Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 02, 2022

Assessment of Immunohistochemical Expression of KI67, P53 in Urinary Bladder Carcinoma

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Abstract

Background: To assess immunohistochemical expression of Ki67, p53 in urinary bladder carcinoma.**Material and Methods:**A sum total of eighty- eight cases of urinary bladder carcinomas of both genders was included. Tissue samples in 10% buffered formalin were received as TURBT chips or bladder biopsy in histopathology section and processed. 3–5 µ thick H and E stained sections. Immuno histochemical staining of p53 and Ki-67 was performed using primary antibodies DO7 and SP6 respectively.**Results:**Age group (years) 21-40 comprised of 12 males and 0 females, 41-60 had 28 males and 6 females and >60 had 25 males and 17 females. Tumor histology was SCC seen in 2 males and 0 females, urethral cell carcinoma in 62 males and 23 females and adenocarcinoma in 1 male. Pathologic grade was low seen in 30 males and 5 females and high in 35 males and 18 females. Stage was pTa seen in 23 males, pT1 in 35 males and 10 females and pT2 in 7 males and 13 females respectively.**Conclusion:**p53 and Ki 67 immunomarkers in urinary bladder carcinomas may provide additional prognostic information along with histological grading and staging.

Keywords:p53, Ki 67, immunomarkers.

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Introduction

Urothelial carcinoma comprises approximately 90% of all primary bladder tumors with gross or microscopic painless hematuria as common presentation. The gold standard for diagnosing bladder carcinoma is cystoscopy and biopsy of suspicious area.[1]The management and posttreatment monitoring of superficial bladder cancers are largely dependent on stage and grade because approximately 70% of superficial urothelial carcinomas may recur and 10%–20% progress to a higher stage, grade, or metastatic disease. Some previous studies have shown p53 mutations and cell proliferation markers to play an important role in urothelial carcinoma pathogenesis and also as prognostic factors.[2]

P53 and Ki 67 expressions have frequently used urothelial malignancy enzyme labels. P53 is a key tumor suppressor gene involved in genomic balance, genotoxic stress response, and cell cycle apoptosis stimulation. Some studies showed correlations in urothelial bladder cancer between p53 and tumor stage and grade.[3,4]

Urothelial carcinomas (UC) are divided into three groups: pTa, pT1, and ≥ pT2 disease, regarding the local extension. pTa bladder cancers have a variable recurrence rate and progression.[5] About 70% of superficial transitional cell bladder cancers recur and 10-20% progress to a higher stage, grade or metastatic disease.[6] In comparison with superficial transitional cell carcinoma, the prognosis of muscle invasive tumors or metastatic disease is poor.[7] Therefore, immunohistochemical expression of p53 and proliferation marker Ki-67 may be helpful in proper staging and grading of bladder carcinomas. Considering this, we attempted present study to assess immunohistochemical expression of Ki67, p53 in urinary bladder carcinoma.

Material & Methods

This prospective, observational study comprised of sum total of eighty- eight cases of urinary bladder carcinomas of both genders. Ethical approval was obtained from institutional review and clearance committee.

History and clinic-radiological findings were recorded. Tissue samples in 10% buffered formalin were received as TURBT chips or bladder biopsy in histopathology section and processed. 3–5 µ thick H and E stained sections. Immunohistochemical staining of p53 and Ki-67 was performed using primary antibodies DO7 and SP6 respectively. Results of the study was compiled and assessed statistically using Mann Whitney U test with the level of significance set below 0.05.

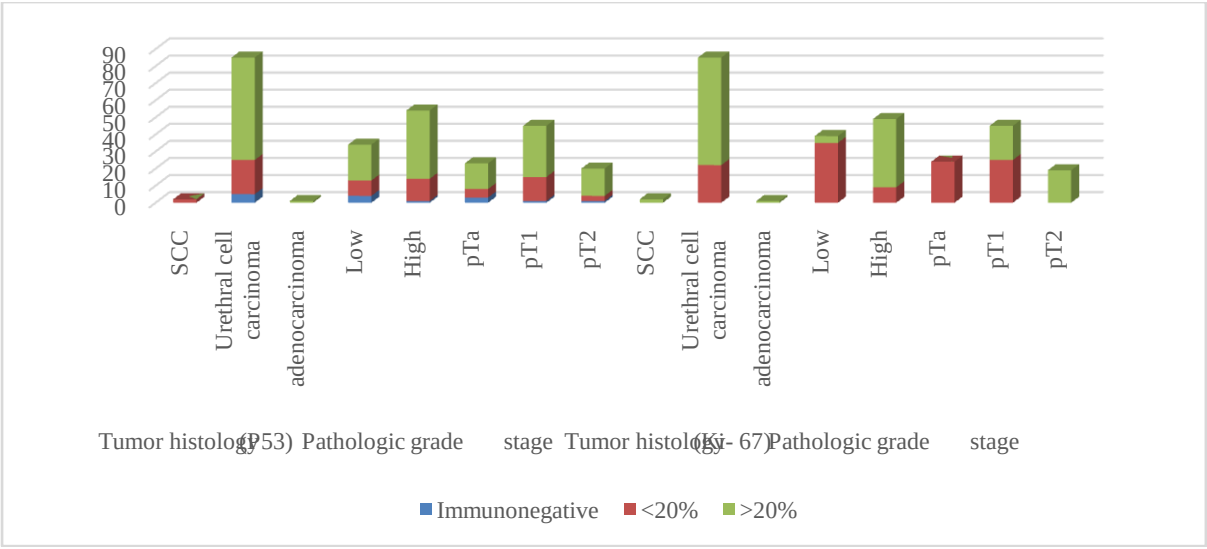
Results

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 02, 2022

Table 1: Distribution pattern of p53 and ki-67 immunohistochemical staining

Parameters	variables	Immunonegative	<20%	>20%	p value
Tumor histology (P53)	SCC	0	2	0	<0.05
	Urethral cell carcinoma	5	20	60	
	adenocarcinoma	0	0	1	
Pathologic grade	Low	4	9	21	<0.05
	High	1	13	40	
stage	pTa	3	5	15	<0.05
	pT1	1	14	30	
	pT2	1	3	16	
Tumor histology (Ki- 67)	SCC	0	0	2	<0.05
	Urethral cell carcinoma	0	22	63	
	adenocarcinoma	0	0	1	
Pathologic grade	Low	0	35	4	<0.05
	High	0	9	40	
stage	pTa	0	24	0	<0.05
	pT1	0	25	20	
	pT2	0	0	19	

In p53, tumor histology, Immunonegative, <20% and >20% under SCC was seen in 0, 2 and 0, under urethral cell carcinoma was seen in 5, 20 and 60 and under adenocarcinoma was seen in 0, 0 and 1. Pathologic grade was low in 4, 9 and 22 and high in 1, 8 and 42. Stage in pTa was 5, 5 and 14, under pT1 was seen in 1, 14 and 30 and under pT2 was seen in 1, 2 and 16. Tumor histology (Ki- 67) in SCC was seen in 0, 0 and 2, in urethral cell carcinoma was seen in 0, 45 and 40, in urethral cell carcinoma was seen in 0, 45 and 40 and under adenocarcinoma was seen in 0, 0 and 1. Pathologic grade was low in 0, 35 and 4 and high in 0, 9 and 40. Stage in pTa was 0, 24 and 0, under pT1 was seen in 0, 25 and 20 and under pT2 was seen in 0, 0 and 19. A significant difference was observed (P< 0.05) (Table I, graph I).



Graph 1: Distribution pattern of p53 and ki-67 immunohistochemical staining

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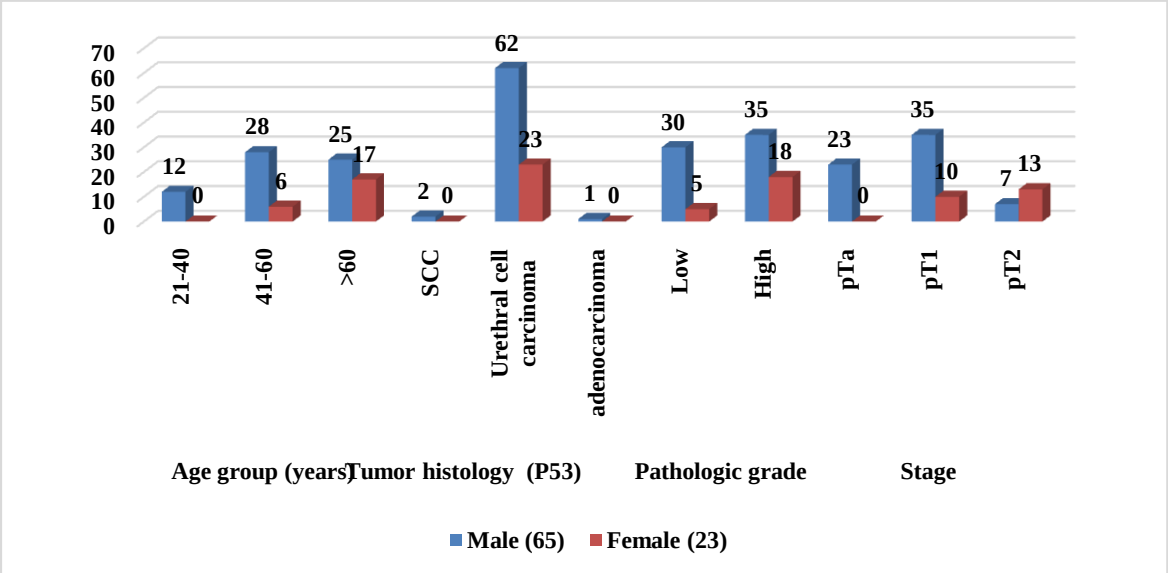
Table 2: Pattern of bladder carcinoma based on gender

Parameters	Variables	Male (65)	Female (23)	P value
Age group (years)	21-40	12	0	<0.05
	41-60	28	6	
	>60	25	17	
Tumor histology (P53)	SCC	2	0	<0.05
	Urethral cell carcinoma	62	23	
	adenocarcinoma	1	0	
Pathologic grade	Low	30	5	<0.05
	High	35	18	
Stage	pTa	23	0	<0.05
	pT1	35	10	
	pT2	7	13	

Age group (years) 21-40 comprised of 12 males and 0 females, 41-60 had 28 males and 6 females and >60 had 25 males and 17 females. Tumor histology was SCC seen in 2 males and 0 females, urethral cell carcinoma in 62 males and 23 females and adenocarcinoma in 1 male. Pathologic grade was low seen in 30 males and 5 females and high in 35 males and 18 females. Stage was pTa seen in 23 males, pT1 in 35 males and 10 females and pT2 in 7 males and 13 females respectively. A significant difference was observed (P< 0.05) (Table II, graph II).



Graph 2: Pattern of bladder carcinoma based on gender

41 subjects had Varices of various grades with a mean velocity of 3.16 ± .33, whereas it was 3.30 in subjects without varices.[Table3]

Table 3: Correlation of p53 and Ki-67 immunoexpression

Stage	Grade	Number	Mean		P value
			p-53	Ki- 67	
pTa	Low	23	26.3	6.51	<0.05
pT1	Low+high	45	31.7	15.4	<0.05
pT2	High	20	35.9	32.8	<0.05

The mean value of p- 53 expression in low grade was 26.3 and for pT1 was 31.7 and for pT2 was 35.9. The mean expression of Ki- 67 for pTa was 6.51, for pT1 was 15.4 and for pT2 was 32.8. A significant correlation was found between tumour markers and stage and grade (P< 0.05).

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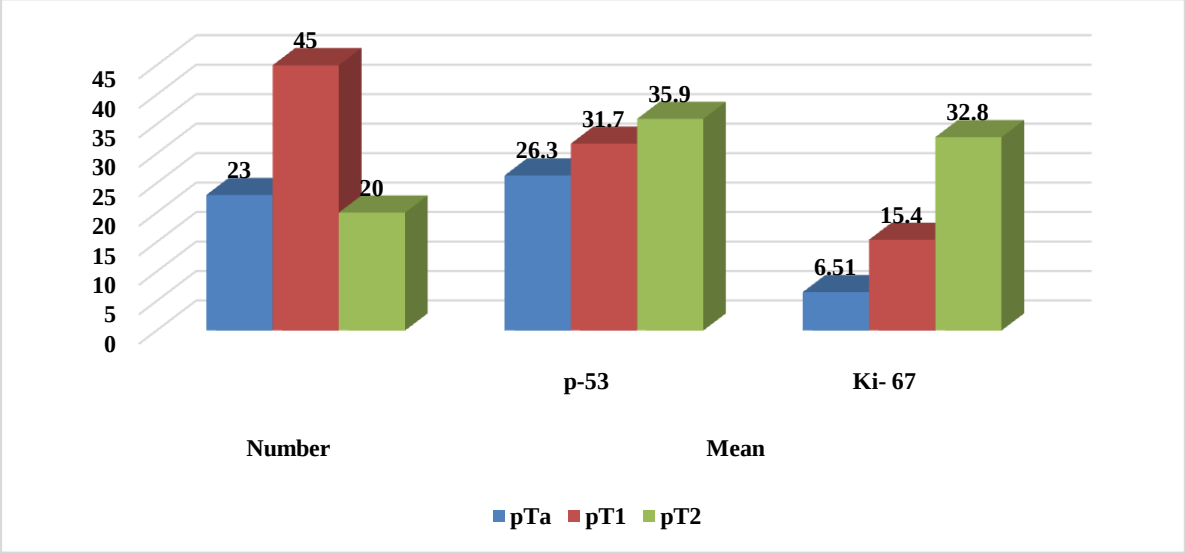

Graph3: Correlation of p53 and Ki-67 immunoexpression

Discussion

p53 is the most frequently mutated tumor suppressor gene identified in human cancers.[8] Tumor suppression functions of p53 stem, in part, from its capabilities to induce cell cycle arrest in late G1 and/or apoptosis in response to genotoxic stress and hypoxia, and mutational inactivation of p53 is associated with an increased risk of tumorigenesis.[9] Alterations in the p53 pathway contribute to bladder tumor progression and are likely to provide relevant prognostic information to assist in the management of bladder cancer patients.[10,11] The evidence shows that over-expression of p53 is a promising prognostic factor and several studies have addressed the association of p53 mutation with high grade, high stage bladder cancer, and an unfavorable prognosis. p53, Ki67, and p73 are members of the p53 gene family involved in development, differentiation, and response to cellular stress.[12] We assessed immunohistochemical expression of Ki67, p53 in urinary bladder carcinoma.

Our results showed that in p53, tumor histology, immunonegative, <20% and >20% under SCC was seen in 0, 2 and 0, under urethral cell carcinoma was seen in 5, 20 and 60 and under adenocarcinoma was seen in 0, 0 and 1. Pathologic grade was low in 4, 9 and 22 and high in 1, 8 and 42. Stage in pTa was 5, 5 and 14, under pT1 was seen in 1, 14 and 30 and under pT2 was seen in 1, 2 and 16. Tumor histology (Ki- 67) in SCC was seen in 0, 0 and 2, in urethral cell carcinoma was seen in 0, 45 and 40, in urethral cell carcinoma was seen in 0, 45 and 40 and under adenocarcinoma was seen in 0, 0 and 1. Pathologic grade was low in 0, 35 and 4 and high in 0, 9 and 40. Stage in pTa was 0, 24 and 0, under pT1 was seen in 0, 25 and 20 and under pT2 was seen in 0, 0 and 19. In the study by KoyuncuerA[13], totally 62 urinary bladder transurethral resection materials diagnosed with urothelial carcinoma were included. When pTa was evaluated in terms of Ki67 immunoreactivity, no statistically significant difference was observed between LGPUC and HGPUC, non-invasive papillary UC, regarding staining percentages, whereas statistically significant relation was observed for pT1 and pT2 regarding Ki67 staining percentages. For pTa, no statistically significant relation was observed between LGPUC and HGPUC, non-invasive papillary UC, in terms of p53 staining percentages. However, highly significant relationship was observed for pT1 and pT2 in terms of p53 staining percentages. No significant relationship was observed between the staining percentages of p53 and Ki67.

Our results showed that age group (years) 21-40 comprised of 12 males and 0 females, 41-60 had 28 males and 6 females and >60 had 25 males and 17 females. Tumor histology was SCC seen in 2 males and 0 females, urethral cell carcinoma in 62 males and 23 females and adenocarcinoma in 1 male. Pathologic grade was low seen in 30 males and 5 females and high in 35 males and 18 females. Stage was pTa seen in 23 males, pT1 in 35 males and 10 females and pT2 in 7 males and 13 females respectively. Sahar Ali et al[14] in their study sixty-two cases of bladder neoplasm were investigated. Grading and staging was done. An immunohistochemical assay for p53 and Ki 67 was performed in altogether cases, with relation to clinicopathological parameter. There was a significant association of p53 and Ki 67 overexpression in high grade with the epithelial type (P=0.0001) & (P=.0.01) respectively. While there was a statistically significant association of high expression of P53 in PT1 compared to PTa and PT2. There was a significant correlation between Ki 67 in staging pT1

The mean value of p- 53 expression in low grade was 26.3 and for pT1 was 31.7 and for pT2 was 35.9. The mean expression of Ki- 67 for pTa was 6.51, for pT1 was 15.4 and for pT2 was 32.8. A significant correlation was found between tumour markers and stage and grade. Thakur et al[15] evaluated 110 cases of bladder tumor. Grading and staging were done according to the WHO-2004 and American Joint Committee on Cancer-TNM staging recommendations. Immunohistochemical staining for p53 and Ki-67 was performed in all the cases,

ISSN: 0975-3583,0976-2833 VOL13, ISSUE 02, 2022

categorized as high and low expression taking 20% positivity as cutoff value. There were 61 cases of high grade and 49 cases of low grade exhibiting urothelial carcinoma as the most common variant (97.3%). Muscle invasive carcinomas (pT2) noted in 29 cases whereas 23 and 58 cases revealed stage pTa and pT1, respectively. Evaluation of p53 and Ki-67 immunoexpression showed a significant association with histological grade and stage individually and also in combination.

Conclusion

p53 and Ki 67 immunomarkers in urinary bladder carcinomas may provide additional prognostic information along with histological grading and staging.

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