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Diagnostic utility of immunohistochemistry using basal cell markers in distinguishing benign from malignant prostatic lesions

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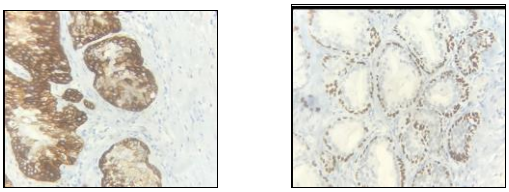
Abstract
Immunohistochemical detection of basal cells plays a significant role in the diagnosis or exclusion of prostatic carcinoma in diagnostically challenging cases. The objective of this research is to study the expression of immunohistochemical markers p63 and high molecular weight cytokeratin (34βE12) in various prostatic lesions and comparing the sensitivity and specificity of 34βE12 and p63 in prostatic lesions. This was a cross sectional study carried out in our institution on 40 cases of prostatic lesions. It was found that p63 is more sensitive than HMWCK in identifying the basal cells in diagnostically challenging cases.

Keywords: Prostate carcinoma, basal cell markers-HMWCK, p63

Introduction
Prostatic disease causes significant morbidity and mortality in elderly men throughout the world. It can be common to underdiagnose small focus of prostatic adenocarcinoma or over diagnose benign lesions mimicking cancer. Immunohistochemistry (IHC) is a valuable adjunctive in the diagnosis of minute foci of prostatic carcinoma and to differentiate it from benign mimickers and precursor lesions [1]. Prostate cancer is now the 5th most common cancerin the world and 2nd most common cancer in men [2].

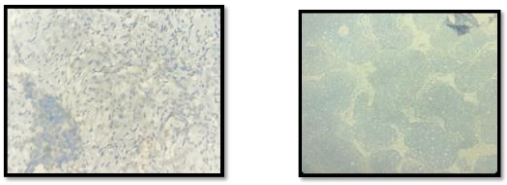
Materials and Methods
This cross sectional study includes 40 cases of prostatic lesions referred from Urology department of SRM Medical College Hospital and Research Centre, Potheri. All types of prostatic specimens including TURP and TRUCUT biopsies were considered. All the prostatic specimens were subjected to a careful and detailed gross examination. Fixation was done by 10% neutral buffered formalin and paraffin embedded tissue sections from these specimens were used for microscopic study. Sections were made manually and staining was done with routine hematoxylin and eosin. The slides were examined thoroughly and looked for the presence of malignancy, prostatic intraepithelial neoplasia, metaplasia, acute and chronic inflammation and other secondary changes associated with benign nodular hyperplasia. Immunohistochemical staining with basal cell specific markers like HMWCK (34βE12) and p63 was done for 40 cases of prostatic lesions including benign and malignant conditions.

Results
Table I shows histopathological diagnosis and the results of expression of HMWCK and p63 in the 40 cases. Table 2 shows the HMWCK staining in benign and malignant prostatic glands. The Sensitivity of HMWCK is 90 % and Specificity of HMWCK is 100%. Table 3 shows p63 staining in Benign and malignant prostatic glands with Sensitivity and Specificity to be 100%. From Table 1 and 2, it is apparent that all of the malignant glands showed total absence of HMWCK leading to a specificity of 100% for both HMWCK and p63. The results of our study has demonstrated that p63 and HMWCK are specific for basal cells in the prostate gland and are negative in the areas of prostatic carcinoma. After statistical analysis p63 is found to be more sensitive than HMWCK in staining basal cells in prostatic specimens.



HMWCK-Cytoplasmic positivity, p63-Nuclear positivity

Fig 1: Benign prostatic hyperplasia-HMWCK and p63 positivity



HMWCK negativity p63 negativity

Fig 2: Prostatic adenocarcinoma -HMWCK and p63 negativity

Table 1: Histopathological diagnosis and the results of expression p63 and HMWCK

Sl.No	Path no	HPE DIAGNOSIS	p63	HMWCK
1	5723/18	Benign Prostatic Hyperplasia	Positive	Positive
2	6519/18	Benign Prostatic Hyperplasia	Positive	Positive
3	5568/18	Benign Prostatic Hyperplasia	Positive	Positive
4	7277/18	Benign Prostatic Hyperplasia	Positive	Positive
5	9391/18	Benign Prostatic Hyperplasia	Positive	Positive
6	6522/18	Benign Prostatic Hyperplasia	Positive	Positive
7	8286/18	Benign Prostatic Hyperplasia	Positive	Positive
8	5385/18	Benign Prostatic Hyperplasia	Positive	Positive
9	7634/18	Benign Prostatic Hyperplasia	Positive	Positive
10	6700/18	Benign Prostatic Hyperplasia	Positive	Positive
11	8929/18	Benign Prostatic Hyperplasia	Positive	Positive
12	6289/18	Benign Prostatic Hyperplasia	Positive	Positive
13	8939/18	Benign Prostatic Hyperplasia	Positive	Positive
14	5876/18	Benign Prostatic Hyperplasia	Positive	Negative
15	8019/18	Benign Prostatic Hyperplasia	Positive	Positive
16	6737/18	Benign Prostatic Hyperplasia	Positive	Positive
17	5703/18	Benign Prostatic Hyperplasia	Positive	Positive
18	8423/18	Benign Prostatic Hyperplasia	Positive	Positive
19	9222/18	Benign Prostatic Hyperplasia	Positive	Positive
20	7320/18	Benign Prostatic Hyperplasia	Positive	Negative
21	6858/18	Benign Prostatic Hyperplasia	Positive	Positive
22	7755/18	Benign Prostatic Hyperplasia	Positive	Positive
23	7631/18	Benign Prostatic Hyperplasia	Positive	Negative
24	231/19	Benign Prostatic Hyperplasia	Positive	Positive
25	1561/18	Benign Prostatic Hyperplasia	Positive	Positive
26	1184/19	Benign Prostatic Hyperplasia	Positive	Positive
27	1444/18	Benign Prostatic Hyperplasia	Positive	Positive
28	592/18	Benign Prostatic Hyperplasia	Positive	Positive
29	2214/19	Benign Prostatic Hyperplasia	Positive	Positive
30	1248/19	Benign Prostatic Hyperplasia	Positive	Positive
31	1406/19	Prostatic Adenocarcinoma	Negative	Negative
32	2051/19	Prostatic Adenocarcinoma	Negative	Negative
33	5271/18	Prostatic Adenocarcinoma	Negative	Negative
34	9217/18	Prostatic Adenocarcinoma	Negative	Negative
35	8352/18	Prostatic Adenocarcinoma	Negative	Negative
36	6330/18	Prostatic Adenocarcinoma	Negative	Negative
37	1999/19	Prostatic Adenocarcinoma	Negative	Negative
38	6729/18	Prostatic Adenocarcinoma	Negative	Negative
39	6387/18	Prostatic Adenocarcinoma	Negative	Negative
40	9216/18	Prostatic Adenocarcinoma	Negative	Negative

Table 2: HMWCK staining in benign and malignant prostatic glands

HMWCK	BENIGN	MALIGNANT	TOTAL
POSITIVE	27	0	27
NEGATIVE	3	10	13
TOTAL	30	10	40

Sensitivity of HMWCK = 90%
Specificity of HMWCK = 100%
Positive predictive value=100%

Table 3: p63 staining in Benign and malignant prostatic glands

p63	BENIGN	MALIGNANT	TOTAL
POSITIVE	30	0	30
NEGATIVE	0	10	10
TOTAL	30	10	40

Sensitivity of p63 = 100%
Specificity of p63 = 100%
Positive predictive value = 100%

Discussion

M.H. Weinstein *et al.* proved that p63 is more superior in demonstrating Prostatic Basal Cells when compared to HMWCK [4] which correlated with our study. Our results reveal high expression of p63 (40 of 40, 100%) in normal basal cells and confirm the superiority over HMWCK. Even though the diagnosis of prostatic lesions are analysed through histopathological examination, sometimes diagnosis can be challenging when pathologists are faced with certain problems such as small foci of carcinoma or benign mimickers. In these situations, Immunohistochemical detection of basal cells play an important role. The most commonly used basal cell specific markers are high molecular weight cytokeratin [HMWCK] and newly described basal cell marker p63 [5]. Signorette *et al.* [6] also highlighted the role of p63 in the development of prostate gland and showed that p63 is expressed in virtually all the basal cells of prostatic glands including a subset negative for 34βE12. HMWCK shows cytoplasmic positivity where as p63 shows nuclear positivity [7].The results of our study demonstrate that p63 and HMWCK are specific for basal cells in the prostate gland. This correlated with the study of Shah *et al.* [8] who reported the absence of basal cell staining both with HMWCK and p63 in prostatic adenocarcinoma. Multhaupt *et al.* [9] found that 88% benign glands in the transition zone obtained by transurethral resections of the prostate lost their HMWCK antigenicity if antigen retrieval was not used. Michael *et al.* [10] also showed same effect as above.

Conclusion

In this study of 40 cases of prostatic lesions, histopathological analysis and the diagnostic role of Immunohistochemical markers were studied. It was found that immunohistochemical p63 staining is diagnostically reliable in identifying basal cells in prostatic lesions and has an edge over HMWCK staining. In addition, p63 staining shows a nuclear reaction which is easy to interpret than HMWCK which shows cytoplasmic reaction.

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