Journal of Carcinogenesis
Covering Genesis to Therapeutics

Journal of Carcinogenesis, ISSN: 1477-3163
2026; Vol 25: Issue 1, https://carcinogenesis.com/

Study of Gata-3 Expression in Urothelial Neoplasms and its Correlation with Histomorphological Parameters

Dr Sristi J Shetty[1], Dr Usha M[2], Dr Rashmi K[3], Dr Laxmi Ronada[4], Dr Fayeza M Malvi[5]

[1]Post graduate, Department Of Pathology, Ramaiah Medical College, Ramaiah University Of Applied Sciences, MSR Nagar, Mathikere, Bangalore – 560054

[2]Associate Professor, Department Of Pathology, Ramaiah Medical College, Ramaiah University Of Applied Sciences, MSR Nagar, Mathikere, Bangalore – 560054

[3]Associate Professor, Department Of Pathology, Ramaiah Medical College, Ramaiah University Of Applied Sciences, MSR Nagar, Mathikere, Bangalore – 560054

[4]Assistant Professor, Department Of Pathology, Ramaiah Medical College, Ramaiah University Of Applied Sciences, MSR Nagar, Mathikere, Bangalore – 560054

[5]Post graduate, Department Of Pathology, Ramaiah Medical College, Ramaiah University Of Applied Sciences, MSR Nagar, Mathikere, Bangalore – 560054

ABSTRACT

Background Urothelial neoplasms are among the most common tumors affecting the urinary tract and are known for their high recurrence rates and variable clinical behavior. The prognosis and management of these tumors depend on histomorphological parameters like tumor grade and invasion into the muscularis propria mainly. However, assessment based only on morphology may be limited in certain cases. GATA3, a transcription factor expressed in urothelial cells has gained importance as an immunohistochemical marker. Studying its expression and its correlation with histomorphological parameters will help in better characterization of tumors and their prognostication. Materials and Methods This cross-sectional study was carried out in the Department of Pathology, Ramaiah Medical College, Bengaluru, over a period from March 2024 to February 2026. A total of 68 cases of urothelial neoplasms from cystoscopic biopsies, TURBT, and radical cystectomy specimens. Using light microscopy, the tumor morphology was examined. The evaluation of GATA3 expression was done by immunohistochemistry. The scoring was done using and immunoreactivity scoring system based on the intensity of staining and the proportion of positive tumor cells. Descriptive statistics and Chi-square test were used for statistical analysis and for the analysis of the association between GATA3 expression and histomorphological parameters respectively. Results A total of 68 cases of urothelial neoplasms were studied and evaluated, of which majority showed GATA3 positivity. The correlation between GATA3 expression and various histomorphological parameters was found to be statistically significant. Most low grade tumors with mild nuclear pleomorphism, low mitotic activity, no invasion, absence of necrosis and increased TILs showed strong expression of GATA3. The high grade tumors comparatively showed weak GATA3 expression. These findings indicate that GATA3 may serve not only as a diagnostic marker but also has prognostic significance. Conclusion The present study confirms that GATA3 is a highly sensitive immunohistochemical marker in urothelial neoplasms and demonstrates significant association with multiple histopathological prognostic parameters. The findings further strengthen the role of GATA3 as a marker of tumor differentiation and biological behavior. Importantly, the study expands the existing knowledge by demonstrating associations with mitotic activity, necrosis and TILs, suggesting a broader role of GATA3 in tumor biology.

Keywords: *Urothelial carcinoma; GATA3; Immunohistochemistry, Histomorphological parameters; Tumor grade; Tumor infiltrating lymphocytes; Necrosis; Mitotic activity*

How to Cite: Dr Sristi J Shetty, Dr Usha M, Dr Rashmi K, Dr Laxmi Ronada, Dr Fayeza M Malvi, (2026) Study of Gata-3 Expression in Urothelial Neoplasms and its Correlation with Histomorphological Parameters, *Journal of Carcinogenesis, Vol.25, No.1*, 703-714

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

1. INTRODUCTION

Urothelial carcinoma (UC) is a common urinary tract cancer with high global incidence and mortality. Its classification into non-invasive and invasive types particularly the presence of muscle invasion is critical, as muscle-invasive UC is aggressive and life-threatening. Prognosis and treatment decisions depend on the cancer's extent, highlighting the need for reliable biomarkers to enable early detection, risk stratification, and personalized treatment for better clinical outcomes.1-3

Bladder cancer is among the top ten cancers globally, with approximately 550,000 new cases reported annually.4 Urothelial carcinoma is the most common subtype, being 3–4 times more frequent in males than females and more prevalent in individuals over 60.5 In India, the gender disparity is even more pronounced, with incidence 8.6 times higher in males. It ranks 17th in incidence and 19th in mortality within the Indian population.6,7

Approximately 75% of bladder cancers are pure conventional urothelial carcinomas (CUC), while the remaining 25% contain histological subtypes (HSs). Histological subtypes of urothelial carcinoma are often associated with conventional urothelial carcinoma (CUC), but may occur in pure form occasionally. In some cases, more than one histological subtype can be seen within the same tumor8. Urothelial carcinomas with any histological subtypes are generally more aggressive than pure CUCs9. Hence such tumors are classified as high risk (even in the absence of muscle invasion) by the European Association of Urology and Japanese Urology Association. Therefore it is very important to recognize and report these histological subtypes for risk stratification, prognostic evaluation and treatment planning10-12. At the time of initial diagnosis, most urothelial tumors are superficial and 70% of these tumors follow a prolonged clinical course with frequent recurrences even after local excision, but without any significant progression. In contrast, a small proportion of tumors rapidly progress and show aggressive behavior. This unpredictable clinical course necessitates long-term surveillance, thereby making urothelial carcinoma one of the costliest cancers to manage13,14.

Histopathology is very much essential for guiding treatment and assessing prognosis in urothelial tumors, but it is limited by subjectivity and poor specificity in certain situations. Various immunohistochemical markers including p63, cytokeratin 7, cytokeratin 20, uroplakin, S100P, and thrombomodulin have been investigated to improve staging, grading, and metastatic site specificity. However, none have proven clinically useful, as they are also expressed in other epithelial cancers like breast, ovary, and lung, limiting their diagnostic value at metastatic sites.15-17

The identification of reliable biomarkers for invasive urothelial carcinoma (UC) is essential for early detection, risk stratification, and personalized treatment. GATA-binding protein 3 (GATA3) has emerged as a promising biomarker for UC.2,3,18 It is a transcription factor involved in cell differentiation and proliferation, commonly expressed in urothelial and breast epithelial cells. GATA3 regulates luminal differentiation in breast tissue and may also play a role in the development or maintenance of skin, hair, and vascular endothelial cells.19,20

The management and prognostication of urothelial carcinoma patients largely depend on the histomorphological parameters. This study is designed to assess the hypothesis that GATA-3 expression intensity and proportion show significant association with the histomorphological parameters and may play an important role in stratifying high-risk patients. Hence, this study aims to explore the utility of GATA-3 expression in urothelial neoplasms arising along the urinary tract and its correlation with histomorphological parameters.

2. MEHTODOLOGY

This cross-sectional study included patients with urothelial neoplasms who underwent TURBT, cystoscopic biopsy, or radical cystectomy at the Department of Pathology, Ramaiah Medical College and Hospitals, Bengaluru, over a period of two years. Written informed consent was obtained from all participants, who were enrolled based on the predefined inclusion and exclusion criteria. A total of 68 subjects were included in the study based on the predetermined sample size.
Inclusion Criteria:

Cystoscopic biopsies, TURBT, and radical cystectomy from patients aged more than 18 years with urothelial neoplasms were included in the study.

Exclusion Criteria:
Cases with extensive tumor necrosis without sufficient viable tumour cells for accurate evaluation of the immunohistochemical results were excluded from the study.

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

3. METHOD OF DATA COLLECTION

The cystoscopic biopsies, TURBT and radical cystectomy specimens of urothelial neoplasms were received in the Pathology Department in 10% formalin. After a detailed gross specimen examination, multiple representative tissue bits were taken from the tumor and processed as per standard protocol. Five micrometer thick sections were cut from the formalin fixed paraffin embedded blocks and stained with hematoxylin and eosin (H&E) stain. The H&E stained slides were evaluated and reported as per WHO / International Society of Urologic Pathology (ISUP) classification of bladder tumors, 2022. Special emphasis was laid on tumor grade, nuclear pleomorphism, muscle invasiveness, mitosis, necrosis and TILs.

4. PROCESSING FOR IMMUNOHISTOCHEMISTRY (IHC)

Sections of 3 µm thickness were mounted on coated glass slides, deparaffinised in three changes of xylene for 10 minutes each and rehydrated through descending grades of alcohol (100%, 90%, 70% and 50%). The sections were rinsed in running tap water, distilled water and Tris buffer.

Endogenous peroxidase activity was blocked using peroxidase blocking solution for 15 minutes, followed by Tris buffer washes. Antigen retrieval was performed using Tris-EDTA buffer by microwave heating for four cycles of 8 minutes of boiling followed by 5 minutes of cooling. After washing, protein blocking was performed for 15 minutes, followed by incubation with the primary antibody for 45–60 minutes in a moist chamber.

Following Tris buffer washes, post-primary block was applied for 30 minutes, followed by Poly-HRP secondary antibody for 30 minutes. Immunoreactivity was visualised using DAB chromogen for 5 minutes. The sections were counterstained with haematoxylin for 20 seconds, washed, dehydrated, cleared and mounted using DPX. Positive and negative controls were included with each staining batch.

Evaluation of IHC Staining:
A positive immunoreaction was defined by brown nuclear staining of tumour cells. Expression was assessed using the immunoreactivity score (IRS), calculated by multiplying the proportion of positively stained tumour cells (score 0–4) by staining intensity (score 0–3). Tumours were categorised as having negative, weak, moderate or strong expression based on the IRS.

5. RESULTS

The majority of cases belonged to the 61-70 years age group (39.7%), followed by 51-60 years (27.9%) and >70 years (22.1%). Only 2.9% of cases were below 40 years of age, indicating that urothelial carcinoma in the present study predominantly affected older adults.

Males constituted 73.5% of the study population, whereas females accounted for 26.5%. Thus, a clear male predominance was observed, with an approximate male: female ratio of 2.8:1.

Table 1. Distribution according to GATA3 expression

	Frequency (n)	Percentage (%)
Negative	1	1.5
Mild	36	52.9
Strong	31	45.6

Mild GATA3 expression was observed in 52.9% of cases, strong expression in 45.6%, and negative expression in only 1.5%. Hence, most urothelial tumors in the present study were GATA3 positive.

Table 2. Association of GATA3 expression with tumor grade

	Negative n (%)	Mild n (%)	Strong n (%)
High	1 (2.2)	33 (73.3)	11 (24.4)
Low	0 (0.0)	2 (9.5)	19 (90.5)
Not applicable	0 (0.0)	1 (50.0)	1 (50.0)

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

There was a statistically significant association between GATA3 expression and tumor grade (Pearson chi-square test, p = <0.001). High-grade tumors showed predominantly mild GATA3 expression (73.3%), whereas low-grade tumors showed predominantly strong expression (90.5%). This indicates that stronger GATA3 expression was associated with lower-grade tumors.

Graph 1. Graph showing Association of GATA3 expression with tumor grade

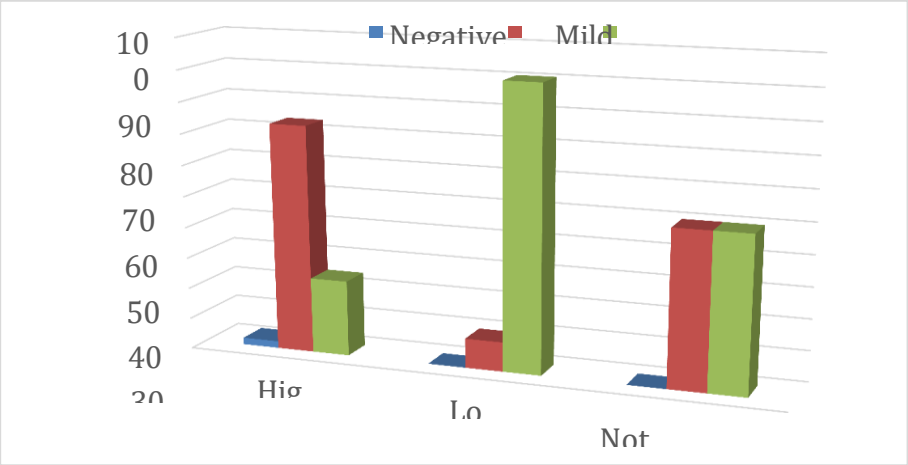


Table 3. Association of GATA3 expression with nuclear pleomorphism

	Negative n (%)	Mild n (%)	Strong n (%)
Mild	0 (0.0)	2 (11.7)	15 (88.3)
Moderate	0 (0.0)	18 (60.0)	12 (40.0)
Severe	1 (4.8)	16 (76.2)	4 (19.0)

A statistically significant association was noted between GATA3 expression and nuclear pleomorphism (Pearson chi-square test, p = 0.002). Tumors with mild pleomorphism showed predominantly strong expression (88.3%), whereas tumors with severe pleomorphism showed mainly mild expression (76.2%) with occasional negativity (4.8%). This suggests that GATA3 expression decreases as pleomorphism becomes more severe.

Graph 2. Graph showing Association of GATA3 expression with nuclear pleomorphism

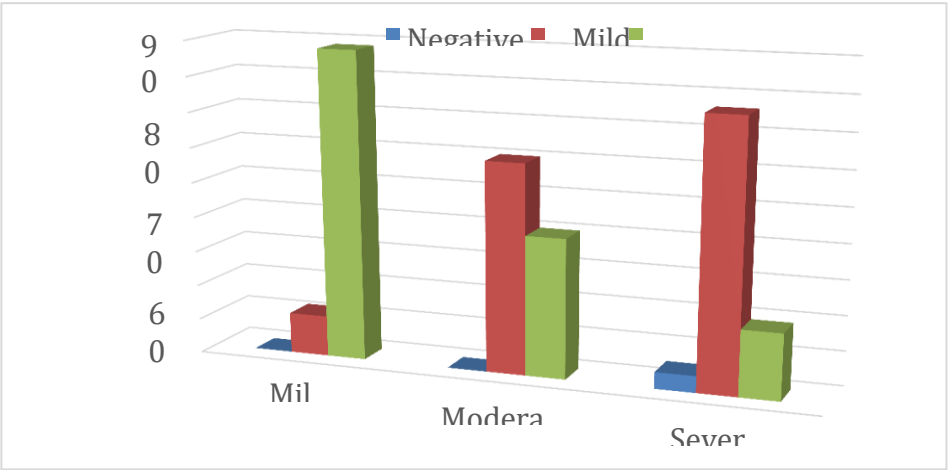


Table 4. Association of GATA3 expression with invasion

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

	Negative n (%)	Mild n (%)	Strong n (%)
Lamina propria invasion	0 (0.0)	11 (64.7)	6 (35.3)
Muscle invasion	1 (2.9)	23 (65.7)	11 (31.4)
No invasion	0 (0.0)	2 (12.5)	14 (87.5)

There was a statistically significant association between GATA3 expression and invasion (Pearson chi-square test, p = 0.004). Tumors without invasion showed predominantly strong GATA3 expression (87.5%), while both lamina propria invasive tumors (64.7%) and muscle-invasive tumors (65.7%) predominantly showed mild expression. This indicates lower GATA3 expression in more invasive tumors.

Graph 3. Graph showing Association of GATA3 expression with invasion

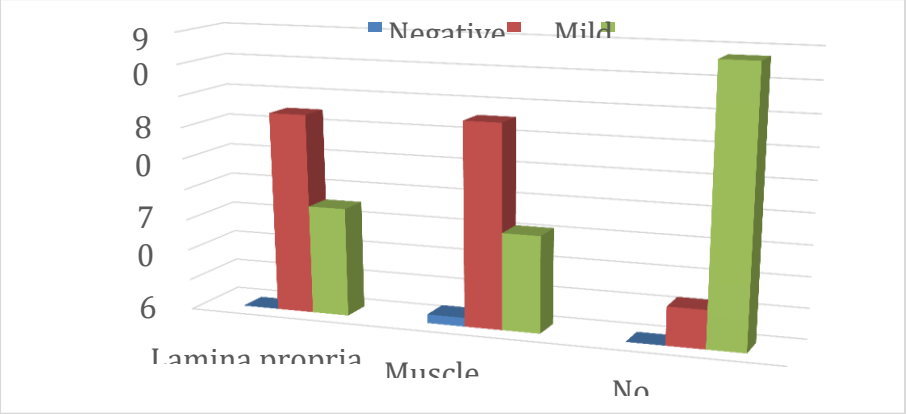


Table 5. Association of GATA3 expression with mitotic activity

	Negative n (%)	Mild n (%)	Strong n (%)
<5/10hpf	0 (0.0)	19 (40.4)	28 (59.6)
5-10/10hpf	1 (4.8)	17 (81.0)	3 (14.3)

p value: 0.001 A statistically significant association was observed between GATA3 expression and mitotic activity (Pearson chi-square test, p = 0.001). Tumors with

<5/10hpf mitosis more often showed strong expression (59.6%), whereas tumors with 5-10/10hpf mitosis predominantly showed mild expression (81.0%). Thus, higher mitotic activity was associated with reduced GATA3 expression.

Graph 4. Graph showing Association of GATA3 expression with mitotic activity

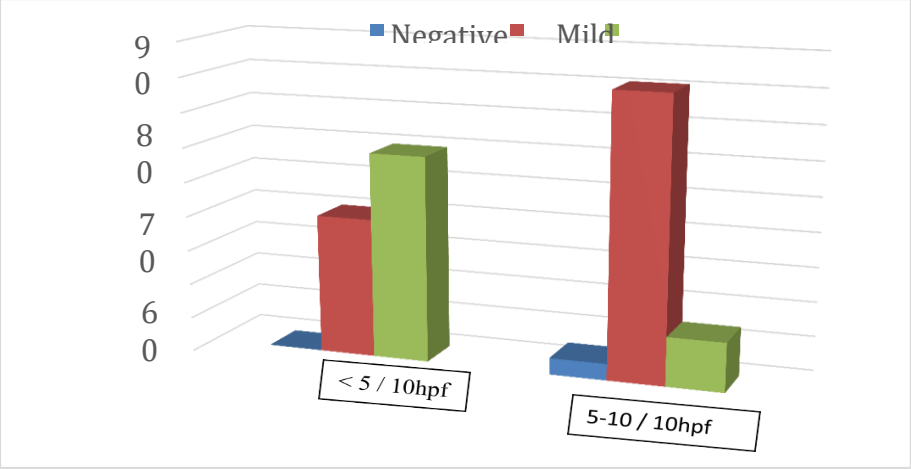


Table 6. Association of GATA3 expression with necrosis

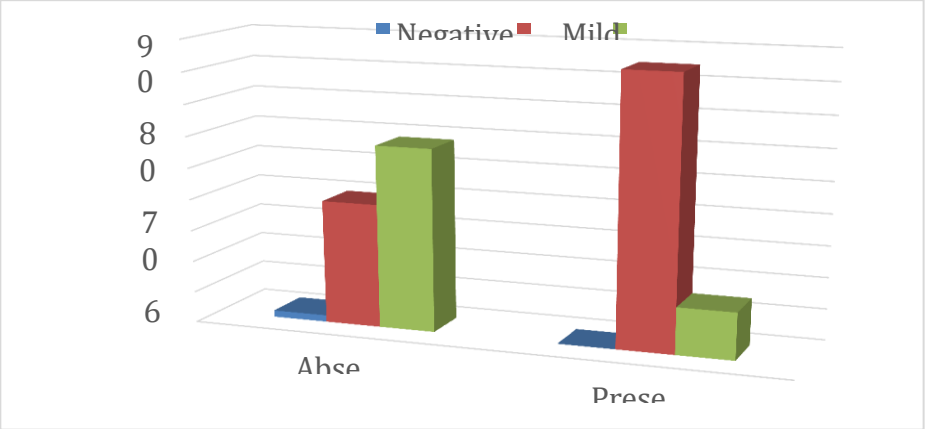
© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

	Negative n (%)	Mild n (%)	Strong n (%)
Absent	1 (2.1)	19 (39.6)	28 (58.3)
Present	0 (0.0)	17 (85.0)	3 (15.0)

p value: 0.003

Necrosis showed a statistically significant association with GATA3 expression (Pearson chi-square test, p = 0.003). In tumors without necrosis, strong GATA3 expression was more common (58.3%), whereas tumors with necrosis predominantly showed mild expression (85.0%). Therefore, presence of necrosis was associated with lower GATA3 expression

Graph 5. Graph showing Association of GATA3 expression with necrosis



6. DISCUSSION

The present study evaluated GATA-3 expression in urothelial neoplasms and demonstrated that it is strongly expressed in the majority of cases, with significant associations observed with tumor grade, invasion, nuclear pleomorphism, mitotic activity, necrosis, and tumor infiltrating lymphocytes. These findings support the idea that GATA3 is not just a diagnostic marker, but also reflects tumor differentiation and overall biological behavior. The results of the present study are discussed below in comparison with previously published studies.

Age Distribution

In the present study, most patients belonged to the sixth and seventh decades of life with peak incidence in the 61-70 years age group. This is in line with global epidemiological data reported by Antoni et al. [1] and Sung et al. [21], which show that the incidence of bladder cancer increases with age.

Similar findings were reported by Gupta et al. [6], who observed that bladder cancer commonly affects individuals in the 6th to 7th decades and that older patients tend to present with more aggressive disease. The findings of the present study closely match with these findings suggesting that the study population follows the typical age pattern seen in urothelial carcinoma.

This age distribution can be explained by prolonged exposure to carcinogens such as tobacco and occupational chemicals over time [23–25]. In addition, molecular studies have shown that urothelial carcinogenesis occurs due to gradual accumulation of genetic alterations [21]. Hence, the findings of this study are consistent with both epidemiological and molecular evidence.

Gender Distribution

The present study showed a clear male predominance, which is consistent with previous studies. Burger et al. [23] and Cumberbatch et al. [26] have reported that bladder cancer is more common in males mainly due to higher exposure to environmental and occupational risk factors.

Similarly, Gupta et al. [6] also observed male predominance and attributed it to smoking and occupational exposure. The findings of the present study are in agreement with these observations.

This male predominance may be due to a combination of factors like greater exposure to carcinogens, hormonal influences and genetic susceptibility [23–25]. Overall, the gender distribution in this study follows the well-established

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

epidemiological pattern.

Histopathological Spectrum:
In the present study, papillary urothelial carcinoma was the most common histological type. This is in accordance with the WHO 2016 classification [12], which identifies conventional urothelial carcinoma as the most common subtype.

Studies by Lopez-Beltran et al. [9] and Lobo et al. [8] have also reported that conventional urothelial carcinoma constitutes the majority of cases while those with histologic subtypes are less common but clinically significant due to their aggressive nature. In this study, only a small proportion of variant histologies were seen.

Thus the histopathological findings of this study are in keeping with the known spectrum of urothelial neoplasms.

GATA-3 Expression:
GATA3 is a transcription factor that plays an important role in cellular differentiation and lineage specification [17]. Its role in urothelial differentiation has been well documented by Higgins et al. [15] and Chou et al. [17].

In the present study, a high overall positivity (approximately 98%) was observed. This is similar to the findings of Liu et al. [38], Chang et al. [39], and Miettinen et al. [42], who also reported high sensitivity of GATA3 in urothelial carcinoma. Plage et al. [41] have shown that reduced or loss of GATA3 expression is associated with tumor progression. This supports the findings of the present study where lower expression was noted in more aggressive tumors.

Therefore, both high positivity and variation in staining intensity seen in this study are well supported by previous research.
GATA-3 Positivity in Urothelial Carcinoma – Present study in comparison with previous studies

Tumor Grade and GATA-3:
This study showed a statistically significant association between GTA3 expression and tumor grade. Strong expression was mainly seen in low grade tumors whereas reduced expression was noted in high grade tumors. This finding is consistent with Agarwal et al. [37], who reported that GATA3 expression correlates with tumor differentiation and can be used in grading. Similar observations were made by Chandra et al. [43] and Hussain et al. [44], who also reported decreased expression in high grade tumors.

The meta-analysis by Yoo et al. [40] further confirmed the prognostic significance of GATA-3, demonstrating better outcomes in tumors with higher expression.

At the molecular level, studies have shown that low-grade tumors follow a luminal differentiation pathway, characterized by expression of markers such as GATA-3 [63–65]. In contrast, high-grade tumors exhibit genomic instability and loss of differentiation markers [23].

Therefore, the findings of the present study not only corroborate previous studies but also align with current molecular understanding of bladder cancer.

GATA-3 Expression vs Tumor Grade - Present study in comparison with previous studies
Tumor Invasion:
The present study demonstrated reduced GATA-3 expression in invasive tumors, with significant association.
This is consistent with Yoo et al. [40], who reported higher expression in non-muscle-invasive bladder cancer compared to muscle-invasive tumors. Similarly, Plage et al. [41] demonstrated that loss of GATA-3 is associated with tumor progression.

Molecular studies have shown that invasive tumors are associated with basal-like phenotype and epithelial–mesenchymal transition [29, 28]. These tumors typically show reduced expression of luminal markers such as GATA-3.

Thus, the present findings strongly align with both histopathological and molecular evidence.

GATA-3 Expression vs Tumor Invasion - Present study in comparison with previous studies

Nuclear Pleomorphism:
The present study showed that tumors with mild pleomorphism had strong GATA-3 expression, whereas those with severe pleomorphism showed reduced expression.

Although specific studies on nuclear pleomorphism and GATA-3 are limited, this finding is consistent with the general

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

observation that poorly differentiated tumors exhibit loss of lineage-specific markers [22]. Thus, the present study provides additional evidence linking GATA-3 expression with cytological differentiation.

Mitotic Activity:
The present study demonstrated a significant inverse relationship between GATA-3 expression and mitotic activity. While Hussain et al. [44] did not find a significant association, the present study showed a clear correlation. This difference may be due to variation in sample size and tumor characteristics.

Studies on proliferative markers such as Ki-67 [34, 35] have shown that increased proliferation is associated with aggressive tumor behavior. The reduced expression of GATA-3 in highly proliferative tumors observed in the present study supports this concept.

Tumor Necrosis: Comparative Analysis
A significant association between reduced GATA-3 expression and tumor necrosis was observed. Necrosis is a known indicator of aggressive tumor biology and is associated with hypoxia and rapid tumor growth. Molecular pathways such as p53 mutation and PI3K/AKT activation contribute to this phenomenon [33, 30].

Although Hussain et al. [44] did not find a significant association, the present study suggests that GATA-3 expression may reflect tumor aggressiveness more comprehensively.

Tumor Infiltrating Lymphocytes (TILs):
The present study demonstrated a significant association between GATA-3 expression and TILs.

Recent studies have emphasized the role of tumor immune microenvironment in bladder cancer [31, 32]. GATA-3 is known to regulate T-cell differentiation [36], suggesting a possible link between tumor biology and immune response.

However, limited literature is available on this specific association, making this an important contribution of the present study.

When all findings are considered together, a consistent pattern emerges:

Strong GATA-3 expression → well-differentiated, less aggressive tumors

Reduced expression → poorly differentiated, aggressive tumors

7. CONCLUSION

The present study demonstrates that GATA-3 is a highly sensitive immunohistochemical marker for urothelial neoplasms, supporting its utility in establishing urothelial origin, particularly in morphologically challenging and metastatic cases. Reduced GATA-3 expression showed an inverse association with adverse histopathological features, including higher tumour grade, increased mitotic activity, nuclear pleomorphism and necrosis, suggesting a potential association with tumour dedifferentiation and aggressive biological behaviour.

The association between GATA-3 expression and tumour-infiltrating lymphocytes (TILs) further highlights its possible relationship with the tumour microenvironment and warrants further investigation.

Overall, GATA-3 is a valuable diagnostic marker with potential prognostic significance in urothelial neoplasms. Further studies incorporating molecular analysis are required to elucidate its role in tumour progression and biology.

REFERENCES

[1] Antoni S, Ferlay J, Soerjomataram I, Znaor A, Jemal A, Bray F. Bladder cancer incidence and mortality: A global overview and recent trends. Eur Urol. 2017;71(1):96-108.
[2] Wu XR. Urothelial tumorigenesis: A tale of divergent pathways. Nat Rev Cancer. 2005;5(9):713-725.
[3] Knowles MA, Hurst CD. Molecular biology of bladder cancer: New insights into pathogenesis and clinical diversity. Nat Rev Cancer. 2015;15(1):25-41.
[4] Richters A, Aben KKH, Kiemeney LALM. The global burden of urinary bladder cancer: An update. World J Urol. 2020;38(8):1895-1904.
[5] Rabbani F, Cordon-Cardo C. Mutation of cell cycle regulators and their impact on superficial bladder cancer. Urol Clin North Am. 2000;27(1):83-102.
[6] Gupta P, Jain M, Kapoor R, Muruganandham K, Srivastava A, Mandhani A. Impact of age and gender on the

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

clinicopathological characteristics of bladder cancer. Indian J Urol. 2009;25(2):207-210.
[7] Mishra V, Balasubramaniam G. Urinary bladder cancer and its associated factors—An epidemiological overview. Indian J Med Sci. 2021;73(2):239-248.
[8] Lobo N, Shariat SF, Guo CC, et al. What is the significance of variant histology in urothelial carcinoma? Eur Urol Focus. 2020;6(4):653-663.
[9] Lopez-Beltran A, Henriques V, Montironi R, Cimadamore A, Raspollini MR, Cheng L. Variants and new entities of bladder cancer. Histopathology. 2019;74(1):77-96.
[10] Babjuk M, Burger M, Compérat EM, et al. European Association of Urology guidelines on non-muscle-invasive bladder cancer (TaT1 and carcinoma in situ)—2019 update. Eur Urol. 2019;76(5):639-657.
[11] Matsumoto H, Shiraishi K, Azuma H, et al. Clinical practice guidelines for bladder cancer 2019 update by the Japanese Urological Association: Summary of the revision. Int J Urol. 2020;27(9):702-709.
[12] Humphrey PA, Moch H, Cubilla AL, Ulbright TM, Reuter VE. The 2016 WHO classification of tumours of the urinary system and male genital organs—Part B: Prostate and bladder tumours. Eur Urol. 2016;70(1):106-119.
[13] Ploeg M, Aben KKH, Kiemeney LALM. The present and future burden of urinary bladder cancer in the world. World J Urol. 2009;27(3):289-293.
[14] Han H, Wolf EM, Liang G. Epigenetic alterations in bladder cancer and their potential clinical implications. Adv Urol. 2012;2012:546917.
[15] Higgins JP, Kaygusuz G, Wang L, Montgomery K, Mason V, Zhu SX, et al.
[16] Placental S100 (S100P) and GATA3: Markers for transitional epithelium and urothelial carcinoma discovered by complementary DNA microarray. Am J Surg Pathol. 2007;31(5):673-680.
[17] Esheba GE, Longacre TA, Atkins KA, Higgins JP. Expression of the urothelial differentiation markers GATA3 and placental S100 (S100P) in female genital tract transitional cell proliferations. Am J Surg Pathol. 2009;33(3):347-353.
[18] Chou J, Provot S, Werb Z. GATA3 in development and cancer differentiation: Cells GATA have it. J Cell Physiol. 2010;222(1):42-49.
[19] Yagi R, Zhu J, Paul WE. An updated view on transcription factor GATA3-mediated regulation of Th1 and Th2 cell differentiation. Int Immunol. 2011;23(7):415-420.
[20] Sellheyer K, Krahl D. Expression pattern of GATA-3 in embryonic and fetal human skin suggests a role in epidermal and follicular morphogenesis. J Cutan Pathol. 2010;37(3):357-361.
[21] Song H, Suehiro J, Kanki Y, Kawai Y, Inoue K, Daida H, et al. Critical role for GATA3 in mediating Tie2 expression and function in large vessel endothelial cells. J Biol Chem. 2009;284(43):29109-29124.
[22] Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2021;71(3):209-249.
[23] Mathur P, Sathishkumar K, Chaturvedi M, Das P, Sudarshan KL, Santhappan S, et al. Cancer statistics, 2020: Report from National Cancer Registry Programme, India. JCO Glob Oncol. 2020;6:1063-1075.
[24] Burger M, Catto JWF, Dalbagni G, Grossman HB, Herr H, Karakiewicz P, et al.
[25] Epidemiology and risk factors of urothelial bladder cancer.Eur Urol.2013;63(2):234-241.
[26] Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Gobal cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide. CA Cancer J Clin. 2018;68(6):394-424.
[27] Cumberbatch MGK, Rota M, Catto JWF, La Vecchia C. The role of tobacco smoke in bladder and kidney carcinogenesis: A comparison of exposures and meta-analysis of incidence and mortality risks. Eur Urol. 2016;70(3):458-466.
[28] Cumberbatch MGK, Cox A, Teare D, Catto JWF. Contemporary occupational carcinogen exposure and bladder cancer: A systematic review and meta-analysis. JAMA Oncol. 2015;1(9):1282-1290.
[29] Li Y, Yang K, Li K, et al. Clinical and molecular characteristics of bladder urothelial carcinoma subtypes. J Cell Biochem. 2019;120(6):9956-9963.
[30] Guo CC, Bondaruk J, Yao H, et al. Assessment of luminal and basal phenotypes in bladder cancer. Sci Rep. 2020;10(1):9743.
[31] Fong MHY, Feng M, McConkey DJ, Choi W. Update on bladder cancer molecular subtypes. Transl Androl Urol. 2020;9(6):2881-2889.
[32] Chen K, Xing J, Zhang YL, et al. Research progress of PI3K/AKT/mTOR pathway inhibitors in bladder cancer. Chin J Cancer Med. 2023;31(3):575-579.
[33] Wang C, Xu Z, Li W, Jiao Y, et al. Analysis of the correlation between E2F3 expression and the number of tumor-infiltrating CD8+ T cells in invasive bladder cancer tissues. Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi. 2018;34(1):1-8.
[34] Sharifi L, Nowroozi MR, Amini E, et al. A review on the role of M2 macrophages in bladder cancer: Pathophysiology and targeting. Int Immunopharmacol. 2019;76:105880.
[35] Petitjean A, Achatz MI, Borresen-Dale AL, et al. TP53 mutations in human cancers: Functional selection and impact on cancer prognosis and outcomes. Oncogene. 2007;26:2157-2165.
[36] Quintero A, Alvarez-Kindelan J, Luque RJ, et al. Ki-67 MIB-1 labelling index and the prognosis of primary TaT1

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

urothelial carcinoma of the bladder. J Clin Pathol. 2006;59(1):83-88.
[37] Margulis V, Shariat SF, Ashfaq R, et al. Ki-67 is an independent predictor of bladder cancer outcome in patients treated with radical cystectomy for organ-confined disease. Clin Cancer Res. 2006;12(24):7369-7373.
[38] Yu Q, et al. T cell factor 1 initiates the T helper type 2 fate by inducing the transcription factor GATA-3 and repressing interferon-γ. Nat Immunol. 2009;10(9):992-999.
[39] Goswami R, et al. STAT6-dependent regulation of Th9 development. J Immunol.
[40] 2012;188(3):968-975.
[41] Liu H, Shi J, Wilkerson ML, Lin F. Immunohistochemical evaluation of GATA3 expression in tumors and normal tissues. Am J Clin Pathol. 2012;138(1):57-64.
[42] Chang A, Amin A, Gabrielson E, Illei P, Roden RB, Sharma R, et al. Utility of GATA3 immunohistochemistry in the diagnosis of urothelial carcinoma. Hum Pathol. 2012;43(11):1963-1968.
[43] Yoo D, Kim K, Kim JH. Diagnostic and prognostic significance of GATA3 expression in urothelial carcinoma: A systematic review and meta-analysis. Medicina (Kaunas). 2023;59(8):1452.
[44] Plage H, et al. Loss of GATA3 expression is associated with progression in urothelial carcinoma. Pathol Res Pract. 2022;229:153702.
[45] Miettinen M, McCue PA, Sarlomo-Rikala M, Rys J, Czapiewski P, Wazny K, et al. GATA3: A multispecific but potentially useful marker in surgical pathology—A systematic analysis of 2500 epithelial and non-epithelial tumors. Am J Surg Pathol. 2014;38(1):13-22.
[46] Chandra K, Mishra A, Singh SK, Kumar N, Upadhyay R, Kumar U, et al. Role of GATA-3 expression in urothelial carcinoma and its correlation with p53 by immunohistochemistry. J Datta Meghe Inst Med Sci Univ. 2023;18(3):392-397.
[47] Hussain NA, Kehiosh HJ. Correlation of GATA3 expression with histopathological parameters in patients with urothelial carcinoma. World J Adv Healthc Res. 2023;7(3):101-107.

IMAGES:



Figure 1. Radical cystectomy specimen showing a solid, grey white mass measuring 3.8x3x2cm

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

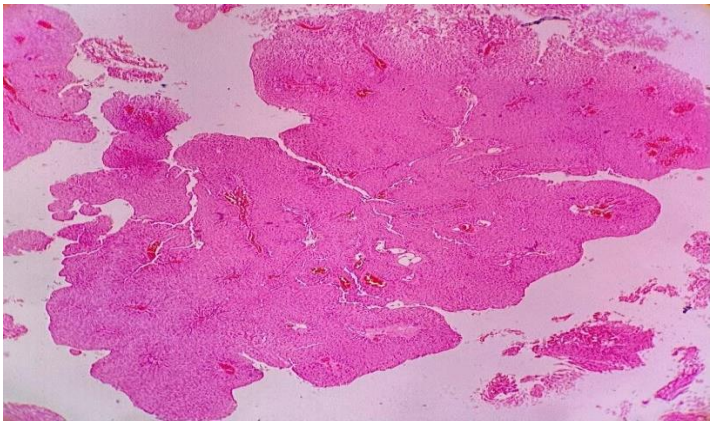


Figure 2. Photomicrograph showing Papillary Architecture in Low-Grade Urothelial Carcinoma (H&E, 4×)

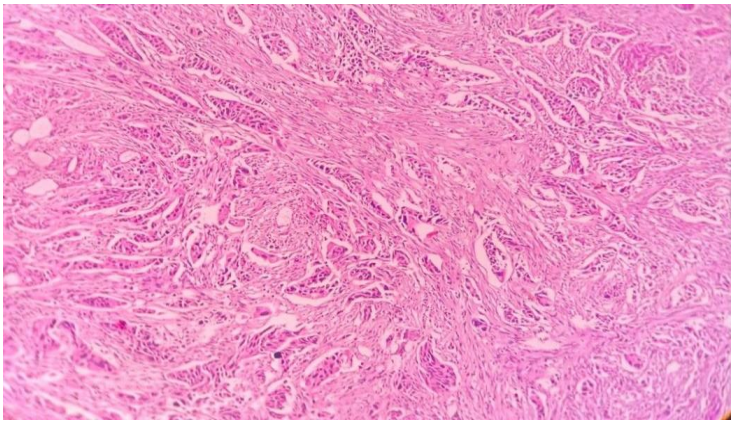


Figure 3. Photomicrograph Demonstrating Lamina Propria Invasion by Urothelial Carcinoma (H&E, 10×)

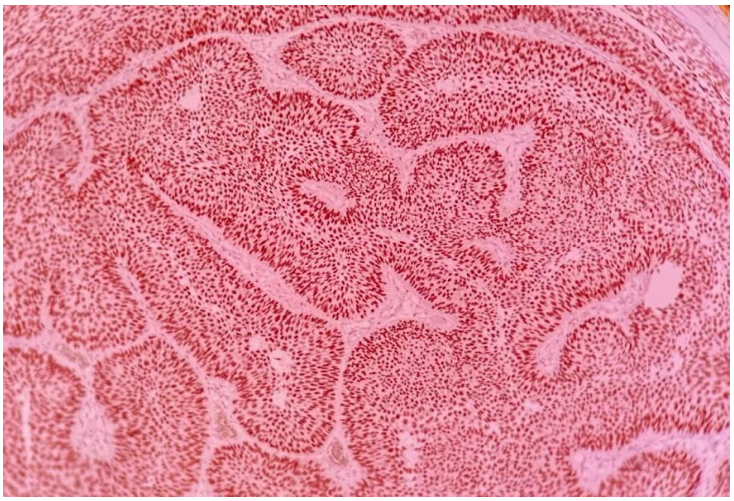


Figure 4. Photomicrograph of Low-Grade Papillary Urothelial Carcinoma Showing Strong Nuclear GATA3 Positivity in >90% Tumor Cells (10x)

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow

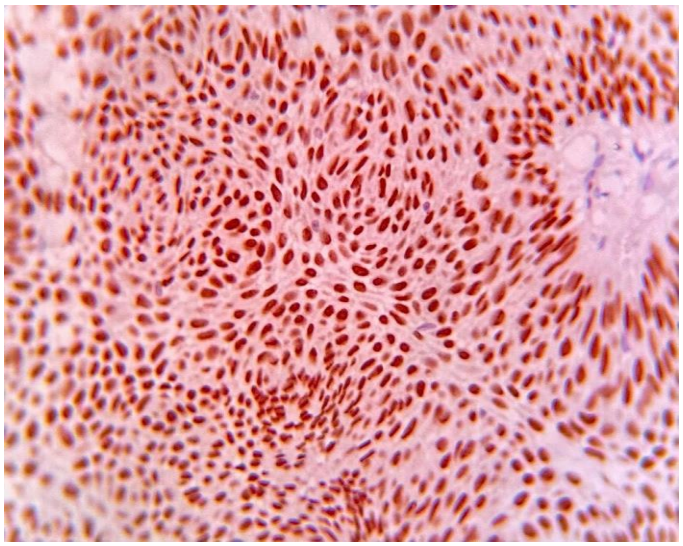


Figure 5. Photomicrograph of Low-Grade Papillary Urothelial Carcinoma Showing Strong Nuclear GATA3 Positivity in >90% Tumor Cells (40x)

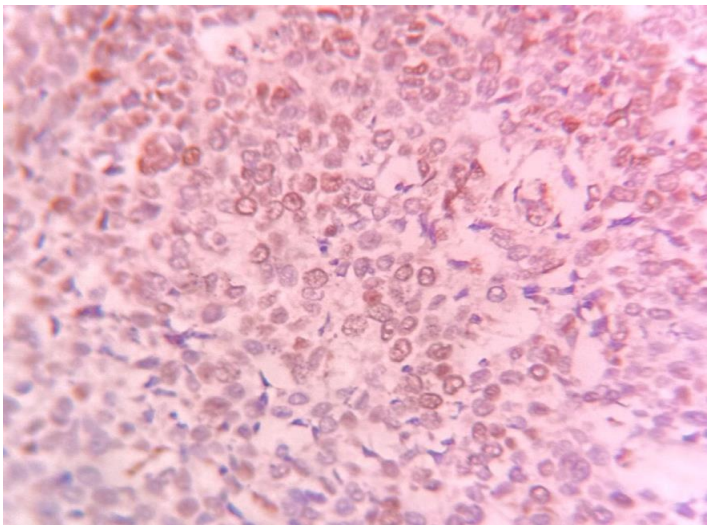


Figure 6. Photomicrograph of High-Grade Papillary Urothelial Carcinoma Showing Moderate Nuclear GATA3 Positivity in 40% Tumor Cells (40x)

© 2026 Journal of Carcinogenesis | Published for Carcinogenesis Press by Wolters Kluwer-Medknow