaluation. Immunohistochemical (IHC) analysis was performed to assess p53 expression using the GenomeMe antibody. Data on age, histological type, and histological grade were collected. Statistical analysis included Chi-square test was conducted to evaluate associations between p53 overexpression and clinicopathological parameters.

Results: The study analyzed 50 cases, revealing significantly higher p53 expression in prostatic adenocarcinoma compared to BPH. The majority of participants were aged between 61 and 70 years (46%). There were 50% patients with adenocarcinoma, 26% with BPH, 20% with BPH and chronic prostatitis, and 4% with BPH with prostatic intraepithelial neoplasia. There were strong associations between p53 overexpression and specific diagnoses, histological type, and histological grade (Gleason scores) in prostate cancer.

Conclusion: The study findings suggest that p53 overexpression is closely linked to malignant prostate conditions and could potentially serve as a valuable biomarker for distinguishing between benign and malignant prostatic diseases, as well as predicting tumor aggressiveness.

Keywords: Prostate Tumors, Gleason Score, Immunohistochemistry, Molecular Marker.

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INTRODUCTION

Prostate gland is one of the most commonly affected organs in male with increasing age, accounting for significant morbidity and mortality. The prostate is affected by a variety of pathological processes, of which benign prostatic hyperplasia (BPH) and prostate cancer are two of the most common neoplastic growths that occur in elderly men. Both of these conditions are rare before age 50 years, but by age 80, more than 80% of men have evidence of BPH histology and more than 50% have at least microscopic foci of prostate cancer [1]. While BPH and prostate adenocarcinoma are distinct entities, they share a common anatomical origin and often coexist in clinical settings, complicating diagnosis and management.

BPH is characterized by the proliferation of prostatic cells, leading to an enlargement of the prostate gland. This enlargement can result in urethral obstruction and lower urinary tract symptoms, such as hesitancy, weak stream, and incomplete emptying of the bladder. These symptoms can significantly impact a man's quality of life, causing discomfort and inconvenience [2]. On the other hand, prostate cancer is the second most frequent malignancy (after lung cancer) in men worldwide and accounted for 3.8% of all cancer deaths in males in 2018 [3]. At its indolent stage, the condition may be asymptomatic or may mimic symptoms that may also arise from prostatic hypertrophy. Many prostate cancers are detected on the basis of elevated plasmatic levels of prostate-specific antigen, a glycoprotein normally expressed by prostate tissue. However, because men without cancer have also been found with elevated PSA, a tissue biopsy is the standard of care to confirm cancer's presence [3].

The molecular mechanisms underlying the progression from benign prostatic conditions to malignant states are complex and not fully understood. One key molecule implicated in prostate cancer development is the tumor suppressor protein, p53 [4,5]. Known as the "guardian of the genome," p53 plays a crucial role in regulating the cell cycle, apoptosis, and genomic stability [6]. Mutations in the TP53 gene, which encodes the p53 protein, are among the most common genetic alterations in human cancers, including prostate adenocarcinoma. Abnormal expression of p53 has been associated with poor prognosis and aggressive disease in various cancers [7].

Understanding the clinicopathological correlation of p53 expression in benign and malignant prostate conditions could provide insights into prostate cancer pathogenesis and progression. This understanding could also help differentiate between BPH and prostate adenocarcinoma, aiding in more accurate diagnosis and personalized treatment strategies. Therefore, the present study aimed to assess clinicopathological parameters in patients with BPH and prostate adenocarcinoma, and evaluate their correlation with p53 overexpression in these prostatic conditions.

METHODS

This was an ambispective observational study conducted in the Department of Pathology at a single tertiary care hospital in North India from 2022 to 2024. The study was approved by the Institutional Ethics Committee and participants were enrolled after obtaining informed written consent. The study was conducted on patients of all ages diagnosed with benign prostatic hypertrophy (BPH) or prostatic adenocarcinoma and confirmed through histopathological examination. The sample included prostatic trucut biopsies, transurethral prostatic resection (TURP) chips, and radical prostatectomy specimens. The study excluded patients with incomplete medical records or insufficient

tissue samples for analysis. Furthermore, those who did not consent to participate in the study or with prostatic carcinoma other than adenocarcinoma such as squamous and neuroendocrine histologic type were excluded from the study.

A total of 50 cases were selected based on availability and adequate tissue samples for immunohistochemical analysis. After obtaining the specimens, conventional processing and embedding in paraffin wax were carried out. Sections of 5µm thickness were cut using a microtome and stained with hematoxylin and eosin (H&E) for histopathological examination. These stained slides were evaluated for tumor histology, Gleason grade, and other relevant histological features according to standard reporting protocols.

Method of immunohistochemical analysis and scoring of p53 Immunoreactivity

To assess p53 expression, additional 4 µm sections cut from paraffin-embedded tumor tissue blocks were prepared for immunohistochemistry (IHC) and staining was conducted following standard protocol.

Only nuclear immunoreactivity was considered for scoring. The immunohistochemical staining was evaluated semi-quantitatively based on the percentage of positively stained tumor cell nuclei:

- Score 0: No staining observed
- Score 1: Less than 10% of tumor cell nuclei stained
- Score 2: 10–33% of tumor cell nuclei stained
- Score 3: More than 33% of tumor cell nuclei stained

For all study participants, patient demographics, clinical presentation, and histopathological parameters included Gleason score and histological grade. The association of p53 expression with these variables was assessed.

Statistical analysis

Data were entered into a Microsoft Excel spreadsheet and analyzed using the Statistical Package for the Social Sciences (SPSS) version 20.0. Descriptive statistics were used to calculate the means as well as standard deviations (SDs) of the data. The Chi-square test was used to assess associations between categorical variables. A p-value <0.05 was considered statistically significant.

RESULT

Out of 50 study participants, the majority of the patients were aged between 61 and 70 years, accounting for 46% (n=23) of the total population. This was followed by 28% in the 50–60 age group (n=14) and 26% in the 71–80 age group (n=13).

The distribution of diagnoses reveals that nearly half of the patients (n=25, 50%) have adenocarcinoma of the prostate. BPH accounts for 26% (n=13), BPH with chronic prostatitis (BPHCP) for 20% (n=10), and BPH with prostatic intraepithelial neoplasia (PIN) for 4% (n=2) (Fig. 1). Overall, 50% of the patients had benign conditions of the prostate.

Gleason's scoring and grading were done to categorize the aggressiveness of prostate cancer. Of all, the most common grade was 5 (n=10, 20%), indicating higher-grade tumors. Grades 1, 2, and 3 each accounted for 8% of the patients (n=4), while Grade 4 accounted for 6% (n=3).

Tumor grading also revealed that while 50% had no detectable tumor content, 7 cases (14%) had grade 1 tumor, 9 cases (18%) had grade 2 tumor, and another 9 cases (18%) had grade 3 tumor.

IHC staining of specimen revealed that tumors of 25 patients (50%) were negative for p53 overexpression, while 7 patients (14%) had <10% p53 overexpression, 9 patients (18%) had 10–33% p53 overexpression, and remaining 9 patients (18%) had >33% p53 overexpression (Fig. 2).

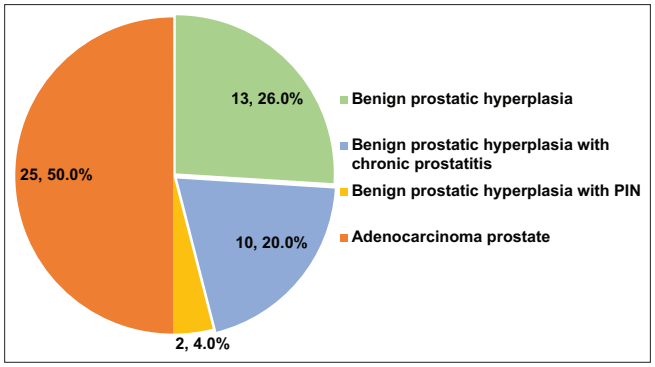

Fig. 1: Pie diagram showing distribution of diagnoses

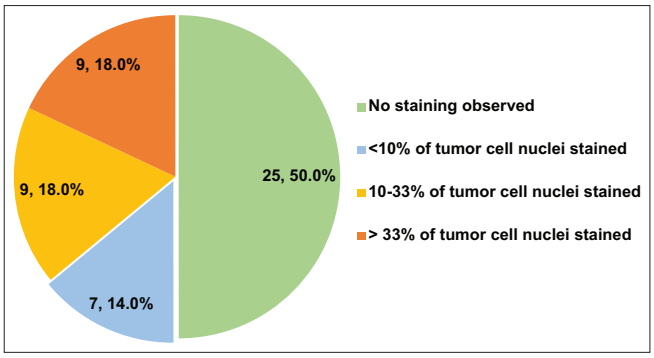

Fig. 2: Pie diagram showing distribution of p53 immunoreactivity

A significant association was observed between p53 expression in tumors and various diagnoses (p<0.001). Out of 25 cases with negative p53 overexpression, only 12% cases were adenocarcinoma prostate, while 52% cases were of BPH and 36% cases were of BPH with chronic prostatitis. On the contrary, 57% of cases with <10% p53 overexpression, 100% cases with 10–33%, and >33% p53 overexpression were prostate adenocarcinoma (Table 1).

Cumulatively, there was a statistically significant association between histological type and p53 overexpression (Table 2).

Tumors with Gleason grades 1 and 2 also predominantly show low extent of p53 overexpression. However, as the Gleason grade increases, particularly for grade 3 to 5, there is a marked increase in p53 overexpression; and the association between p53 overexpression and histological grade is statistically significant (Table 3).

However, there was no statistically significant association between p53 overexpression and age of patients (p=0.581) (Table 4).

DISCUSSION

The p53 protein is a critical tumor suppressor involved in maintaining genomic stability by regulating the cell cycle, inducing apoptosis, and promoting DNA repair. It halts the cell cycle at the G1/S checkpoint to allow DNA repair and triggers apoptosis if the damage is irreparable, preventing cancer development. Mutations in the TP53 gene, which encodes p53, are among the most common in human cancers, including PCa. These mutations lead to the loss of p53 function, resulting in uncontrolled cell growth, genomic instability, and resistance to apoptosis, all contributing to cancer progression [8].

Studying p53 expression in prostate diseases offers significant diagnostic and prognostic value. In prostate carcinoma, high levels of p53 expression or the presence of TP53 mutations often correlate with higher tumor grades, advanced stages, and poorer prognoses. This makes p53 a potential biomarker for distinguishing between BPH and

Table 1: p53 overexpression in tumor and their association with diagnosis

Diagnosis	Total n (%)	0% n (%)	<10% n (%)	10–33% n (%)	>33% n (%)	p-value
Adenocarcinoma prostate	25 (50.0)	3 (12.0)	4 (57.15)	9 (100.0)	9 (100.0)	<0.001*
BPH	13 (26.0)	13 (52.0)	0 (0.0)	0 (0.0)	0 (0.0)	
BPH with chronic prostatitis	10 (20.0)	9 (36.0)	1 (14.29)	0 (0.0)	0 (0.0)	
BPH with PIN	2 (4.0)	0 (0.0)	2 (28.57)	0 (0.0)	0 (0.0)	
Total	50 (100.0)	25 (100.0)	7 (100.0)	9 (100.0)	9 (100.0)	

Table 2: p53 overexpression in tumor and their association with histological type

Histological type	Total n (%)	0% n (%)	<10% n (%)	10–33% n (%)	>33% n (%)	p-value
Benign	25 (50.0)	22 (88.0)	3 (42.86)	0 (0.00)	0 (0.00)	<0.001*
Malignant	25 (50.0)	3 (12.0)	4 (57.14)	9 (100.0)	9 (100.0)	
Total	50 (100.0)	25 (100.0)	7 (100.0)	9 (100.0)	9 (100.0)	

Table 3: p53 overexpression in tumor and their association with histological grade

Histological grade	Total n (%)	0% n (%)	<10% n (%)	10–33% n (%)	>33% n (%)	p-value
Benign (no grade)	25 (50.0)	22 (88.0)	3 (42.86)	0 (0.0)	0 (0.0)	<0.001*
Grade 1	4 (8.0)	3 (12.0)	1 (14.29)	0 (0.0)	0 (0.0)	
Grade 2	4 (8.0)	0 (0.0)	2 (28.57)	2 (22.22)	0 (0.0)	
Grade 3	4 (8.0)	0 (0.0)	0 (0.0)	4 (44.44)	0 (0.0)	
Grade 4	3 (6.0)	0 (0.0)	0 (0.0)	1 (11.11)	2 (22.22)	
Grade 5	10 (20.0)	0 (0.0)	1 (14.29)	2 (22.22)	7 (77.78)	
Total	50 (100.0)	25 (100.0)	7 (100.0)	9 (100.0)	9 (100.0)	

Table 4: p53 overexpression in tumor and their association with age

Age	Total n (%)	0% n (%)	<10% n (%)	10–33% n (%)	>33% n (%)	p-value
50–60 years	14 (28.0)	8 (32.0)	2 (28.57)	1 (11.11)	3 (33.33)	0.581
61–70 years	23 (46.0)	12 (48.0)	3 (42.86)	6 (66.67)	2 (22.22)	
71–80 years	13 (26.0)	5 (20.0)	2 (28.57)	2 (22.22)	4 (44.44)	
Total	50 (100.0)	25 (100.0)	7 (100.0)	9 (100.0)	9 (100.0)	

prostate carcinoma and a prognostic marker influencing management and therapeutic decisions. This study investigated the association of p53 overexpression in these prostatic conditions with clinicopathological parameters.

In the present study, the 28% of the patients were aged between 50 and 60 years while majority were in the 61–70 age group (46%). This age distribution reflects the typical demographic pattern seen in both BPH and prostate adenocarcinoma, as these conditions primarily affect older men, and tend to increase in prevalence with age [2,9], which is consistent with the higher frequency observed in the 61–70 age group in this study. Our study is similar to the study of Bhat *et al*. reported 45% in the 61–70 age group, 30% in the 50–60 age group, and 25% in the 71–80 age group [10], while Verma *et al*. found 48% in the 61–70 age group, 27% in the 50–60 age group, and 25% in the 71–80 age group [11]. Interestingly, the age group data showed no significant association with p53 overexpression (p=0.581), indicating that age alone may not be a determining factor for p53 mutation status or expression levels in these conditions. Similar lack of statistical association was reported by Schitcu *et al*. [12] and Teroerde *et al*. [13].

Benign prostatic conditions, including BPH (26%), BPH with chronic prostatitis (20%), and BPH with prostatic intraepithelial neoplasia (PIN) (4%), accounted for half of the diagnoses, while prostate adenocarcinoma was present in the other half of the patients. The presence of BPH with chronic prostatitis and PIN underscores the complexity of benign prostatic disease and its potential overlap with malignancy in clinical settings. A significant association was found between p53 expression levels and specific diagnoses (p<0.001). In particular, all cases with higher p53 expression (>10%) were adenocarcinoma, suggesting a strong link between p53 overexpression and malignant transformation. Conversely, most benign cases (52% BPH and 36% BPH with chronic prostatitis) had no p53 overexpression, supporting the role of p53 as a marker of malignancy rather than benign prostatic conditions.

The study revealed a significant association between p53 expression and histological type (p<0.001). While all benign cases were predominantly negative for p53 overexpression (88%), a stark contrast was observed in malignant cases, where 100% of the tumors with more than 10% p53 overexpression were adenocarcinomas. This finding aligns with the literature that suggests p53 mutations and overexpression are more commonly associated with malignant transformations and could serve as a distinguishing feature between benign and malignant prostate conditions.

Gleason scoring is a critical method for assessing the aggressiveness of prostate cancer. In this study, 20% of patients were classified with Gleason grade 5, which represents high-grade tumors. Lower grades (1–4) were less common, with each comprising 6–8% of the cohort. A statistically significant association was observed between p53 overexpression and higher Gleason grades (p<0.001). Specifically, higher Gleason grades (3–5) were associated with increased p53 overexpression, indicating that p53 mutations or accumulation may

be linked to tumor progression and poor differentiation in prostate adenocarcinoma. Conversely, lower grades and benign cases showed minimal to no p53 expression, suggesting that p53 overexpression could serve as an indicator of tumor aggressiveness and malignancy. Over observations are aligned with the findings reported by Wahid *et al*. [14] and Bhat *et al*. [10], showing a significant correlation between p53 expression in tumors and Gleason scores. Wahid *et al*. reported a higher p53 expression in tumors with Gleason scores of 8–10, with 75% p53 positivity in high-grade tumors ($p<0.001$) [14]. Bhat *et al*. found similar results, with 80% p53 positivity in Gleason scores of 9–10 and 65% in scores of 7–8 ($p< 0.001$). Our study also showed that 77.78% of those with >33% p53 immunoreactivity had a Gleason score of 5, reinforcing the strong correlation.

In the context of recent therapeutic advancements, it needs to be highlighted that understanding p53 status is crucial not only for diagnostic and prognostic purposes but also for predicting responses to certain therapies, thereby guiding the development of personalized treatment plans. Ongoing research aims to develop drugs that restore p53 function in cancer cells with TP53 mutations and explore combination therapies to enhance treatment efficacy [15,16], underscoring the importance of p53 in prostate disease research.

This study has some limitations, including a small sample size of 50 participants, which restricts the generalizability of the findings. In addition, the study did not account for the molecular heterogeneity of prostate cancer, potential confounding factors, or the functional status of p53, which could impact the interpretation of its role in disease progression. Furthermore, the reliance on semi-quantitative assessment of p53 immunoreactivity may be subject to inter-observer variability, which may affect the consistency of the results.

CONCLUSION

The findings of this study suggest that while age does not significantly correlate with p53 expression, there are strong associations between p53 overexpression and specific diagnoses, histological type, and histological grade (Gleason scores) in prostate cancer. p53 overexpression is closely linked to malignant prostate conditions and could potentially serve as a valuable biomarker for distinguishing between benign and malignant prostatic diseases, as well as predicting tumor aggressiveness. These results highlight the importance of incorporating molecular markers like p53 in the diagnostic and prognostic evaluation of prostate cancer.

CONFLICTS OF INTEREST

The authors declare no potential conflicts of interest.

AUTHORS' CONTRIBUTIONS

All authors contributed equally in the design of the study, data collection, analysis, and manuscript writing.

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