EUROPEAN ACADEMIC RESEARCH
Vol. IV, Issue 2/ May 2016

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

Immunohistochmical Evaluation of P63 Marker in Prostatic Carcinoma and Benign Prostatic Hyperplasia in Small Foci of Sudanese Patients

MOHAMED H. ELHAG
MSc student, Faculty of Medical Laboratory Sciences
Al-Neelain University, Khartoum, Sudan
ELSADIG A. ADAM
Department of Pathology, Al-Ribat University Khartoum, Sudan
ELTAYEB E. ELTAYEB
MSc student, Faculty of Medical Laboratory Sciences
Al-Neelain University, Khartoum, Sudan
NADA S. SALIH
Senior of Histopathology Department
Khartoum Radiation and Isotopes Center Khartoum, Sudan

Abstract:

Background: *Prostate cancer is a major health problem throughout the world. Immunohistochemistry plays a very important role in the diagnosis of minimal prostatic carcinoma and to exclude one of its benign mimickers, but it should always be interpreted in the context of the H&E appearances. In some cases of minimal prostate cancer morphologic features do not allow a diagnosis of carcinoma. In such situation, the absences of basal cell marker (p63) confirm the presence of prostate cancer.*

The aim: *Assessing the usefulness of immunohistochemical analysis with p63 to confirm the diagnosis of minimal prostate cancer.*

Methods: *Fifty needles biopsy specimens, including Twenty with small foci of prostatic carcinoma and Thirty benign prostate (≤ 1mm or <5% of needle core tissue) were stained immunohistochemically with P63 antibodies.*

Results: *Of 20 cases of small foci of prostatic carcinoma, 14 (70%) expressed for basal cell staining p63 (nuclear stain). All benign*

glands were recognized easily by basal cell marker (p63) positivity. P value was statically significant.

Conclusions: *Immunohistochemical staining with the p63 could improve the diagnostic performance and helped in avoid carrying out new biopsies in small foci of prostatic carcinoma detection. Therefore we propose that this marker can be applied along with other prostate cancer diagnostic factors.*

Key words: Immunohistochmical Evaluation, P63 Marke, Prostatic Carcinoma, Benign Prostatic Hyperplasia, Small Foci, Sudanese Patients

INTRODUCTION:

Prostatic carcinoma is a major health problem worldwide, prostatic carcinoma is the second most common malignancy in men after lung cancer [1]. Diagnosis of prostate cancer glands can sometimes present a diagnostic challenge for pathologists, since; prostatic carcinoma can mimic benign prostate glands [2]. The diagnosis of prostatic cancer, especially in needle biopsy samples, can occasionally be challenging, either because they only show small foci of prostatic carcinoma, or because of the difficulty in distinguishing prostatic cancer from benign mimickers [3]. The difficulty in the diagnosis of prostatic carcinoma is mostly seen with minimal (limited<1mm) carcinoma in needle tissue [4]. Many major and minor histological features important for the diagnosis of minimal prostatic carcinoma should be assessed specifically at low- and high-power magnification. The first of the major criteria is an infiltrative growth pattern which frequently presents as the presence of small malignant glands between larger, more complex (and often paler), benign glands [5]. Immunohistochemistry plays a very important role in the diagnosis of minimal prostatic carcinoma and to exclude one of

its benign mimickers, but it should always be interpreted in the context of the H\&E appearances. In some cases of minimal prostate cancer morphologic features do not allow a diagnosis of carcinoma [6]. P63 gene is expressed in the regenerative epithelial compartment of several organs, and shares extensive homology with p53 [7].

Prostate requires p63 expression for its development and it is expressed like in breast, in myoepithelial cells surrounding normal acinar glands, therefore p63 is routinely used to evaluate the presence of normal basal cells thus distinguishing between benign and malignant glands [8, 9]. In adenocarcinoma, p63 tends to be under expressed and in prostatic carcinoma specifically, negative immunohistochemical staining of p63 is clinically useful tool for identifying benign mimickers [10, 11]. Other studies have identified p63 as important in signatures of advanced disease. We aimed in our study to correlate between immunohistochemical expression of p63 in small focal prostatic carcinoma and benign prostatic hyperplasia BPH in true cut needle biopsies.

MATERIALS AND METHODS:

Sample:

Patients with prostatic carcinoma with age ranged from 40 to 90 years (mean = 61), and Patient with benign prostate hyperplasia (BPH) with age ranged from 60 to 85 years (mean = 72.5± 3.1) obtained from the department of histopathology in IBNSENA hospital and RADIO AND ISOTOPE CENTER OF KHARTOUM (RICK) during the period from August 2015 to January 2016.

Slides preparation:

Total of 20 sections of small foci were obtained from paraffin embedded tissue (previously diagnosed as prostatic carcinoma

by H&E) and was confirmed by two pathologists, and 30 sections of benign prostate hyperplasia BPH (≤ 1mm of needle core tissue). Using a rotary microtome and taken in thermal coated slide and dried in hot plate oven at 80ºC for one hour

Immunohistochemical Analysis:

Staining was carried out using streptoavidin-biotin immunoperoxidase technique (thermo fisher). Three to five micrometer thick sections, cut from formalin fixed paraffin embedded blocks, were deparaffinized in Xylene and rehydrated in graded alcohol. The mounted sections were immersed in target retrieval solution, tris buffer EDTA (PH 9.0), then boiled in this solution in PT link for 20 min and then washed in phosphate buffer saline (pH 7.2).Then the slides were then incubated 20 minute using a polyclonal anti-p63 antibody ready to use thermofisher), After a buffer rinse, bound antibodies were detected with the thermo Envision System. Slides were counterstained with hematoxylin, and rinsed again. The slides were allowed to air dry and were cover slipped with permanent mounting media. Negative controls, in which the primary antibodies were replaced by PBS, were carried out for each primary antibody for p63; prostatic carcinoma was used as positive internal control [12].

Result interpretation:

- Results obtained from two sections were detected by researcher and confirmed by experienced histopathologist.
- Negative and positive controls were used for evaluation of the test sections.
- Ethical clearance for this study is provided by ethical committee of AL-Neelain University -faculty of medical laboratory science.

Statistical analysis:

The results of the study were statistically analyzed using SPSS version 18 statistical program. Data were expressed as mean± SD for quantitative variables, numbers and percentage. For categorical variables, student test was used for statistical analysis of Gleason's grading Spearman's statistical test was used $P< 0.05$ was considered the significant limit.

RESULTS:

Staining results with p63

A total of 50 prostate needle biopsy specimens, prostatic carcinoma in all sample were 20 (40%), while the benign prostatic hyperplasia specimens were 30(60%) shown in Table (1).

Out of 20 cases of small biopsy of prostatic carcinoma 14 (70%) expressed p63, and 6 (30%) did not expressed p63, while in 30 cases of small biopsy of benign prostatic hyperplasia specimens had 27(90%) expressed p63 and 3(10%) Table (2) .The expression of p63 in prostatic carcinoma is less than benign prostatic hyperplasia BPH which is statically significance P value: 0.001

Table (1) showing the frequency of prostate carcinoma and begin prostatic hyperplasia BPH among study population

Sample	Frequency	Percent
Prostatic carcinoma	20	40.0%
Benign Prostatic Hyperplasia	30	60.0%
Total	50	100.0%

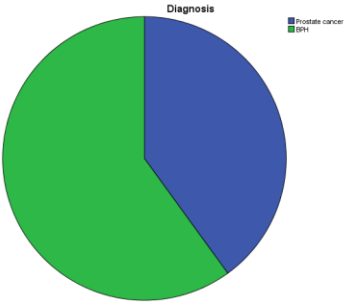

Table (2):-showing the frequency of expression of p63 among study population.

Diagnosis			Result		Total
			Positive	Negative	
	Prostate cancer	Count	14	6	20
		% within Diagnosis	70.0%	30.0%	100.0%
		% within Result	34.1%	66.7%	40.0%
	BPH	Count	27	3	30
		% within Diagnosis	90.0%	10.0%	100.0%
		% within Result	65.9%	33.3%	60.0%
Total		Count	41	9	50
		% of Total	82.0%	18.0%	100.0%

DISCUSSION:

Prostatic carcinoma is one of the most important cancers in men. With a worldwide incidence of 25.3 per 100,000 it is the second most common cancer in men [13].

In this study patient's age ranged from 47 to 96 years mean age 61.5, the result showed there was an increase susceptibility of prostate cancer PCa with increasing age. This finding was supported with (Zhang, Qian et al. 2013) who showed that positively associated of prostate size with increasing age [14]

In this study we found that expression of p63 in benign prostate hyperplasia BPH 27 (90%) of 30 cases. This finding was compatible with (Rashed, H. E., A. A. Hegazy, et al. 2015) who found that all benign prostate glands were recognized

easily by basal cell marker (p63) positivity [15], and supported with (Memarzadeh, S., L. Xin, et al. 2007) who showed that p63 staining is at least as sensitive and specific for the identification of basal cells in diagnostic prostate specimens [16].

The expression of p63 in prostatic carcinoma is less than BPH which is statically significance P value: 0.0001, this finding agreed with (Dhillon, P. K., M. Barry, et al. 2009) which is a rare expression pattern for a protein that is normally absent in prostatic carcinoma and that usually exhibits strong nuclear staining in basal cells of benign prostate[17].

CONCLUSIONS:

Immunohistochemical staining with the p63 could improve the diagnostic performance and helped in avoid carrying out new biopsies in small foci of prostatic carcinoma detection. Therefore we propose that this marker can be applied along with other prostate cancer as diagnostic factors.

REFERENCES:

1. Ferlay, J., et al., *IARC CancerBase No. 5. version 2.0. Lyon: IARCPress; 2004.* 2002, GLOBOCAN.
2. Gaudin, P. and V. Reuter, *Benign mimics of prostatic adenocarcinoma on needle biopsy*. Anatomic pathology (Chicago, Ill.: annual), 1996. **2**: p. 111-134.
3. Hameed, O. and P.A. Humphrey, *Immunohistochemistry in the diagnosis of minimal prostate cancer.* Current Diagnostic Pathology, 2006. **12**(4): p. 279-291.
4. Thorson, P. and P.A. Humphrey, *Minimal adenocarcinoma in prostate needle biopsy tissue.* American journal of clinical pathology, 2000. **114**(6): p. 896-909.

5. Epstein, J.I., *Diagnostic criteria of limited adenocarcinoma of the prostate on needle biopsy.* Human pathology, 1995. **26**(2): p. 223-229.
6. Rashed, H.E. and I. Kateb, *Evaluation of minimal prostate cancer in needle biopsy specimens using AMACR (P504S), P63 and KI67.* MARSLAND PRESS, 2012. **9**: p. 12-21.
7. Yang, A., et al., *p63, a p53 homolog at 3q27–29, encodes multiple products with transactivating, death-inducing, and dominant-negative activities.* Molecular cell, 1998. **2**(3): p. 305-316.
8. Reis-Filho, J.S., et al., *Distribution of p63, cytokeratins 5/6 and cytokeratin 14 in 51 normal and 400 neoplastic human tissue samples using TARP-4 multi-tumor tissue microarray.* Virchows Archiv, 2003. **443**(2): p. 122-132.
9. Hameed, O., J. Sublett, and P.A. Humphrey, *Immunohistochemical stains for p63 and α-methylacyl-CoA racemase, versus a cocktail comprising both, in the diagnosis of prostatic carcinoma: a comparison of the immunohistochemical staining of 430 foci in radical prostatectomy and needle biopsy tissues.* The American journal of surgical pathology, 2005. **29**(5): p. 579-587.
10. Di Como, C.J., et al., *p63 expression profiles in human normal and tumor tissues.* Clinical Cancer Research, 2002. **8**(2): p. 494-501.
11. Signoretti, S., et al., *p63 is a prostate basal cell marker and is required for prostate development.* The American journal of pathology, 2000. **157**(6): p. 1769-1775.
12. Bancroft, J.D. and M. Gamble, *Theory and practice of histological techniques*. 2008: Elsevier Health Sciences.
13. Patel, H., et al., *Does Oral Lycopene Reduce Benign Prostate Enlargement/Hyperplasia (BPE/BPH).* Oncol Cancer Case Rep, 2016. **1**(108): p. 2.
14. Zhang, S.-J., et al., *Relationship between age and prostate size.* Asian J Androl, 2013. **15**(1): p. 116-20.

15. Rashed, H.E., A.A. Hegazy, and R.A. Ahmed, *Minimal Adenocarcinoma in Prostate Needle Biopsy Tissue: Immunohistochemical Study*. International Journal of Current Research and Review, 2015. **7**(6): p. 7.
16. Memarzadeh, S., et al., *Enhanced paracrine FGF10 expression promotes formation of multifocal prostate adenocarcinoma and an increase in epithelial androgen receptor*. Cancer cell, 2007. **12**(6): p. 572-585.
17. Dhillon, P.K., et al., *Aberrant cytoplasmic expression of p63 and prostate cancer mortality*. Cancer Epidemiology Biomarkers & Prevention, 2009. **18**(2): p. 595-600.