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Histopathological Study of Prostatic Lesion and Expression of p63 Immunohistochemical Marker in Tertiary Care Centre

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Abstract: ***Background**: Prostatic lesions, including benign prostatic hyperplasia (BPH) and prostatic carcinoma, are common in aging males. Histopathology plays a critical role in diagnosis; however, the overlap in features often leads to diagnostic challenges. p63, a basal cell marker, has emerged as a valuable immunohistochemical marker in differentiating benign from malignant prostatic lesions. **Objective**: To evaluate the utility of p63 immunohistochemistry in distinguishing benign from malignant prostatic lesions in a tertiary care setting. **Methods**: This prospective observational study was conducted at Gajra Raja Medical College, Gwalior, from April 2023 to October 2024. 80 prostatic biopsy specimens were analyzed using histopathology and p63 immunohistochemistry. Data was collected on patient demographics, clinical findings, histopathological diagnosis, PSA levels, and p63 expression. Descriptive statistics and Chi-square tests were used for analysis. **Results**: The study found that 88.75% of cases were p63 positive, correlating with benign diagnoses, while 100% of malignancies were p63 negative. PSA levels were significantly elevated in malignant cases. Histologically, BPH with chronic prostatitis was most common, while prostatic adenocarcinoma accounted for 10% of cases. **Conclusion**: p63 immunohistochemistry is a reliable tool for differentiating benign from malignant prostatic lesions, offering high specificity and sensitivity. Combined with PSA testing, it improves diagnostic accuracy in ambiguous cases.*

Keywords: Prostatic Lesions, p63, Immunohistochemistry, Benign Prostatic Hyperplasia, Prostate Cancer

1. Introduction

Prostatic lesions are among the most frequently encountered urological conditions in aging males, encompassing a spectrum from benign hyperplasia to malignant carcinoma. In India, the rising geriatric population has led to a growing clinical burden of prostate-related diseases in tertiary healthcare institutions. Histopathological examination remains the gold standard for diagnosing these lesions; however, morphological overlap between benign and malignant conditions often poses diagnostic challenges. In such situations, immunohistochemical markers like p63—a nuclear transcription factor expressed in basal cells serve as valuable adjuncts to differentiate benign from malignant prostatic lesions.

Benign prostatic hyperplasia (BPH) is the most common non-neoplastic condition affecting elderly men, while prostate carcinoma is the second most frequent malignancy in men worldwide. The overlap in histological features of high-grade prostatic intraepithelial neoplasia (HGPIN), BPH, and prostatic adenocarcinoma often complicates diagnosis. In a histopathological study by Suba et al., p63 expression was found consistently in all benign prostatic glands and was absent in malignant glands, confirming its diagnostic relevance [1].

The utility of p63 lies in its exclusive expression in the basal cells of benign glands, whereas these cells are absent in adenocarcinoma. This was further validated in a large immunohistochemical study by Ibrahim et al., which concluded that p63 is highly specific and sensitive for non-carcinomatous lesions and can aid in distinguishing carcinoma from mimicking benign lesions [2].

In Indian clinical settings, where diagnostic ambiguity is common, the use of p63 alongside other markers has significantly improved diagnostic accuracy. Alampally et al. conducted a study on 60 prostatic biopsies and emphasized the role of p63 in resolving suspicious cases, especially when histomorphology alone is inconclusive [3]. The study concluded that combined use of p63 and AMACR enhances the reliability of prostate lesion diagnosis.

A comparative analysis by Akoijam et al. examined the efficacy of two basal cell markers—p63 and 34βE12 and found no significant difference in their sensitivity, but p63 offered more consistent nuclear staining, making it more practical for routine diagnostic use [4]. The study also highlighted that all malignant lesions were negative for both markers, supporting their role in identifying cancer.

In a detailed evaluation of 60 cases, Sreela demonstrated that 90% of benign lesions showed p63 positivity, while 100% of carcinoma cases showed p63 negativity, establishing its specificity. The study also introduced the significance of stromal markers like calponin, but emphasized that p63 remains a primary marker for epithelial differentiation [5].

Koshy and Bavikar investigated the immunostaining profiles of 130 prostatic samples and found that p63 exhibited a sensitivity of 92.86% and specificity of 100%, making it a

dependable tool in differentiating benign from malignant lesions [6]. They advocated its use particularly in morphologically difficult and ambiguous biopsies.

In the Nigerian context, Madubuike et al. applied p63 staining to 151 prostatic Tru-Cut biopsies and reported 100% diagnostic concordance between morphology and p63-based immunohistochemistry. The study supports the universal applicability of p63 as a basal cell marker, even in resource-limited settings [7].

A study conducted in Pakistan by Sarwar et al. provided similar results, stating that all benign cases expressed p63, while none of the carcinoma cases did, highlighting its value in South Asian diagnostic practices [8]. This consistency across populations strengthens the reliability of p63 as a diagnostic marker.

Agarwal et al. explored the use of p63 in differentiating urothelial carcinomas from prostatic adenocarcinomas, given the frequent anatomical and histological overlap. Their study found that 92% of urothelial carcinomas expressed p63, while none of the prostatic carcinomas did, reinforcing p63's specificity across urological malignancies [9].

Finally, a foundational study by Wen investigated p63 expression across benign, premalignant, and malignant lesions and found that all 30 carcinoma cases were negative for p63, while strong expression was observed in benign and low-grade PIN lesions, providing critical validation of its diagnostic role [10].

The study aimed to assess the histopathological patterns of prostatic lesions and evaluate the role of p63 immunohistochemical staining in differentiating benign from malignant prostate conditions in a tertiary care setting.

2. Methodology

1) Study Design
This was a prospective observational study designed to evaluate the histopathological spectrum of prostatic lesions and the diagnostic role of p63 immunohistochemical staining. A structured approach with predefined inclusion and exclusion criteria ensured uniform case selection and minimized bias. The primary goal was to assess the utility of p63 in distinguishing benign from malignant prostate lesions.

2) Study Setting
The study was conducted in the Department of Pathology, Gajra Raja Medical College and JA Group of Hospitals, Gwalior. This tertiary care center receives diverse urological cases and has well-equipped histopathology and immunohistochemistry labs. Tissue samples were referred by the Department of Surgery and processed in-house.

3) Study Duration
The study was conducted over 18 months, from April 2023 to October 2024. This duration allowed for adequate patient enrollment, sample processing, immunostaining, data analysis, and follow-up when required.

4) Participants – Inclusion and Exclusion Criteria
Inclusion criteria were patients with clinically and histologically confirmed prostatic lesions, adequate tissue samples, and informed consent. Exclusion criteria included critically ill patients, inadequate tissue, refusal to participate, or history of prior prostate cancer treatment.

5) Study Sampling
Purposive sampling was used to include clinically relevant cases. Patients with suspected prostatic pathology underwent biopsy, and those meeting inclusion criteria with suitable tissue were selected for histopathological and p63 immunohistochemical analysis.

6) Study Sample Size
A total of 80 cases were included, based on a calculated sample size using a 71.16% expected p63 positivity rate, 5% significance level, and 10% absolute precision. This ensured adequate statistical power for analysis.

7) Study Groups
Patients were grouped histologically into benign (BPH, PIN) and malignant (prostatic adenocarcinoma) categories. Each group was evaluated for p63 expression to compare staining patterns between non-neoplastic and neoplastic lesions.

8) Study Parameters
Key parameters included histological features, p63 staining results, PSA levels, and clinical data. The study analyzed correlations between p63 expression and lesion type to determine diagnostic accuracy.

9) Study Procedure
Tissue samples were fixed, processed, sectioned, and stained using standard immunohistochemical protocols. p63 staining involved antigen retrieval, antibody incubation, DAB visualization, and hematoxylin counterstaining to detect basal cell nuclear expression.

10) Study Data Collection
Data were collected using a structured proforma covering demographics, clinical findings, histopathology, and IHC results. Records were digitized for accuracy and confidentiality, ensuring consistent and traceable documentation.

11) Data Analysis
Data were analyzed using SPSS. Descriptive statistics summarized the findings, while Chi-square tests assessed associations between p63 expression and diagnosis. Sensitivity, specificity, PPV, and NPV were calculated with significance at $p < 0.05$.

12) Ethical Considerations
Ethical approval was obtained from the Institutional Ethics Committee. Informed consent was taken from all participants. Patient confidentiality was maintained, and the study followed ethical standards as per the Declaration of Helsinki.

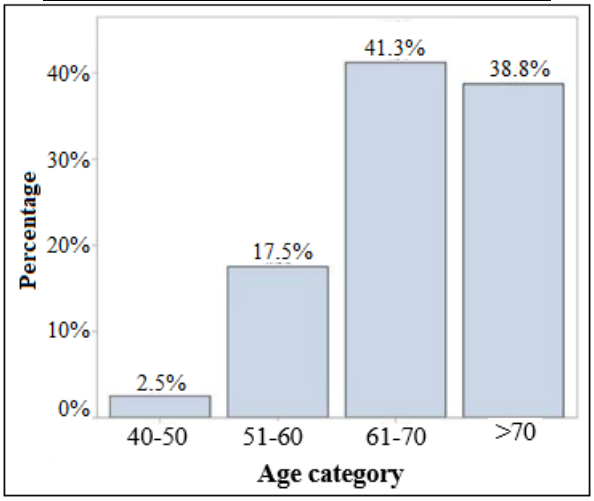
3. Results

1) Age-wise Distribution of Patients with Prostatic Lesions

The highest number of prostatic lesions occurred in patients aged 61–70 years (41.25%), followed by those >70 years (38.75%). This indicates increasing prostatic pathology with advancing age (Table 1).

Table 1: Age-wise Distribution of Patients with Prostatic Lesions

Age category	Frequency	Percent
40-50	2	2.5
51-60	14	17.5
61-70	33	41.25
>70	31	38.75



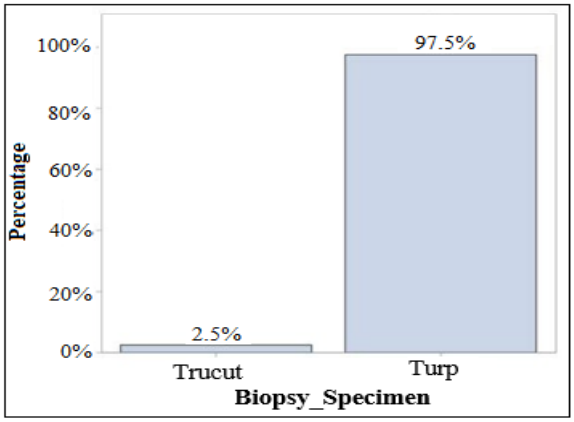
Graph 1: Age-wise Distribution of Patients with Prostatic Lesions

2) Distribution of Biopsy Specimens in Prostatic Lesions

TURP was the predominant method of biopsy (97.5%), highlighting its dual diagnostic and therapeutic utility in prostatic diseases (Table 2).

Table 2: Distribution of Biopsy Specimens in Prostatic Lesions

Biopsy_Specimen	Frequency	Percent
Trucut	2	2.5
Turp	78	97.5



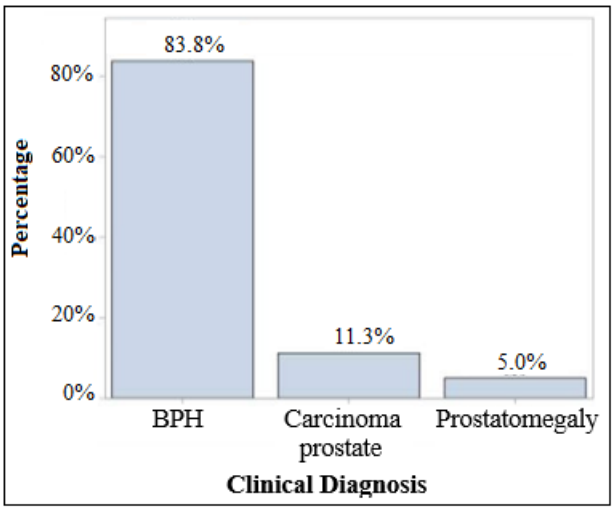
Graph 2: Distribution of Biopsy Specimens in Prostatic Lesions

3) Distribution of Clinical Diagnosis in Patients with Prostatic Lesions

Benign Prostatic Hyperplasia (BPH) was the most common clinical diagnosis (83.75%), whereas carcinoma prostate accounted for 11.25% of cases. (Table 3)

Table 3: Distribution of Clinical Diagnosis in Patients with Prostatic Lesions

Clinical Diagnosis	Frequency	Percent
BPH	67	83.75
Carcinoma prostate	9	11.25
Prostatomegaly	4	5



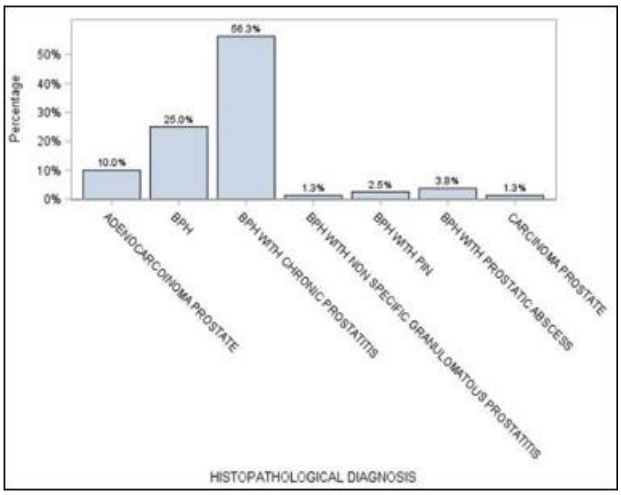
Graph 3: Distribution of Clinical Diagnosis in Patients with Prostatic Lesions

4) Distribution of Histopathological Diagnosis in Prostatic Lesions

Histology confirmed BPH with chronic prostatitis as the most frequent diagnosis (56.25%), while adenocarcinoma was found in 10% of cases (Table 4).

Table 4: Distribution of Histopathological Diagnosis in Prostatic Lesions

Histopathological_Diagnosis	Frequency	Percent
Adenocarcinoma Prostate	8	10
BPH	20	25
BPH With Chronic Prostatitis	45	56.25
BPH With Non-Specific Granulomatous Prostatitis	1	1.25
BPH With Pin	2	2.5
BPH With Prostatic Abscess	3	3.75
Carcinoma Prostate	1	1.25



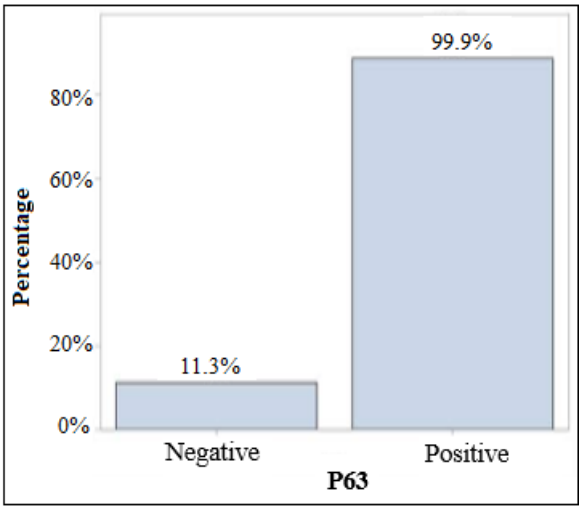
Graph 4: Distribution of Histopathological Diagnosis in Prostatic Lesions

5) Expression of p63 Immunohistochemical Marker in Prostatic Lesions

p63 expression was positive in 88.75% of cases, consistent with benign histology, and negative in 11.25%, mostly correlating with malignancy (Table 5).

Table 5: Expression of p63 Immunohistochemical Marker in Prostatic Lesions

P63	Frequency	Percent
Negative	9	11.25
Positive	71	88.75



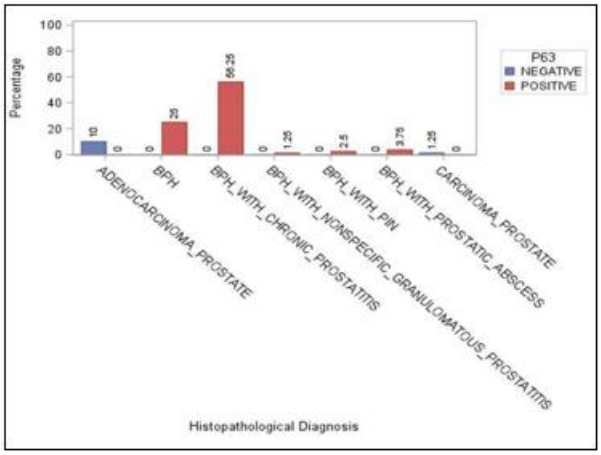
Graph 5: Expression of p63 Immunohistochemical Marker in Prostatic Lesions

6) Distribution of p63 Expression by Histopathological Diagnosis

All malignant cases showed negative p63 expression, while all benign variants showed positive staining, confirming p63's diagnostic specificity (Table 6).

Table 6: Distribution of p63 Expression by Histopathological Diagnosis

Histopathological_ Diagnosis	p63 Negative	p63 Positive	Total	p-value
Adenocarcinoma Prostate	8 (10%)	0 (0%)	8	<.0001
BPH	0 (0%)	20 (25%)	20	
BPH With Chronic Prostatitis	0 (0%)	45(56.25%)	45	
BPH With Non-Specific Granulomatous Prostatitis	0 (0%)	1 (1.25%)	1	
BPH with Pin	0 (0%)	2 (2.50%)	2	
BPH With Prostatic Abscess	0 (0%)	3 (3.75%)	3	
Carcinoma Prostate	1 (1.25%)	0 (0%)	1	



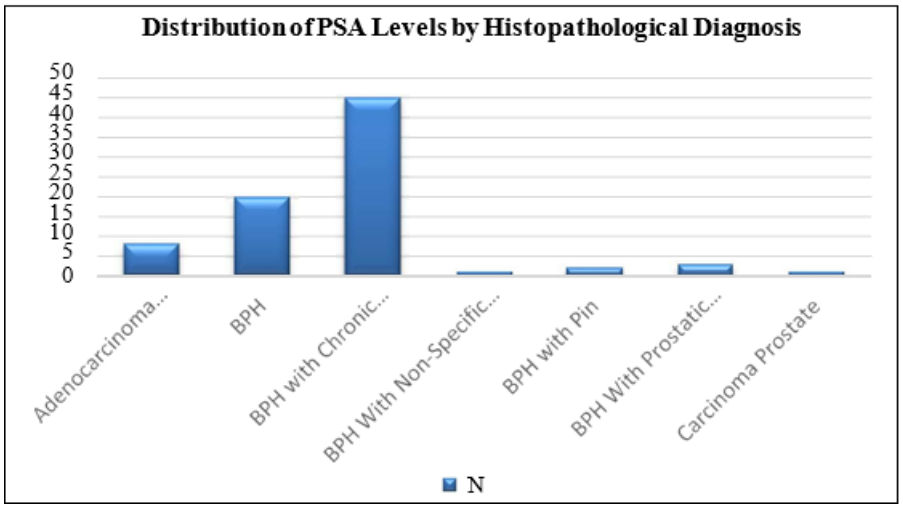
Graph 6: Distribution of p63 Expression by Histopathological Diagnosis

7) Distribution of PSA Levels by Histopathological Diagnosis

Mean PSA levels were significantly higher in adenocarcinoma (17.63 ng/ml) compared to benign lesions like BPH (4.6 ng/ml), supporting PSA's value in malignancy screening (Table 7).

Table 7: Distribution of PSA Levels by Histopathological Diagnosis

Histopathological Diagnosis	N	Mean	Std Dev	Minimum	Maximum	p-value
Adenocarcinoma Prostate	8	17.63	3.02	11	21	
BPH	20	4.6	0.82	4	7	
BPH with Chronic Prostatitis	45	5.18	1.43	3	8	
BPH With Non-Specific Granulomatous Prostatitis	1	5	.	5	5	<.0001
BPH with Pin	2	5	0	5	5	
BPH With Prostatic Abscess	3	5.33	1.53	4	7	
Carcinoma Prostate	1	19	.	19	19	



Graph 7: Distribution of PSA Levels by Histopathological Diagnosis

Histopathological Images

Figure 1: Prostatic CHIPS

Figure 2: Test Block for IHC and H&E

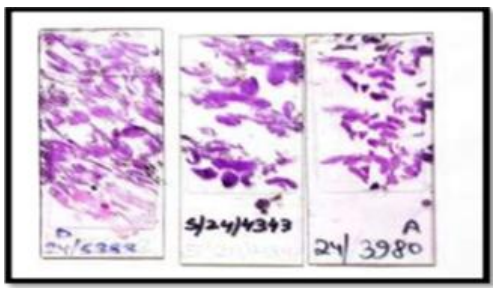


Figure 3: H&E slides

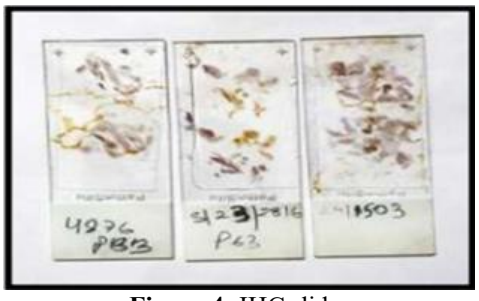


Figure 4: IHC slides

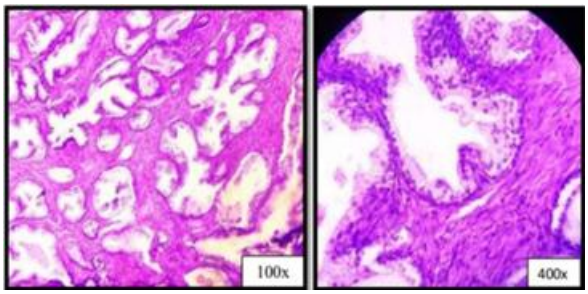


Figure 5: Benign prostatic hyperplasia

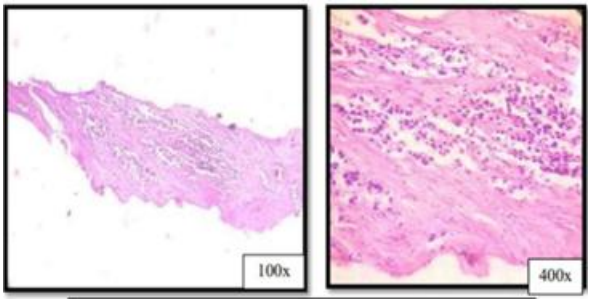


Figure 6: Adenocarcinoma Prostate gleason score 3+5=8, Grade=4

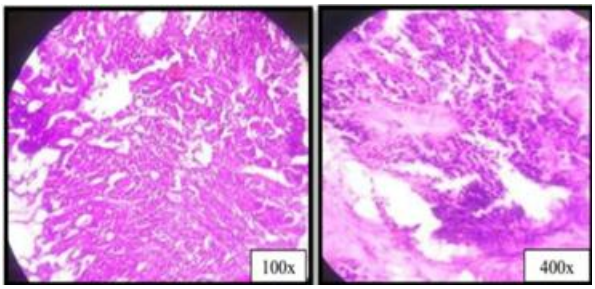


Figure 7: Adenocarcinoma prostate, Gleason score 4+5=9, Grad

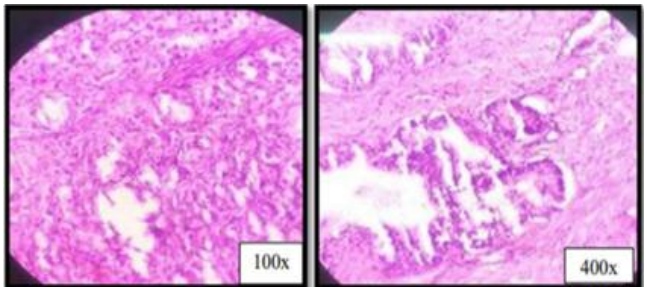


Figure 8: Adenocarcinoma prostate, Gleason score 3+4=7, Grade =2

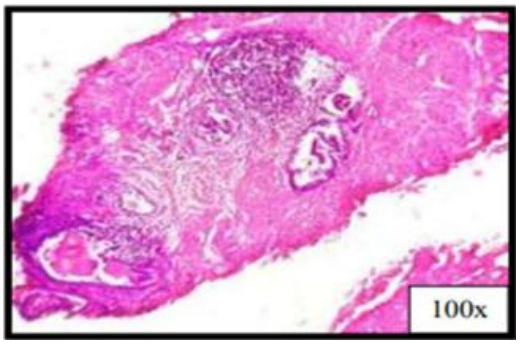


Figure 9: Prostatic adenocarcinoma with chronic prostatitis

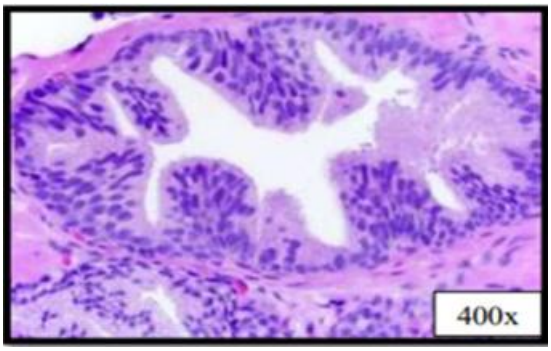


Figure 10: PIN lesion

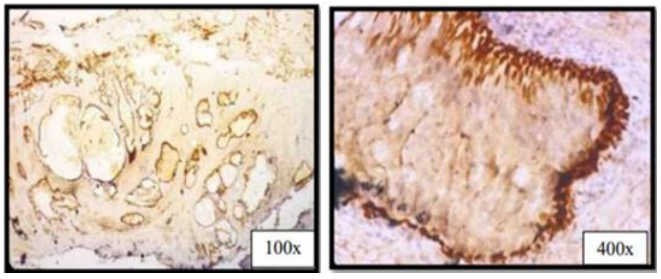


Figure 11: p63 positive

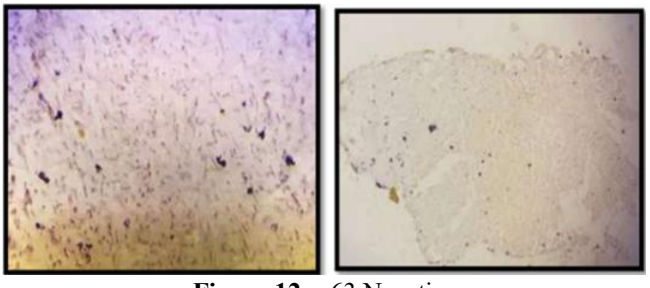


Figure 12: p63 Negative

4. Discussion

The present study aimed to evaluate the histopathological spectrum of prostatic lesions and the role of p63 immunohistochemical staining in differentiating benign from malignant conditions. Our findings are in line with several previous studies, reinforcing the diagnostic value of p63 as a basal cell marker.

In our study, the majority of patients were above 60 years, with the 61–70 years age group being the most affected (41.25%), followed by those above 70 years (38.75%). This age distribution corresponds well with findings from Suba et al. (2022), who also noted a similar prevalence of prostatic lesions among elderly males, underscoring the importance of prostate screening in this age group [1].

Histopathologically, Benign Prostatic Hyperplasia (BPH) with chronic prostatitis (56.25%) was the most common diagnosis, consistent with Alampally et al. (2019), who observed BPH and associated inflammation as the predominant pathology in TURP specimens [3]. Adenocarcinoma accounted for 10% of cases in our study, which is comparable to the malignancy rates reported in tertiary care settings by Madubuike et al. (2022) [7].

The expression of p63 was observed in 88.75% of cases and was absent in all malignant lesions, confirming its reliability as a benign basal cell marker. This aligns with the findings of Sreela (2018) and Nisar et al. (2017), who emphasized that p63 positivity is limited to benign glands due to the presence of intact basal cells [5, 8]. Our results also correlate with Koshy and Bavikar (2021), who reported p63 as a valuable tool in identifying basal cell presence and excluding malignancy [6].

Moreover, elevated PSA levels in malignant cases (mean 17.63 ng/ml) were significantly higher than benign conditions, reaffirming PSA's role as a screening marker. However, overlap in PSA values, as also reported by Agarwal et al. (2021), highlights the necessity of combining PSA with histopathological and immunohistochemical assessments for accurate diagnosis [9].

Our findings strongly support the use of p63 as a reliable immunohistochemical marker for distinguishing benign from malignant prostatic lesions, consistent with global literature.

5. Conclusion

In conclusion, our study underscores the diagnostic value of p63 immunohistochemistry in differentiating benign from malignant prostatic lesions. The high specificity and sensitivity of p63 for benign prostatic lesions, with consistent negativity in malignant cases, confirm its reliability as a diagnostic tool. Elevated PSA levels further complement histopathological and immunohistochemical findings, reinforcing the importance of a combined diagnostic approach for accurate differentiation, especially in ambiguous cases. The use of p63 enhances diagnostic accuracy and aids in the management of prostate-related diseases.

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