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Original Article

The expression of epidermal growth factor receptor (EGFR) in urinary bladder carcinoma: An immunohistochemical study

Mankirat Kaur[1], Menka Khanna[1], Karamjit Singh Gill[1], Sukirat Kaur[2], Arshdeep Kaur[3], Satinder Kaur[1], Jaspreet Singh[1], Harwinder Kaur[1]

[1]*Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India*
[2]*Punjab Institute of Medical Sciences, Jalandhar, Punjab, India*
[3]*Department of Pathology, Adesh Medical College, Bathinda, India*

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ABSTRACT

Background: Urinary bladder carcinoma is one of the most prevalent malignancies of the genitourinary tract. The Epidermal Growth Factor Receptor (EGFR), a transmembrane tyrosine kinase receptor, plays a crucial role in cell proliferation, differentiation, and survival. Its expression has been implicated in the pathogenesis and progression of various cancers, including bladder carcinoma.

Materials and Methods: This cross-sectional study was conducted on 60 histopathologically confirmed cases of urinary bladder carcinomas diagnosed via transurethral resection of bladder tumor specimens. Immunohistochemistry for Epidermal Growth Factor Receptor was performed using a rabbit monoclonal antibody; membranous tumor cell staining was considered positive, and the proportion and intensity of positive cells were scored. The correlation between EGFR expression and tumor grade, stage, and other clinicopathological parameter were statistically analyzed.

Results: The peak incidence of urinary bladder carcinoma was observed in the 6th to 7th decade of life. The majority (77%) of the patients were males. Painless hematuria was the most common presenting symptom. EGFR positivity was observed in 93% of cases. Based on histological grading, 77% of cases were high-grade, and 23% were low-grade urinary bladder carcinoma cases. A statistically significant correlation was found between the EGFR score and tumor grade (p value < 0.001) and tumor stage (p value = 0.03).

Conclusion: EGFR expression was predominantly observed in high-grade and advanced-stage tumors, suggesting its association with aggressive disease and poor prognosis. Routine IHC assessment of EGFR in bladder carcinoma may provide valuable prognostic information and assist in patient risk stratification.

Correspondence:
Dr. Mankirat Kaur, MD
Department of Pathology
Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar, Punjab, India
ORCID ID: 0009-0000-1845-5116
Email- 123mankiratkaur@gmail.com

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INTRODUCTION

Urinary Bladder carcinoma (UBC) is one of the most prevalent malignancies of the genitourinary tract and represents a significant global health concern. Worldwide, it ranks as the tenth most frequently diagnosed cancer and the thirteenth leading cause of cancer-related mortality. Urothelial carcinoma is the most prevalent subtype, accounting for more than 90% of bladder cancer cases in industrialized nations.[1] UBC predominantly affects older adults, with major risk factors including tobacco smoking, exposure to chemicals, and chronic bladder inflammation.[2]

Urothelial carcinomas can develop in any portion of the urinary tract lined with urothelium. Notably, 90% – 95% of cases originate in the lower urinary tract (bladder and urethra), while 5% – 10% occur in the upper urinary tract (renal pelvis and ureter).[3, 4]

Common presenting symptoms of UCBs include gross or microscopic hematuria, increased urinary frequency, and unexplained pelvic pain. Advanced disease may present with urinary retention, lower back pain, anorexia, unintended weight loss, and bone pain. Early diagnosis and prompt treatment are essential in improving patient outcomes.[5]

The urinary bladder is chronically exposed to environmental carcinogens, primarily through tobacco smoke and occupational exposure to aromatic amines. These substances can cause DNA damage through adduct formation. Other risk factors include chronic cystitis, schistosomiasis, radiation therapy, chemotherapeutic agents (e.g., cyclophosphamide), anti-diabetic drugs (e.g., pioglitazone), and arsenic-contaminated drinking water.[6]

Early detection of bladder cancer is essential for effective treatment, as early-stage tumors are typically small and non-invasive. Several diagnostic methods are available to aid in early detection, including urinalysis, urine cytology, intravenous pyelogram, retrograde pyelogram, cystoscopy, and imaging modalities such as ultrasound, computed tomography (CT), and magnetic resonance imaging (MRI). The accuracy of diagnosis and prognosis can be further improved through histopathological examination, molecular marker analysis, cytogenetics, and immunohistochemistry (IHC).[7, 8]

Various IHC markers like Uroplakin III, Uroplakin II, GATA3, CK20, CK7, CK5/6, S100P, Human Epidermal Growth Factor Receptor (HER2/neu), Programmed Cell Death Ligand 1 (PD-L1), Thrombomodulin, p53, and Paired Box Gene 8 (PAX8), play a crucial role in diagnosis as well as in aiding in predicting disease progression and prognosis.[8,9] The detection and interpretation of abnormal expression patterns in these biomarkers offer significant potential as prognostic and predictive tools in the clinical management of bladder cancer.[10,11]

The epidermal growth factor receptor (EGFR), encoded by the c-erbB1 oncogene, is a transmembrane receptor tyrosine kinase that regulates key cellular processes, including proliferation, differentiation, migration, and survival. In bladder carcinoma, EGFR overexpression is one of the most frequently observed molecular alterations and is particularly associated with high-grade and muscle-invasive tumors. Activation of EGFR stimulates downstream oncogenic pathways such as RAS/MAPK, PI3K/AKT, and STAT3, which collectively promote uncontrolled cell division, enhanced invasive potential, angiogenesis, and resistance to apoptosis. These molecular events contribute to tumor progression, recurrence, and poorer clinical outcomes.[12]

The objective of the study is to assess IHC expression of EGFR in urinary bladder carcinoma and to correlate the expression of EGFR with clinicopathological variables like age, tumor size, histological grade, invasion of the tumor, and pathological staging.

MATERIALS AND METHODS

This was a cross-sectional study conducted from 1st August 2023 to 28th February 2025 in the Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. Ethical clearance was obtained from the Institutional Ethics Committee of Sri Guru Ram Das Institute of Medical Sciences and Research. Specimens were obtained from Transurethral Resection of Bladder Tumor (TURBT). Histopathological examination was performed on formalin-fixed, paraffin-embedded sections, stained with Hematoxylin and Eosin. Histopathologically confirmed cases of UBC that were adequate for IHC were included in the study, while benign tumors of bladder, poorly preserved or inadequate samples were excluded from the study.

Reagents used for immunohistochemistry: Poly-L-lysine hydrobromide-coated slides, a rabbit monoclonal primary antibody (Biomedical Care), protein block, post-primary block, and a polymer-based enzyme conjugate. DAB (3, 3′-diaminobenzidine) was used as the chromogen. The procedure also required phosphate-buffered saline (PBS), citrate buffer (pH 6.0), and Tris buffer (pH 7.4–7.6) for antigen retrieval. Hydrogen peroxide was used for peroxidase blocking. Additional materials included methanol, a heater and a decloaker.

Immunohistochemistry analysis: IHC was performed on 3–5 µm formalin-fixed, paraffin-embedded tissue sections mounted on 0.1% Poly-L-lysine-coated slides. Sections were dried overnight at 37°C, deparaffinized in xylene, and rehydrated. Antigen retrieval was carried out using the Decloaker method with Diva Decloaker solution at 95°C for 1 hour, followed by cooling to room temperature. Endogenous peroxidase activity was blocked using hydrogen peroxide in methanol for 5 minutes. Slides were washed in phosphate-buffered saline (PBS) or Tris-buffered saline (TBS), and incubated with a protein block for 5 minutes. A rabbit monoclonal primary antibody against EGFR was applied for 1 hour in a moist chamber, followed by incubation with a post-primary block and polymer detection system. Visualization was achieved using 3, 3'-diaminobenzidine (DAB) as the chromogen. Slides were counterstained with hematoxylin, dehydrated in propanol, cleared in xylene, and mounted using DPX. All procedures followed the universal kit guidelines, with minor time adjustments as per laboratory standardization. Finally, slides were examined under a light microscope. EGFR immunopositivity was identified by brownish staining localized to cell membrane of tumor cells. Colorectal carcinoma tissue served as the positive control.

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Assessment protocol: The stained slides were scored independently by one pathologist. A second pathologist reviewed a subset of cases to assess interindividual reproducibility, which showed high concordance in scoring, with 93% agreement between observers based on manual count. Both membranous and cytoplasmic staining were evaluated, but final scoring was primarily based on membranous staining intensity and percentage, as EGFR is a transmembrane receptor that resides primarily on the cell membrane, membranous staining is considered more specific for its expression.

EGFR expression was assessed using the Remmele and Stegner Immunoreactive Score (IRS) system. The staining intensity was scored on a semi quantitative 4-point scale, 0 staining was equivalent to the negative control, 1 represented weak cytoplasmic staining, 2 denoted moderate staining and 3 indicated intense staining. The percentage of stained cells were also scored on a semi-quantitative 5-point scale as follows: 0 was assigned when no positive cells were observed, 1 corresponded to 0–25% stained cells, 2 was assigned to 26–50% stained cells, 3 corresponded to 51–75% stained cells, and 4 was assigned to more than 75% of stained cells. Final scoring was then based on the composite score obtained by multiplying the score of staining intensity and percentage of stained cells (Table 1).[13]

Table 1: Scoring of EGFR expression in Urinary Bladder Carcinoma

Score	Interpretation
0	Negative
1-4	+ (weak)
5-8	++ (moderate)
9-12	+++ (strong)

Statistical analysis: The statistical significance of EGFR expression was calculated by correlating EGFR expression with clinicopathological variables such as age, tumor size, histological grade, depth of tumor invasion, and pathological stage using statistical package of the Social Sciences (SPSS), and the chi-square test was applied. Significance was assumed at a p-value less than 0.05.

RESULTS

Histopathologically proven cases of UBC in TURBT specimens totalling 60 were included, all diagnosed at the Department of Pathology, Sri Guru Ram Das Institute of Medical Sciences and Research, Amritsar. All cases were histologically diagnosed as Papillary Urothelial Carcinoma as per the latest WHO/ISUP classification. Most of the patients (77%) were male, reflecting the known male predominance of bladder carcinoma. Among these evaluated cases, 14 (23%) were graded as low-grade tumors and 46 (77%) as high-grade tumors. Out of the total 60 cases, 56 cases (93%) showed immunopositivity for EGFR, while the remaining four cases (7%) were immunonegative. Among the 56 EGFR-positive cases, 25 cases (45%) exhibited a strong score (+++), 25 cases (45%) showed a moderate score (++), and six cases (10%) had a weak score (+) for EGFR expression.

In the present study, the age of patients ranged from 39 to 91 years, with the peak incidence of UBC observed in the 6th to 7th decades of life. EGFR expression was highest (100%) in the 71–90 years age group, followed by 92% in the 51–70 years age group, and 88% in patients aged ≤50 years. Although there was a trend toward increased EGFR positivity with advancing age, the correlation was not statistically significant (p = 0.596) (Table 2).

Tumor size, assessed radiologically or cystoscopically, varied from 0.40 to 7.2 cm. Maximum EGFR positivity was observed in all cases (100.0%) with tumor size > 6.1 cm, followed by 95% in tumors between 3.1 – 6.0 cm, and 92% in tumors ≤3.0 cm. Although EGFR expression appeared to increase with larger tumor size, the association was not statistically significant (p = 0.808) (Table 2).

A significant correlation was observed between EGFR expression and the histological grade of urinary bladder carcinoma. Among the 46 high-grade tumors, 45 cases (98%) were EGFR positive, whereas only one case (2%) was negative. In contrast, of the 14 low-grade tumors, 11 cases (79%) were EGFR positive and three cases (21%) were negative (p = 0.036) (Table 2).

All cases of UBC were evaluated for lamina propria and muscle invasion, along with their corresponding EGFR expression. Among the 50 cases with lamina propria invasion, 47 cases (94%) were EGFR positive, while three cases (6%) were negative (Table 2). Additionally, muscle invasion was assessed in all 60 cases. Of the nine cases showing muscle invasion, all (100%) demonstrated EGFR positivity (Table 2). Despite this observation, no significant correlation was found between EGFR expression and lamina propria invasion (p = 0.643) or muscle invasion (p = 0.616).

A trend of increasing EGFR positivity with tumor stage was observed. All T2 cases (100%) were EGFR positive, compared to 93% in T1 and 90% in Ta stages. However, the association was not statistically significant (p = 0.849) (Table 2).

Table 2: EGFR expression with respect to clinicopathological parameters in urinary bladder carcinoma

	EGFR Negative n (%)	EGFR Positive n (%)	Total n (%)
Age (years)			
≤ 50	1 (12.0)	7 (88.0)	8 (100.0)
51 - 70	3 (8.0)	35 (92.0)	38 (100.0)
71 - 90 Year	0 (0.0)	14 (100.0)	14 (100.0)
Tumor Size (cm)			
≤ 3.0	3 (8.0)	34 (92.0)	37 (100.0)
3.1 - 6.0	1 (5.0)	19 (95.0)	20 (100.0)
≥ 6.1	0 (0.0)	3 (100.0)	3 (100.0)
Histological Grade			
High Grade UBC	1 (2.0)	45 (98.0)	46 (100.0)
Low Grade UBC	3 (21.0)	11 (79.0)	14 (100.0)
Invasion Into lamina propria			
Not Seen	1 (10.0)	9 (90.0)	10 (100.0)
Seen	3 (6.0)	47 (94.0)	50 (100.0)
Invasion into muscularis propria			
Not Seen	4 (8.0)	47 (92.0)	51 (100.0)
Seen	0 (0.0)	9 (100.0)	9 (100.0)
T Stage			
Ta	1 (10.0)	9 (90.0)	10 (100.0)
T1	3 (7.0)	38 (93.0)	41 (100.0)
T2	0 (0.0)	9 (100.0)	9 (100.0)

An analysis of EGFR staining intensity and percentage of stained cells revealed a significant association between EGFR score and tumor grade. Among the high-grade tumors, 50% demonstrated strong (+++) EGFR expression, 46% showed moderate (++), and only 2% each showed weak (+) or negative staining. In contrast, among low-grade tumors, strong positivity was seen in just 14%, while 29% showed moderate, 36% weak, and 21% were EGFR negative. The association between EGFR score and tumor grade was statistically highly significant ($p < 0.001$) (Table 3).

On further evaluation, a significant correlation was observed between EGFR score and tumor stage ($p = 0.036$). The majority of T1 and T2 stage tumors demonstrated strong (+++) and moderate (++) EGFR expression. Specifically, T1 tumors showed the highest proportion of strong (44%) and moderate (44%) EGFR positivity, while T2 tumors had 56% strong and 44% moderate expression. In contrast, Ta stage tumors predominantly exhibited weak EGFR expression (40%) and lower rates of moderate (30%) and strong (20%) staining. These findings indicate that higher EGFR scores are more frequently associated with invasive or more advanced stages (T1 and T2), whereas early-stage (Ta) tumors tend to exhibit weaker EGFR expression *(*Table 3*)*.

Table 3: Correlation of EGFR score with histological grade and tumor stage in urinary bladder carcinoma.

	Negative n (%)	Weak (+) n (%)	Moderate (++) n (%)	Strong (+++) n (%)	Total n (%)
Grade					
High Grade UBC	1 (2.0)	1 (2.0)	21 (46.0)	23 (50.0)	46 (100.0)
Low Grade UBC	3 (21.0)	5 (36.0)	4 (29.0)	2 (14.0)	14 (100.0)
T Stage					
Ta	1 (10.0)	4 (40.0)	3 (30.0)	2 (20.0)	10 (100.0)
T1	3 (7.0)	2 (5.0)	18 (44.0)	18 (44.0)	41 (100.0)
T2	0 (0.0)	0 (0.0)	4 (44.0)	5 (56.0)	9 (100.0)

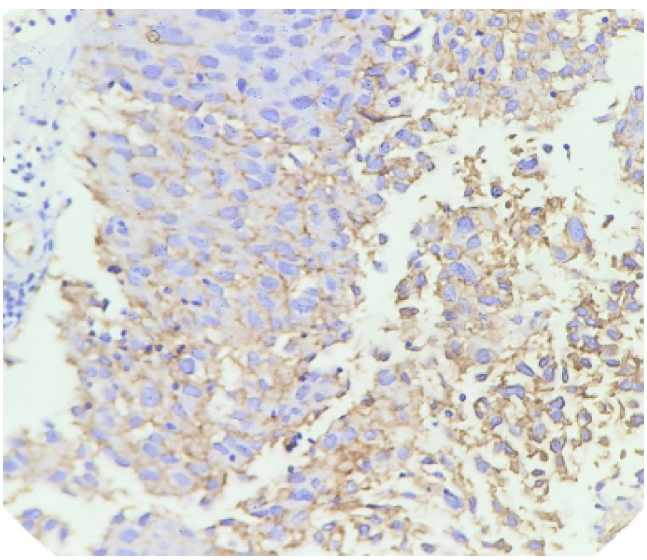

Figure 1: *Photomicrograph showing weak EGFR staining intensity in urinary bladder carcinoma [IHC, 400X]*

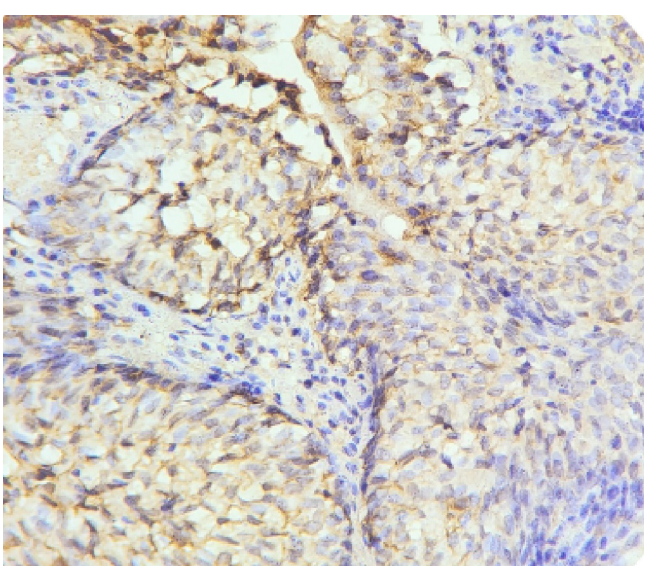

Figure 2: *Photomicrograph showing moderate EGFR staining intensity [IHC, 400x]*

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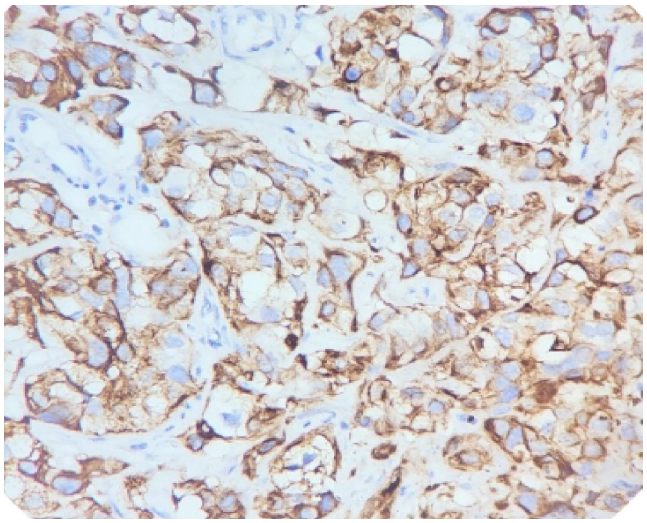

Figure 3: *Photomicrograph showing strong EGFR staining intensity in urinary bladder carcinoma [IHC, 400x]*

DISCUSSION

Urinary bladder carcinoma represents a major global health concern with substantial impact on patient morbidity and mortality. Early detection and the identification of reliable prognostic biomarkers are essential for improving treatment strategies and patient outcomes. The ErbB receptor family, also known as the epidermal growth factor receptor (EGFR) family, is a key group of receptor tyrosine kinase (RTK) proto-oncogenes involved in cellular regulation. When one of EGFR's ligands activates it, a series of intracellular signalling events takes place that trigger transcriptional activation and cell division. This study investigates the expression of EGFR in urinary bladder carcinoma using immunohistochemistry, due to its established link with more aggressive tumor behavior and poor prognosis.[13,14]

The present study, conducted within the local population, observed that 93% of urinary bladder carcinoma cases exhibited positive EGFR expression. Various studies from different countries have reported a wide range of EGFR positivity in urinary bladder carcinoma, varying from 23% to 96%.[10,13-19] This variation may be due to differences in population genetics, tumor biology, or geographical and methodological factors. Our study found an association between Epidermal Growth Factor Receptor (EGFR) expression and several clinicopathological factors, including patient age, tumor size, tumor grade, extent of invasion and tumor staging.

Demographically, this research demonstrated EGFR positivity across different age groups, revealing a notable trend. Patients aged 71 – 90 years showed 100% EGFR positivity, followed by 92% in the 51 – 70 years group, and 8% in those aged ≤ 50 years. These findings align with previous reports by Sharma et al.[13], Li et al.[20], and Barua et al.[19], all of whom observed higher EGFR expression in older age groups. This suggests that EGFR expression tends to be more pronounced in elderly patients compared to younger individuals.

In terms of tumor size, EGFR positivity was assessed across three categories, tumors larger than 6.0cm demonstrated 100% EGFR positivity, those measuring between 3.1cm and 6.0cm showed 95%, while tumors 3.0 cm or smaller exhibited 92% positivity. Although the difference is subtle, larger tumors consistently showed higher EGFR expression compared to smaller ones. This pattern is in agreement with findings from Sharma et al.[13], who reported EGFR positivity in 97% of larger tumors versus 96% in smaller tumors, and Li et al.[20], who noted EGFR positivity in 61% of large tumors compared to 60% in small tumors. Despite slight variations, these studies support the observation that EGFR expression tends to be higher in larger tumors.

Notably, patients in older age groups also exhibited higher levels of EGFR expression, and when considered alongside the trend of increased EGFR expression in larger tumors, these findings further suggest that EGFR may play an important role in tumor growth and progression. The correlation of EGFR with both age and tumor size highlights its potential as a marker of more advanced disease biology.

Importantly, we observed that EGFR expression was significantly more common in high-grade urinary bladder carcinoma (UBC) cases (98%) compared to low-grade cases (79%). This indicates that tumors with higher histological grades, which are typically more aggressive, are more likely to show increased EGFR expression. Our findings are supported by similar results reported in other research groups.[10, 19]

The role of EGFR expression in how invasive urothelial bladder carcinoma (UBC) is, gives us important clues about tumor behavior. In this study, 94% of tumors that had invaded the lamina propria were EGFR-positive. This is similar to the findings of Parvin et al.[18] and Yazdi et al.[21], who found EGFR positivity in 84% and 79% of such cases, respectively. Among muscle-invasive cases (T2 stage), all (100%) were EGFR positive, suggesting a potential link between EGFR expression and deeper tumor invasion. This supports the idea that higher EGFR expression is linked to more aggressive forms of the cancer. Similar results were reported by Barua et al.[19] and Yazdi et al.[21], who also found 100% EGFR positivity in muscle-invasive bladder cancers.

In the current study, EGFR positivity was highest in T2 stage (100%). These findings are consistent with those of Yazdi et al.[21] who also reported 100% EGFR positivity in T2 cases, and with Barua et al.[19] who found similar results. A clear association was observed between EGFR expression and tumor stage in urinary bladder carcinoma. Also, higher EGFR scores were more commonly seen in advanced-stage tumors (T1, lamina propria invasion and T2, muscle invasion), while early-stage tumors (Ta) generally showed lower or weaker EGFR expression. This supports the idea

that EGFR expression may be linked to tumor aggressiveness and progression in bladder cancer.

Finally, EGFR expression has also been associated with poor prognosis. Altered or dysregulated activity of growth factor receptors, EGFR, is believed to influence cancer progression and overall outcomes in affected patients. EGFR is closely linked to critical tumor behaviors, including cell proliferation, migration, recurrence, and metastasis—all of which contribute to the aggressive nature of the disease.[12]

CONCLUSIONS

The present study demonstrates that Epidermal Growth Factor Receptor (EGFR) expression is highly prevalent in urinary bladder carcinoma, particularly in high-grade and advanced-stage tumors. EGFR positivity was significantly associated with aggressive tumor characteristics such as higher histological grade and muscle invasion, suggesting its role in tumor progression. Although EGFR expression showed a trend towards correlation with tumor size and patient age, these associations were not statistically significant. Importantly, all muscle-invasive cases exhibited EGFR positivity, underscoring its potential link with tumor invasiveness.

Importance of the Study: This study provides valuable evidence regarding the prognostic significance of EGFR in urinary bladder carcinoma. By demonstrating a clear association between EGFR expression, tumor grade, and tumor stage, the findings strengthen the recognition of EGFR as a practical and accessible biomarker in routine diagnostic pathology. Routine IHC assessment of EGFR in bladder carcinoma may provide valuable prognostic information and assist in effective patient risk stratification. Furthermore, the study highlights the potential utility of EGFR in guiding prognostication and identifying patients who may benefit from EGFR-targeted therapeutic strategies, underscoring its emerging role in personalized management of bladder cancer.

Limitations of the study:

The sample size of this study was relatively small and was derived from a single institution, which may limit generalizability. Molecular analyses such as EGFR mutation testing or assessment of other related pathway markers were also not performed. Future multi-center studies with larger cohorts and molecular profiling are needed to validate and expand upon these findings.

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Conflict of interest: None

REFERENCES

1. Saginala K, Barsouk A, Aluru JS, Rawla P, Padala SA, Barsouk A. Epidemiology of bladder cancer. Med Sci (Basel). 2020;8(1):15. DOI: https://doi.org/10.3390/medsci8010015.
2. Alfred Witjes J, Max Bruins H, Carrión A, et al. European Association of Urology Guidelines on Muscle-invasive and Metastatic Bladder Cancer: Summary of the 2023 Guidelines. Eur Urol. 2024;85(1):17-31. DOI: 10.1016/j.eururo.2023.08.016
3. Missaoui N, Bdioui A, Baccouche A, et al. Significance of p53, p27, Ki-67, E-cadherin, and HER2 expression in upper urinary tract urothelial carcinoma. J Egypt Natl Canc Inst. 2020;32(1):36. DOI: 10.1186/s43046-020-00047-z
4. Leow JJ, Chong KT, Chang SL, Bellmunt J. Upper tract urothelial carcinoma: a different disease entity in terms of management. ESMO Open. 2016;1(6):e000126. DOI: 10.1136/esmoopen-2016-000126
5. American Cancer Society. Bladder cancer signs and symptoms [Internet]. Atlanta (GA): American Cancer Society; 2024. Available from: https://www.cancer.org/cancer/types/bladder-cancer/detection-diagnosis-staging/signs-and-symptoms.html
6. Partin AW, Dmochowski RR, Kavoussi LR, Peters CA, Wein AJ, editors. Campbell-Walsh-Wein Urology. 12th ed. Philadelphia (PA): Elsevier; 2020. Available from: https://www.eu.elsevierhealth.com/campbell-walsh-wein-urology-9780323884051.html
7. Oeyen E, Hoekx L, De Wachter S, Baldewijns M, Ameye F, Mertens I. Bladder cancer diagnosis and follow-up: the current status and possible role of extracellular vesicles. Int J Mol Sci. 2019;20(4):821. DOI: 10.3390/ijms20040821
8. Michel F, Cancrini F, Cancel-Tassin G, et al. A study of the immunohistochemical profile of bladder cancer in neuro-urological patients by the French Association of Urology. World J Urol. 2022;40(8):1939–47. DOI: 10.1007/s00345-022-03942-3
9. Paner GP, Annaiah C, Gulmann C, et al. Immunohistochemical evaluation of novel and traditional markers associated with urothelial differentiation in variants of urothelial carcinoma. Hum Pathol. 2014;45(7):1473–82. DOI: 10.1016/j.humpath.2014.02.024
10. Hashmi AA, Hussain ZF, Irfan M, et al. Prognostic significance of epidermal growth factor receptor overexpression in urothelial carcinoma. BMC Urol. 2018;18(1):59. DOI: 10.1186/s12894-018-0373-0
11. Neal DE, Sharples L, Smith K, Fennelly J, Hall RR, Harris AL. The epidermal growth factor receptor and the prognosis of bladder cancer. Cancer. 1990;65(7):1619–25. DOI: 10.1002/1097-0142(19900401)65:7<1619::aid-cncr2820650728>3.0.co;2-q
12. Wieduwilt MJ, Moasser MM. The epidermal growth factor receptor family: biology driving targeted therapeutics. Cell Mol Life Sci. 2008;65(10):1566–84. DOI: DOI: 10.1007/s00018-008-7440-8
13. Sharma D, Sharma SK, Raina P, Gulati A. EGFR expression in primary epithelial urinary bladder tumors and its correlation with clinicopathological parameters. Indian J Appl Res. 2021;11(6):44–47. DOI: 10.36106/ijar.
14. Naik DSL, Sharma S, Ray A, Hedau S. Epidermal growth factor receptor expression in urinary bladder cancer. Indian J Urol. 2011;27(2):208–14. DOI: 10.4103/0970-1591.82839
15. Chaux A, Cohen JS, Schultz L, et al. High EGFR immunohistochemical expression in urothelial carcinoma of the bladder is not associated with EGFR mutations in exons 19 and 21. Hum Pathol. 2012;43(10):1590–5. DOI: 10.1016/j.humpath.2011.11.016
16. Siddiqui MR, Railkar R, Sanford T, et al. Targeting EGFR and HER2 expressing bladder cancer using combination photoimmunotherapy.

Sci Rep. 2019;9(1):2084. DOI: 10.1038/s41598-019-38575-x

17. Badawy AA, El-Hindawi A, Hammam O, Moussa M, Helal NS, Kamel A. Expression of epidermal growth factor receptor and transforming growth factor-α in schistosomal and non-schistosomal bladder cancer. Curr Urol. 2015;9(4):192–201. DOI: 10.1159/000447140

18. Parvin M, Sabet-Rasekh P, Hajian P, Torbati PM, Mirzaei H. Evaluating EGFR prevalence in transitional cell carcinoma of the bladder and its relationship with prognostic factors. Iran J Cancer Prev. 2016;9(1):e4022. DOI: 10.17795/ijcp-4022

19. Barua SK, Das N, Baruah SJ, Rajeev TP, Bagchi PK, Sarma D, Phukan M. Correlation of EGFR score with prognostic variables in transitional cell carcinoma of the urinary bladder. Int Surg J. 2018;5(9):3083–8. DOI: 10.18203/2349-2902.isj20183727.

20. Li W, Wang Y, Tan S, Rao Q, Zhu T, Huang G, et al. Overexpression of EGFR and HER-2 in bladder carcinoma and clinical associations. Med Sci Monit. 2018;24:7178–85. DOI: 10.12659/MSM.911640

21. Yazdi SA, Asghari F, Tabriz HM, Vesali B, Nazar E. The value of EGFR expression in predicting aggressive behavior of bladder neoplasms. Nephro-Urol Mon. 2023;15(2):e137778. DOI: https://doi.org/10.5812/numonthly-137778