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Diagnostic utility of p53 & ck20 immunohistochemical marker in urothelial malignancy – A meta-analysis.

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Abstract:
Urothelial carcinoma is a one of the major healthproblems throughout the world. It is a recurrent neoplasm with a significant number of cases in which neoplasm progress to invasive aggressive carcinoma. There is an overlap in the extent of the tumor and the accurate microscopic diagnosis of tumor is not always easy. The aim of this study is to evaluate p53 &ck20 immunohistochemical markers expression in non-neoplastic & neoplastic lesions of urinary bladder & its Correlation with morphological findings. The immunohistochemicalexpression of p53 &ck20 should be assessed in all the cases of urothelial carcinoma as there markers allow the identification of tumor with higher rate & cell growth. They also permit develop of prognostic factors as their expression increase with higher grade & these patient can be benefited with the appropriate targeted treatment leading to increase survival rate.

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I. Introduction

Urothelial carcinoma is the seventh most common cancer on the planet, with around 3,36,000 new cases detected every year. Many components have been known as risk elements of this condition. The most widely recognized risk factors is smoking with the frequency in smokers being 2 to 4 times higher than in the general population and decrease of occurrence up to 1.9 times after quitting smoking[1-7]. The component of tobacco in the pathogenesis of bladder carcinoma isn't known, but different cancer-causing factors have been recognized in cigarette including acrolein, 4-amino benzyl, arylamine& oxygen free radicles[8-12].

Other risk factors incorporate are fatty food varieties, arsenic containing water alongside pain killers, urinary tract diseases, parasites (schistosomiasis), bladder stones, pelvic radiation and chemotherapy medications like cyclophosphamide[14]. The most well-known symptom is hematuria. The frequency of urothelial carcinoma in patient with gross hematuria & in a patient with microscpic hematuria are 20% and 10% individually. IHC markers p53 &ck20 are arising useful markers as pointers of neoplastic change and its correlation with histological findings are very useful in confirming the diagnosis[15].

P53 is a nuclear transcription factor with a pro-apoptotic function. The p53 protein is a tumor suppressor whose mutations are common features in various human tumors. Mutation in p53 and an increased expression of the mutant protein is a predictor of poor prognosis of urothelial tumors.

Cytokeratin 20 (ck20) belongs to the epithelial subgroup of cytoskeleton associated intermediate filaments. It is mostly expressed in superficial & in some intermediate cells of the normal urothelium. Aberrant CK20 expression has been documented in urothelial carcinoma and has proved useful as an diagnostic aid for urinary bladder tumor.

II. Methodology

We conducted a thorough literature search inthe pubmed and Google scholar database on the internet search engine using following keywords: p53, ck20, urothelial tumors. Case reports & case series were not considered cross reference in the chosen article were also checked for additional studies. Publication with available histopathological & IHC correlation were considered for meta-analysis.

In published studies, most Commonly routine histopathological processing was done followed by staining with H&E stain. The studies were observed under Light microscope & diagnosed according to 2004 WHO classification of tumors of urinary system. IHC markers (p53 & ck20) was done in formaline fixed paraffin blocks of each tumors and were mountedonpolylysine coated slides.

Nuclear staining for p53 and cytoplasmic staining for ck20 were interpreted as positive . According to

our assessment the studies used for this review contained a sufficient amount of raw & processeddata.

Table No. 01: Scoring of PS3:

Score	Positive cells and Intensity
0	No staining
1+	< 15 % cells positive , Weak positive
2+	15-50 % cells positive , Moderately postive
3+	>50 % cells positive , Strong positive

Table No. 02: Scoring of CK20:

Score	Positive cells and Intensity
0	No staining
1+	Patchy positivity
2+	<50 % cells positive , Moderately positive
3+	>50 % cells positive , Strong positive

III. Discussion

Urothelial carcinoma is a major health problem throughout the world which is associated with significant morbidity & mortality, Urothelial carcinoma in situ (CIS) is considered to be an important precursor lesion for the invasive carcinoma. Untreated patients have high risk for progression of disease to invasive carcinoma & death. Diagnosis of urinary bladder lesion is difficult so that multiple technique is used for its diagnosis. It is necessary to distinguish between reactive & neoplastic changes. To diagnose the neoplastic changes in the urothelial lesions p53 & ck20 immunohistochemical markers are new emerging marker which havesignificant results. Urothelial carcinoma is recurrent neoplasm with having higher chances to progress into aggressive invasive carcinoma. In our study, we studied use of ck20 and p53 IHC markers expression in bladder carcinoma specimen & correlated with prior as subsequent cancer diagnoses.

MojganAsgari et al observed p53 expression in 12 cases out of 20 cases where ck20 expression seen in 15 cases out of 20 cases. They conclude that both ck20 & p53 markers are useful todiagnose neoplastic changes in urothelial lesions. However, they should be used in a panel &its correlation with morphological features is necessary[7].

ShaziaMumtaz, Atif Ali et al showed p53 Expression was observed in 87 cases out of 95 cases where as ck20 Expression seen in 83 cases out of 95 cases. They conclude that ck20 and p53 expression found in both low & high grade carcinoma &having different expression, so that combined use of markers are more beneficial than single marker[12].

CalmeMalfare, Mireiacastillo et al observed that p53 expression was seen in 40 cases out of 50 cases & ck20 expression seen in 36 cases out of 50 cases. They conclude that IHC markers are important for identify neoplastic changes in urothelial lesion from reactive atypia.

Sayed Abdul Raheem et al observed PS3 expression in 134 cases out of 162 cases. & ck20 Expression observed in 136 cases out of 162 cases. They Conclude that both ck20& p53 are significant in invasive carcinoma butinbetween both CK20 have higher rate of positivity in invasive carcinoma.

Javier A. , Aries Stell et al showed p53 Expression was observed in 57 cases out of 69 cases where as ck20 expression seen in 31 cases out of 69 Cases. JK Mckanney, S.Desai et al showed expression of PS3 in 12 out of 20 cases & ck20 expression in 17out of 21 cases. They conclude that ck20 is the most consistent marker associated with neoplastic lesion and have higher rate of positivity.

Table No. 03:

S. No.		Total No. of Cases	P53 Expression	CK20 Expression
1	MojganAsgari et al	20	12/20	15/20
2	ShaziaMumtaz, Atif Ali et al	95	87/95	83/95
3	CalmeMalfare, Mireiacastillo et al	50	40/50	36/50
4	Sayed Abdul Raheem et al	162	134/162	136/162
5	JK Mckanney, S.Desai et al	21	12/21	17/21
6	Javier A. , Aries Stell et al	69	57/69	31/69

IV. Conclusion:

Ck20 and p53 are among the most commonly used IHC markers for discrimination of urothelial neoplastic lesions from non- neoplastic lesions. However most studies on the use of these antibodies are conducted on specimens with established histologically diagnosed. Urothelial carcinoma have high rate of recurrence &have high chance to progress into the aggressive invasive carcinoma. Accurate diagnosis is

important for better prognosis & outcome. According to our report, we can conclude that our IHC panel composed of p53 and ck20 studying the neoplastic changes in bladder is adequate & useful for confirm the diagnosis. Both markers have different expression according to tumor progression & grade which helps in better treatment & prognosis. However, combined use of ck20 & p53 are more beneficial than single marker expression.

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