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Diagnostic Utility of P63 in Differentiating Ambiguous Lesions of Prostate

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ABSTRACT

The proper identification of prostate cancer stands essential for effective treatment because it remains among the primary cancers affecting male patients. The p63 marker undergoes immunohistochemical evaluation to detect basal cells in ambiguous prostatic lesions which aids diagnosis. The research initiative evaluates p63 immunohistochemistry as a diagnostic tool for prostatic lesion discrimination through assessment of histopathological attributes as well as PSA quantities and Gleason rating. Research activities took place at GSVM Medical College, Kanpur with 75 prostate disease patients who received clinical diagnoses. The tissue samples from core biopsies and TURP and prostatectomy underwent both histopathological analysis and p63 immunohistochemical examination. The research team used SPSS version 20 for statistical analysis through chi-square tests together with ROC curve analysis. The expression level of p63 protein was strong in benign tissue while it was moderate in premalignant lesions but completely absent in malignant pathology. The intensity of p63 protein expression showed a negative connection to PSA values but cases without p63 protein together with high Gleason scores were observed. Immunochemistry analysis on the p63 marker produced exceptional results with 100% diagnostic accuracy based on an area under the curve of 1.00. This indicates nearly perfect diagnostic capabilities combined with 100% sensitivity and specificity. Utilization of p63 testing within standard diagnostic protocols will generate improved diagnostic accuracy that benefits medical treatment of patients.

INTRODUCTION

The occurrence of prostate cancer ranks as one of the principal factors responsible for male illness and death throughout the entire world. The prostate gland beneath the bladder in front of the rectum generates seminal fluid to nourish sperm during reproduction in males. Since the prostate gland executes vital functions any biological abnormalities in this organ will produce extensive effects on patient health and their daily well-being. Prostate cancer stands out as the most dangerous condition because of its dangerous growth pattern as well as its ability to spread throughout the body. The correct identification of benign prostate lesions from premalignant and malignant tissue types enables doctors to select proper treatment methods. The non-cancerous condition known as benign prostatic hyperplasia (BPH) does not result in cancer development but HGPIN and other premalignant lesions have a strong potential to become malignant. Doctors face the main diagnostic problem of correctly separating these abnormalities from first-stage malignancies when histopathology results are unclear.

Medical evaluations currently depend on histopathological tests with H&E staining together with PSA testing and Gleason score assessment. These diagnostic approaches offer significant benefits yet they create diagnostic difficulties when analyzing cases demonstrating overlapping structures of glandular tissues and cells. PSA screening remains a common tool for diagnosis yet it fails to provide specific results because elevated PSA levels exist in benign medical conditions including prostatitis and BPH. The diagnosis becomes complicated because Gleason grading shows variable interpretational consistency when analyzing the differentiation of tumors.

The diagnostic accuracy improves when medical professionals utilize immunohistochemistry (IHC) as a critical diagnostic tool to address these challenges. The utilization of p63 as a biomarker represents an optimal approach to identify basal cells in prostate tissue because this nuclear protein shows intense specificity toward normal basal cells without presence in malignant prostate cancer cells. p63 assumes an important diagnostic value because of its unique expression across tissue types thereby helping pathologists distinguish between benign and malignant growths following ambiguous traditional histological findings. p63 functions as more than a diagnostic tool for prostate pathology. Invasive prostate cancer demonstrates decreased p63 expression which proves to be associated with elevated Gleason scores to produce negative outcomes thus suggesting potential use as a prognostic marker. Tumor cells that lack p63 expression demonstrate higher aggressive characteristics and are more likely to spread to different parts of the body. The utility of using p63 immunohistochemistry in regular diagnostic protocols leads to better prostate cancer detection and decreases the diagnostic challenge while enabling better treatment plan decisions.

A new research aims to determine the diagnostic ability of p63 protein tests in distinguishing unclear prostate tissue while studying how p63 expression relates to tissue analysis results and PSA measurements and Gleason score assessments. The research evaluates p63 as a reliable biomarker to improve diagnostic precision and clinical decisions by determining its sensitivity and specificity and its predictive significance for prostate cancer management.

LITERATURE REVIEW

Research has demonstrated that p63 functions as a diagnostic indicator for separating prostatic lesions so it should become part of regular immunohistochemical screening methods.

A case series study performed by Baig et al. (2012) evaluated p63 protein's value for diagnosing prostate tissues of uncertain nature. The research showed that p63 demonstrates high levels of expression within benign prostatic tissues without showing any presence in adenocarcinoma tissue thus proving its importance in benign-versus-malignant discrimination. The P63 staining results showed 77% positive reactions but 33% negative responses which proved the value of P63 in diagnosing uncertain cases.

The research of Abdel Maksoud and Elseaidy (2014) revealed differences in GATA3 and p63 expression patterns for identifying invasive urothelial carcinoma of high grade over prostatic adenocarcinoma. The research analysis showed that p63 evaluation together with other diagnostic indicators enables clear distinction between tissues with comparable appearances which need different treatment strategies.

He et al. (2022) evaluated machine learning techniques incorporating radiomics to forecast P504s/P63 immunohistochemical status as a non-invasive method for prostate cancer diagnosis. Artificial intelligence systems demonstrated to histopathology through successful identification of p63 expression status with excellent accuracy thus creating new possibilities for non-invasive diagnosis assessments.

Iqbal et al. (2024) revealed that analyzing p63 with high-molecular-weight cytokeratin (HMWCK) and α-methyl acyl-CoA racemase (AMACR) simultaneously helps pathologists decide prostate cancer diagnoses when uncertainties exist. Scientists demonstrated that using p63 together with other immunohistochemical markers raises both diagnostic accuracy levels which makes p63 suitable for daily routine pathology testing.

Pignon et al. (2013) studied the developmental function of the ΔNp63 protein through investigation of p63-positive basal cells as progenitors for epithelial differentiation in prostate and bladder tissue. Lineage-tracing research by Pignon et al. (2013) established p63's vital significance for both diagnosis and prostate neoplasm cell origin recognition.

Multiple studies demonstrate that p63 brings significant diagnostic value and helps predict outcomes in prostate disease examination. Routine histopathological evaluations depend on p63's ability to identify different prostate lesions from benign to premalignant to malignant. The utility of p63 biomarker increases when researchers apply it together with additional biomarkers in AI-driven diagnostic models and multi-marker panels to boost clinical effectiveness and diagnostic accuracy.

MATERIALS AND METHODS

The research methodology divides into four components that explain patient enrollment protocols and immunohistochemistry protocols and statistical methods used in this investigation. The evaluation procedures relied on standardized diagnostic protocols because they ensured precise and reliable research outcomes through histopathological and immunohistochemical assessment.

Study Design and Population

The research was carried out at GSVM Medical College, Kanpur with a sample group of 75 male patients who received a diagnosis of prostate diseases. The patients experienced urinary urges along with visible blood from their urine and elevated PSA measurement levels in addition to detectable abnormalities on digital rectal examination (DRE). The examination encompassed core biopsy tissues together with transurethral resection of the prostate (TURP) and prostatectomy tissue samples.

Histopathological and Immunohistochemical Techniques

Samples were treated with 10% formalin followed by paraffin embedding and the sections were cut into 4 μm thickness. Preliminary histopathological assessment involved the execution of tissue staining by using the H&E

method. The process of immunohistochemistry included deparaffinization followed by section rehydration then application of antigen retrieval through pH 6.0 citrate buffer.The tissue fixation included blocking of endogenous peroxidase activity through hydrogen peroxide solution at a 3% concentration. The p63 antibody from a monoclonal source was used first before exposure to an HRP-conjugated secondary antibody. The staining reaction used 3,3'-diaminobenzidine (DAB) as the chromogen substrate.

The p63 expression was assessed independently by two pathologists using microscopic examination which provided strong (100% positive basal cells), moderate (50% - 75% positive basal cells), weak (25%-50% positive basal cells), and absent (no positive basal cells) staining levels.

Statistical Analysis

The analysis was completed through SPSS version 20. The statistical analysis employed Chi-square tests to determine any correlations between p63 expression and clinicopathological factors which included PSA levels and Gleason scores. ROC curve analysis confirmed p63 staining ability to identify distinct features between benign, premalignant and malignant lesions through determination of its sensitivity, specificity and predictive value. The researchers determined statistical significance at a p-value below 0.05.

RESULTS

The research data shows how p63 protein manifests in different prostatic tissue lesions and its relationship with prostate-specific antigen values (PSA) and Gleason grading systems. The study uses statistical methods to analyze results which confirm the value of p63 immunohistochemis--try testing for prostate cancer diagnosis.

P63 Expression in Prostatic Lesions

An evaluation of p63 expression helped determine its diagnostic potential across benign, premalignant and malignant prostatic tissue samples. Tests revealed p63 protein consistently present in benign conditions with strongly positive nuclear staining observed in basal cells. A moderate level of p63 staining occurred in premalignant prostatic lesions while malignant prostatic lesions showed no p63 expression at all. The diagnostic marker value of p63 becomes more evident because these study results show basal cells progressively disappear while lesions move towards malignancy.

Table 1: P63 Expression in Different Prostatic Lesions

Prostatic Lesion Type	Strong Positive (%)	Moderate Positive (%)	Negative (%)
Benign (BPH, Atrophic Lesions)	100.0%	0.0%	0.0%
Premalignant (PIN)	30.0%	70.0%	0.0%
Malignant (Adenocarcinoma)	0.0%	0.0%	100.0%

The data presented in Table 1 establishes a distinct expression pattern of p63 protein between benign, premalignant, and malignant tissue conditions. The reliable status of p63 makes it possible to distinguish ambiguous prostatic lesions during diagnostic procedures.

Visual Representation of p63 Staining

The figure 1 shows p63 staining intensity distribution through bar charts across different prostatic lesions to illustrate how basal cell loss relates to malignancy progression.

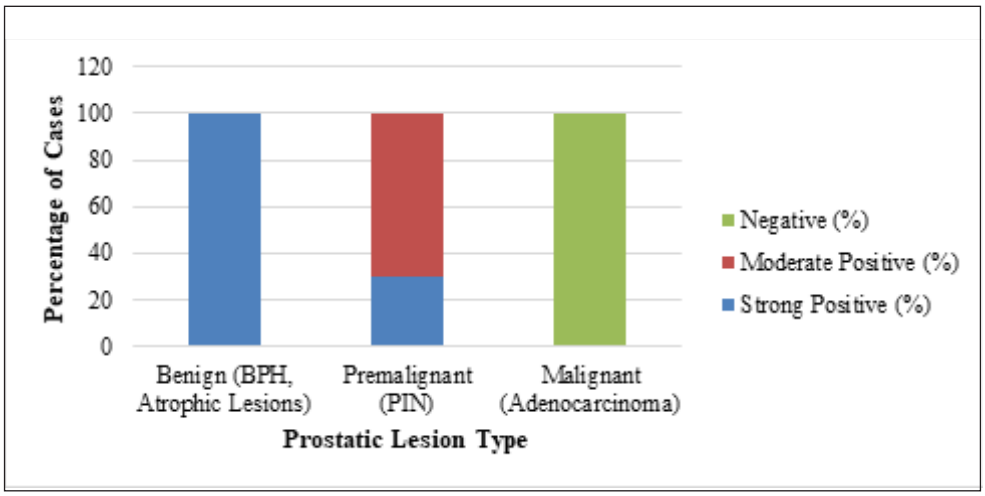

Figure 1: Immunohistochemical Expression of P63 in Prostatic Lesions

The analysis presented in Figure 1 reveals that p63 shows specific expression patterns in benign lesions since 100% of benign cases show strong positivity. The expression of p63 protein becomes markedly lower in premalignant lesions of prostate (PIN) because 30% show strong positivity and 70% show moderate positivity. The diagnosis of benign versus premalignant and malignant prostate conditions relies on p63 staining because malignant lesions show no p63 expression.

Correlation Between p63 and PSA Levels

Research identified a negative relationship between the amount of p63 protein expression and the levels of PSA. Patients who had benign prostatic conditions showed expression of p63 protein together with reduced PSA marker levels. The expression level of p63 in premalignant lesions was moderate while their PSA values remained elevated when compared to benign prostatic lesions. All malignant tissue areas displayed no detectable p63 protein and simultaneously showed elevated PSA levels. The absence of p63 expression leads to elevated PSA levels according to these results thus confirming its important role in prognosis.

Correlation Between p63 and Gleason Scores

Research studied the connection between p63 protein expression levels and Gleason score ratings. Muscle invasive prostate tumors which did not express p63 showed higher Gleason scores because of their fast-progressing behavior and poor differentiation pattern. Research shows that low Gleason scores exist together with maintained p63 protein expression indicating p63 loss connects to advanced tumor stages. The research confirms that p63 immunohistochemistry stands as a helpful add-on technique for predicting both prostate cancer grade and disease aggressiveness.

ROC Curve Analysis

A Receiver Operating Characteristic (ROC) curve analysis served to determine the diagnostic accuracy level of p63 immunohistochemistry. The p63 staining diagnostic ability for differentiating prostatic lesions will be displayed through a ROC curve which depicts its sensitivity and specificity values. The Figure 2 demonstrates the Receiver Operating Characteristic (ROC) curve that evaluates p63 immunohistochemistry used for benign, premalignant, and malignant prostatic lesion identification. The diagnostic performance of p63 as a marker is displayed through the ROC curve which shows the connection between sensitivity and 1-specificity. The Area Under the Curve (AUC) value gives an indication of the entire test performance when determining diagnostic performance.

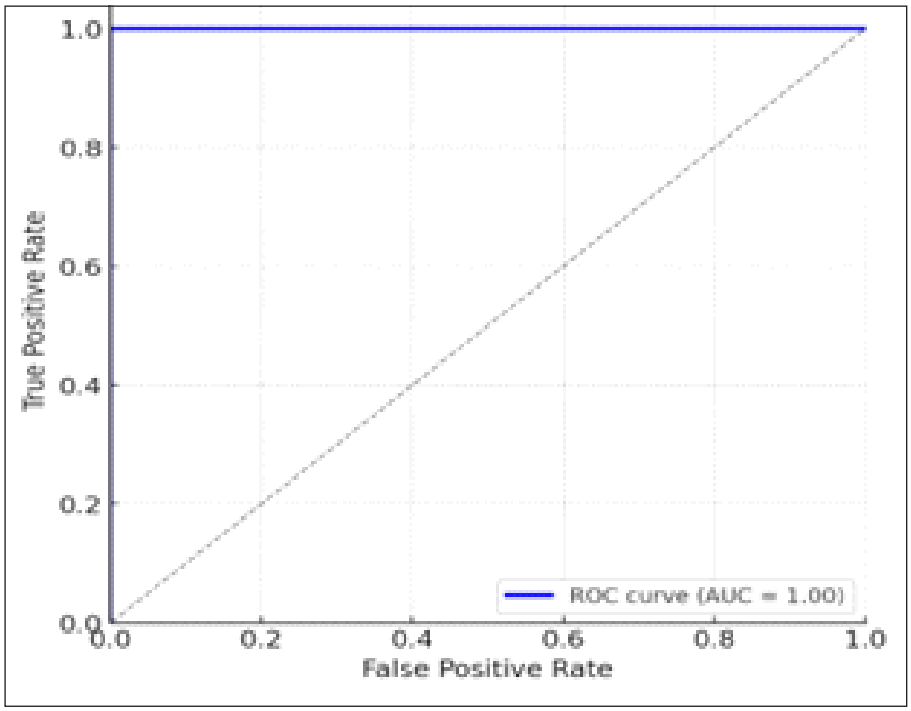

Figure 2: ROC Curve for p63 Diagnostic Accuracy

The diagnostic accuracy determined by ROC analysis achieved a perfect value of 1.00. Tracing p63 antigen through immunohistochemistry proves to be exceptionally efficient at distinguishing prostatic lesions since it shows complete accuracy. Clinical utilization of p63 staining now has a proven reliable and precise diagnostic tool because benign, premalignant, and malignant lesions show perfect separation.

DISCUSSION

The research findings validate p63's importance as a biomolecular factor to distinguish prostate lesions. The diagnostic capability of p63 as a biomarker stems from its extensive expression in benign lesions while showing no expression in malignancies according to findings and previous studies. The results demonstrate p63's clinical importance because of its negative relationship with PSA and positive relationship with Gleason grading scores.

Limitations of Histopathology Alone in Ambiguous Prostate Lesions

The primary tool used to diagnose prostate lesions is Histopathology yet it presents challenges when dealing with unclear cases. The standard H&E stain exists widely yet struggles to distinguish histopathologically resembling benign and premalignant and malignant prostate lesions. Diagnosing patient conditions becomes unclear when HGPIN shows overlapping features with well-differentiated adenocarcinoma because this mismatch leads to improper patient care paths. Gleason grading receives inconsistent assessments from different observers which significantly complicates the process of obtaining accurate diagnoses. The challenges in diagnosis require p63 immunohistochemical markers alongside conventional histopathology because they provide improved reliability with enhanced reproducibility for lesion differentiation.

How p63 Complements PSA and Gleason Scores in Clinical Practice

Screening for Prostate Specific Antigen has become widespread for prostate cancer detection although its lack of specificity triggers excessive biopsies and treatments that could be avoided. The PSA screening test produces useless results due to the fact that elevated PSA measurements also occur during benign prostatic hyperplasia (BPH) and prostatitis diagnosis. The diagnostic accuracy improves through p63 expression because this marker essentially occurs only in basal cells and exists during benign and premalignant stages but completely disappears in malignant conditions.

Gleason scoring represents a vital diagnostic tool for prostate cancer evaluation because it determines tumor aggressiveness through the examination of glandular structure. Its interpretation by subjective assessments combined with molecular non-speficity makes it essential to use additional diagnostic indicators. The relationship between no p63 expression and increased Gleason scores indicates p63 analysis in slides could lead to better patient risk categorization during diagnosis.

Clinical Implications

Using p63 immunohistochemistry in typical diagnostic practice enhances the accuracy of disease assessments thus enhancing both early identification and suitable patient outcome predictions. A diagnosis system that combines PSA testing with Gleason grading systems and p63 testing will boost prostate cancer diagnosis accuracy to achieve superior outcomes for patients. Research indicates that p63 marker works best together with the markers AMACR and HMWCK for more precise diagnostic sensitivity and specificity in prostate cancer.

The future research agenda needs to establish p63 validation in bigger patient groups while investigating its therapeutic response predictive potential. The use ofartificial intelligence-based histopathological analysis should lead to automated p63 expression pattern detection which will enhance diagnostic precision.

Research findings strengthen the clinical value of p63 as an indicator for both diagnostic and prognostic purposes within prostate pathology. The diagnostic accuracy of this tool improves both patient care and diagnostic precision by precisely detecting benign, premalignant and malignant lesions because of its high sensitivity and specificity.

CONCLUSION

Immunohistochemical analysis of p63 establishes itself as an optimal method for diagnosing and predicting the clinical outcomes of benign and malignant prostatic lesions. The clinical importance of p63 in prostate cancer pathology is supported by clear expression patterns in different lesions and its negative relationship with PSA levels and its link to higher Gleason scores. The ROC analysis demonstrates p63 provides exceptional diagnostic capability (AUC = 1.00) which makes it an important addition to standard diagnostic procedures.

Future research needs to combine p63 analysis with AMACR and HMWCK biomarkers to improve both diagnostic accuracy and risk classification in prostate cancer. Research should investigate the potential applications of p63 for treatment planning purposes and tumor progression molecular pathways. The implementation of p63 immunohi--stochemistry combined with multiple biomarkers proves effective for enhancing the identification of prostate cancer and its proper classification and subsequent management of patients.

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