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ORIGINAL RESEARCH ARTICLE

Expression of OCT3/4 in Urinary Bladder Tumors and Its Correlation with Clinicopathological and Prognostic Parameters

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ABSTRACT

Introduction: Urinary bladder carcinoma is a common malignancy with significant recurrence and progression risk. Cancer stem cell markers such as OCT3/4, a pluripotency transcription factor, are implicated in tumor aggressiveness and therapeutic resistance. Assessing OCT3/4 expression may improve prognostic accuracy and aid in risk stratification. The aim of the study is to evaluate OCT3/4 expression in urinary bladder tumors and correlate it with histological type, grade, and prognostic parameters, including lymphovascular invasion and perineural invasion.

Material and Methods: A cross-sectional study was conducted on 40 histologically confirmed urinary bladder tumors in the Department of Pathology, SRMS IMS, Bareilly. Immunohistochemistry for OCT3/4 was performed, and results were analyzed statistically for associations with clinicopathological parameters.

Results: The mean patient age was 61.7 ± 11.1 years, and males constituted 95%. Invasive urothelial carcinoma accounted for 85% of cases, with 65% being high grade and 50% showing muscle invasion. OCT3/4 expression was +1 in 57.5%, +2 in 30%, and +3 in 5% of specimens. No significant association was found with age, sex, or histological type (p >0.05). However, higher OCT3/4 expression correlated significantly with tumor grade (p <0.05), muscular invasion (p <0.05), and perineural invasion, indicating increased expression in aggressive tumors.

Conclusion: OCT3/4 expression is demographically neutral yet biologically informative, enriching risk stratification beyond morphology by associating with high-grade, muscularis propria invasion, and perineural invasion. The predominance of mild positivity with selective enrichment of moderate–strong staining in aggressive phenotypes supports OCT3/4 as a practical adjunct immunomarker for prognostic assessment in urothelial carcinoma.

Keywords: OCT3/4, Urothelial carcinoma, Bladder cancer, Immunohistochemistry, Prognostic biomarker, Tumor grade.

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INTRODUCTION

The urinary bladder is a hollow, muscular organ responsible for temporary storage and periodic expulsion of urine. It is lined by urothelium, a specialized transitional epithelium that maintains a protective barrier while allowing distension during micturition. Disruption of urothelial integrity through chronic irritation, infection, or chemical carcinogens contributes to neoplastic transformation, leading to bladder carcinoma, one of the most frequent malignancies of the urinary tract worldwide.[1] Bladder cancer represents the tenth most common cancer globally, with approximately 573,000 new cases and 213,000 deaths reported in 2020.[1] The disease shows a marked male predominance and is strongly associated with tobacco exposure and industrial carcinogens. Histologically, urothelial carcinoma accounts for nearly 90% of cases and displays significant clinical and molecular heterogeneity.[2] Despite advances in surgical and adjuvant therapy, recurrence and progression rates remain high, particularly in muscle-invasive and high-grade variants, underscoring the need for reliable prognostic biomarkers.[2] Octamer-binding transcription factor 3/4 (OCT3/4), encoded by the POU5F1 gene, is a pivotal regulator of pluripotency in embryonic stem cells and germ cells.[3] Aberrant re-expression of OCT3/4 in somatic tissues confers self-renewal and dedifferentiation potential, favoring oncogenic transformation.[4] Its overexpression has been documented in urothelial carcinomas, suggesting a role in tumor initiation, epithelial-mesenchymal transition, and metastatic behavior.[5,6] Moreover, chemotherapeutic stress may upregulate OCT3/4, contributing to treatment resistance and tumor relapse.[7] The 5th edition of the WHO Classification of Urinary and Male Genital Tumors provides refined morphological and molecular categorization essential for diagnostic precision.[8] Recent Indian and regional studies highlight the prognostic implications of immunohistochemical expression levels in non-muscle-invasive bladder cancer[9] and suggest that OCT3/4 may serve as a predictive biomarker for disease aggressiveness and recurrence.[10]

MATERIAL AND METHODS

Study design: Cross-sectional study

Study setting: The study was conducted in the Department of Pathology, SRMS Institute of Medical Sciences, Bareilly.

Sample Size: 40

All histopathological confirmed cases of transurethral resection specimens of bladder tumors and surgically resected specimens of urinary bladder tumors submitted to the department of pathology were included in the study. Inadequate tissue and poorly fixed/autolyzed tissue were excluded.

Data Analysis

Data on urinary bladder tumors, including demographics, histologic type, grade, LVI, PNI, and OCT3/4 expression, were compiled in Excel spreadsheets and analyzed using appropriate statistical tests.

RESULT

Table 1 shows the distribution of the study population according to age. In our study, the mean age of patients was 61.7 ± 11.1 years, with a range of 35 to 82 years. The maximum number of patients were in the age group of 61 to 70 years (52.5%), followed by 22.5% patients in the age group of 51 to 60 years. 15% of patients were in the age group of 50 to 60 years. 7.5%of the patients were present in the age groups of 31 to 40 years, 41 to 50 years and 71 to 80 years each. 1 patient (2.5%) was >80 years of age.

Table 2 depicts the distribution of the study population according to gender. In our study, out of 40 cases, 95% of the patients were male and 5% were female. This highlights significant male predominance in the study.

Table 3 shows the distribution of the study population according to histological type. In our study, the most common histological type among the patients was invasive urothelial carcinoma (IUC), 34 cases (85%), followed by 4 cases (10%) of non-invasive urothelial carcinoma (NIUC) and 2 cases (5%) of urothelial carcinoma with squamous differentiation (UCSD). This highlights the predominance of invasive urothelial carcinoma in the study sample.

Table 4 shows the distribution of the study population according to the histological grading of tumors. In our study, out of 40 cases, 26 cases (65%) accounted for high grade tumor and 14 cases (35%) for low grade tumor. Table 5 Shows distribution of the study population according to the presence of muscular invasion. In our study, out of 40 cases, 20 (50%) cases show muscle invasion.

Table 6 shows the association of OCT3/4 scoring with demographic variables of the patients. In our study, maximum OCT3/4 expression was observed in age

Table1: Distribution of the study population according to age (n=40)

Age (years)	*Frequency (n)*	*Percentage (%)*
31–40	3	7.5
41–50	3	7.5
51–60	9	22.5
61–70	21	52.5
71–80	3	7.5
>80	1	2.5
Total	40	100
Mean age	61.7 ± 11.1	
Range	35–82	

Table 2: Distribution of the study population according to gender

Sex	*Frequency (n)*	*Percentage (%)*
Female	2	5
Male	38	95
Total	40	100

Table 3: Distribution of the study population according to histological type

Histologic type	*Frequency (n)*	*Percentage (%)*
Invasive urothelial carcinoma (IUC)	34	85
Non-invasive urothelial carcinoma (NIUC)	4	10
Urothelial carcinoma with squamous differentiation (UCSD)	2	5
Total	40	100

Table 4: Distribution of the study population according to histological grading of tumors

Tumor grade	*Frequency (n)*	*Percentage (%)*
High grade	26	65
Low grade	14	35
Total	40	100

Table 5: "Distribution of the study population according to presence of muscular invasion"

Muscular invasion	*Frequency (n)*	*Percentage (%)*
Present	20	50
Absent	20	50
Total	40	100

groups of 41 to 50 & 71 to 81 years in 2 cases. On statistical correlation, *p-value* 0.864 and 1.00 are obtained, which are greater than the common significance level (*p-value* >0.05). This indicates that there is no significant association between OCT3/4 and the age and sex of the patient.

Table 7 shows the association of OCT3/4 scoring with histological type. In our study out of 40 cases 36 (90%) cases includes Invasive urothelial carcinoma and invasive urothelial carcinoma with squamous differentiation and 4 (10%) were non-invasive urothelial carcinoma. 2 out of 36 cases (5.5%) of IUC express +3 positivity of OCT3/4, 12 (33%) out of 36 cases express +2 positivity, 20 (55%) cases show +1 positivity while 2 (5.5%) cases were negative. Among the 4 non-invasive carcinomas, none of the cases showed +2, +3 positivity, while 3 cases were +1 and 2 cases were negative for OCT3/4. Hence, stronger OCT3/4 expression +2, +3 is predominantly observed in invasive urothelial carcinoma while absent in non-invasive urothelial carcinoma. There was no statistically significant association between the histological type of tumor and OCT3/4 score (p >0.05).

Table 8 shows the association of OCT3/4 scoring with tumor grade. In our study, out of 26 high-grade tumors, 42.3% of cases had a +1 score, 46.2% had a +2 score and 7.7% of cases had a +3 score, suggesting that moderate to high OCT3/4 expression is predominant in high-grade tumors. 3.8% of cases had a score of 0. In total, 14 low-grade cases, 85.7% of cases had +1 score, 14.3% had a score of 0 and none of the low -grade tumors had +2 or +3 scores, indicating that strong OCT3/4 expression is absent in low-grade cases. Overall *p-value* <0.05 shows a statistically significant association between tumor grade and OCT3/4 scores.

Table 9 shows the association of OCT3/4 scoring with muscular invasion. In our study, out of 40 cases, 50% of cases show muscular invasion,[3] cases show +3 (strong)

Table 6: Association of OCT3/4 scoring with demographic variables of the patients (n=40)

Demographic variable	*OCT3/4 score n (%)*				*p-value*
	0	*+1*	*+2*	*+3*	
Age (years)					
31–40	1 (33.3)	1 (33.3)	1 (33.3)	0 (0)	0.864
41–50	0 (0)	2 (66.7)	1 (33.3)	0 (0)	
51–60	0 (0)	5 (55.6)	3 (33.3)	1 (11.1)	
61–70	2 (9.5)	13 (61.9)	5 (23.8)	1 (4.8)	
71–80	0 (0)	1 (33.3)	2 (66.7)	0 (0)	
>80	0 (0)	1 (100)	0 (0)	0 (0)	
Sex					
Female	1 (50)	0 (0)	1 (50)	0 (0)	1.00*
Male	2 (5.3)	23 (60.5)	11 (28.9)	2 (5.3)	

Table 7: Association of OCT3/4 scoring with histological type

Histologic Type	*OCT3/4 score n (%)*				*p-value**
	0	*+1*	*+2*	*+3*	
Invasive urothelial carcinoma (IUC)	2 (5.9)	20 (58.8)	11 (32.4)	1 (2.9)	1.00
Non-invasive urothelial carcinoma (NIUC)	1 (25)	3 (75)	0 (0)	0 (0)	
Urothelial carcinoma with squamous differentiation (UCSD)	0 (0)	0 (0)	1 (50)	1 (50)	

Table 8: Association of OCT3/4 scoring with tumor grade

Tumor grade	*OCT3/4 score n (%)*				*p-value**
	0	*1*	*2*	*3*	
High grade	1 (3.8)	11 (42.3)	12 (46.2)	2 (7.7)	0.0004
Low grade	2 (14.3)	12 (85.7)	0 (0)	0 (0)	

Table 9: "Association of OCT3/4 scoring with muscular invasion"

Muscular invasion	*OCT3/4 score n (%)*				*p-value*
	0	*+1*	*+2*	*+3*	
Present	0 (0)	8 (40)	10 (50)	2 (10)	0.003
Absent	3 (15)	15 (75)	2 (10)	0 (0)	

Table 10: Association of OCT3/4 scoring with perineural invasion

Perineural invasion	OCT3/4 score n (%)			
	0	1	2	3
Present	0 (0)	0 (0)	1 (50)	1 (50)
Absent	3 (7.9)	23 (60.5)	11 (29)	1 (2.6)

expression, 10 cases show +2 (moderate) expression and 8 cases show+1 (mild) expression. There is a statistically significant association between muscular invasion and OCT 3/4 score (p <0.05).

Table 10 represents the association of OCT3/4 scoring with perineural invasion. In our study, all cases with perineural invasion had +2 (moderate) to +3 (high) OCT3/4 expression. No cases with perineural invasion had +1or 0 (low) OCT3/4. This suggests a potential correlation between high OCT3/4 levels and perineural invasion.

DISCUSSION

In the present study, the mean age of patients was 61.7 ± 11.1 years (range 35–82 years), with most cases in the 61 to 70 year group (52.5%). These findings are comparable to those of Demirci and Ordu (2023),[9] who reported a mean age of 64.25 years in patients with non–muscle-invasive bladder cancer. Similarly, Siddiqui *et al*. (2019)[10] observed a comparable mean age distribution in their North Indian cohort. The slight variation in age range may be attributed to regional demographic differences. Male predominance was pronounced in our study (95%), aligning with Siddiqui *et al*. (2019)[10] and Ahmed *et al*. (2020),[11] both of whom also reported male predominance exceeding 85%, supporting the well-recognized higher incidence of bladder tumors among males. The histological pattern in this series revealed invasive urothelial carcinoma (IUC) as the most common subtype (85%), followed by non-invasive urothelial carcinoma (10%) and urothelial carcinoma with squamous differentiation (5%). Similar predominance of IUC was documented by Ahmed *et al*. (2020)[11] (77.9% urothelial type) and Siddiqui *et al*. (2019).[10] The predominance of invasive histology indicates late clinical presentation or delayed diagnosis. Regarding tumor grade, 65% were high-grade and 35% low-grade lesions, closely mirroring Demirci and Ordu (2023)[9], who observed higher OCT-4 expression and worse outcomes in high-grade cases. Muscle invasion was detected in 50% of our patients, similar to findings by Ahmed *et al*. (2020) [11], who reported a significant association of OCT-4 expression with muscle invasion (p < 0.001). The comparable proportion underscores the clinical aggressiveness of invasive urothelial carcinoma. No unique demographic trends were observed beyond these parameters, reaffirming the consistency of this study's cohort characteristics with regional and global literature. In the present study, OCT3/4 expression showed no significant association with age or sex (p = 0.864 and p = 1.00), indicating that demographic variables did not influence OCT3/4 expression. This finding aligns with Demirci and Ordu (2023)[9], who also observed no significant correlation between OCT4 expression and patient age or sex distribution, suggesting that molecular tumor behavior is largely independent of demographic factors. Similar results were noted by Siddiqui *et al*. (2019)[10], where the prognostic role of OCT-4 was unaffected by baseline demographics, emphasizing that its impact lies primarily in tumor biology rather than host factors.

The analysis of histological type revealed that stronger OCT3/4 expression (+2 and +3) was predominantly observed in invasive urothelial carcinoma (IUC) and urothelial carcinoma with squamous differentiation, while non-invasive tumors lacked strong positivity. Although the association was not statistically significant (p > 0.05), the trend of higher OCT3/4 expression in invasive lesions was consistent with Ahmed *et al*. (2020)[11], who reported OCT4 positivity in 77.9% of cases, significantly associated with muscle invasion (p < 0.001) and higher grade (p < 0.001). Demirci and Ordu (2023)[9] similarly demonstrated stronger OCT4 staining in higher-stage tumors (p < 0.001), reinforcing its role as an indicator of tumor aggressiveness. In the current series, OCT3/4 expression correlated significantly with histological grade (p < 0.05); 53.9% of high-grade tumors exhibited moderate to strong (+2/+3) staining, while none of the low-grade tumors showed such intensity. This parallels Siddiqui *et al*. (2019)[10], who found a significant association of OCT-4 with tumor grade (p = 0.038) and stage (p = 0.003). Comparable findings were also noted by Ahmed *et al*. (2020) [11], confirming the link between OCT4 and high-grade, invasive morphology. Regarding muscular invasion, half of our cases showed invasion, with a statistically significant association between invasion and higher OCT3/4 scores (p < 0.05). This finding corresponds with Ahmed *et al*. (2020) [11], who observed that OCT4 expression is strongly related to muscle invasion. Likewise, cases with perineural invasion in our study all exhibited +2 to +3 expression, supporting OCT3/4's correlation with aggressive histological features. These observations are biologically supported by Abugomaa *et al*. (2020)[12], who described OCT-4 as a cancer stem cell marker driving invasion, metastasis, and chemoresistance in bladder cancer. Overall, mild OCT3/4 positivity predominated (57.5%), representing early transformation activity, while higher expression correlated with invasiveness and poor differentiation, emphasizing its prognostic utility in urothelial carcinoma.

CONCLUSION

The present cross-sectional study evaluated OCT3/4 expression in urinary bladder tumors and its correlation with clinicopathological and prognostic parameters. The findings demonstrated that OCT3/4 expression was independent of age and sex, indicating that its regulation is primarily tumor-intrinsic rather than host-related. Invasive urothelial carcinoma constituted the predominant histological type and exhibited higher OCT3/4 scores, while non-invasive lesions showed only mild or absent staining, reflecting a direct relationship between OCT3/4 activation and tumor invasiveness. A statistically significant association between OCT3/4 expression and histological grade ($p < 0.05$) confirmed that strong expression parallels high-grade morphology, supporting its role in tumor progression. Similarly, muscle invasion and perineural invasion showed marked correlation with moderate to strong OCT3/4 positivity, emphasizing its potential as an indicator of aggressive biological behavior. The predominance of mild OCT3/4 expression in most cases suggests early neoplastic transformation, whereas intense staining identifies tumors with increased malignant potential. Collectively, these observations signify that OCT3/4 serves not merely as a diagnostic adjunct but as a prognostic biomarker capable of identifying cases prone to recurrence or progression. Integrating OCT3/4 immunohistochemistry into routine pathological assessment could enhance risk stratification and guide therapeutic decision-making in urothelial carcinoma of the urinary bladder.

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