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Original Research Article

Ki-67 Immunohistochemical Expression as a Predictive Marker in Urinary Bladder Cancer: A Cross-Sectional Study from a Tertiary Care Centre in Jharkhand, India

Shivani Keshri[1], Sunil Kumar Mahto[2], Anshu Jamaiyar[3], Manoj K. Paswan[4]

[1,2,3,4]Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand, India

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Corresponding author: Dr. Shivani Keshri

Conflict of interest: Nil

Abstract

Background: Urinary bladder cancer (UBC) shows variable clinical behavior despite similar histopathology. Ki-67 is a proliferation marker, but its predictive role in Indian populations, especially eastern India, is understudied.

Methods: A cross-sectional study was conducted over 18 months in 54 histologically confirmed UBC cases. Ki-67 immunohistochemistry was performed, and the labeling index (LI) was calculated. Ki-67 LI ≥20% was considered high. Associations with clinicopathological parameters were analyzed using Chi-square test (SPSS v27).

Results: Mean age was 60.8 years; 70% were male; 67% used tobacco. Non-muscle invasive bladder cancer (NMIBC) comprised 65%; high-grade tumors 72%. Mean Ki-67 LI was 33.5% (SD 23.47); 57% had high Ki-67. No statistically significant association was found between Ki-67 expression and gender, tobacco use, cancer type (NMIBC vs MIBC), tumor grade, multicentricity, CIS, lymph node status, prior BCG therapy, or surgery type ($p > 0.05$ for all).

Conclusion: Although Ki-67 expression was elevated in a majority of UBC patients, it did not correlate with conventional clinicopathological variables in this cohort. Larger prospective studies with standardized cut-offs and longer follow-up are needed to validate Ki-67 as an independent predictive marker.

Keywords: Ki-67, Urinary Bladder Cancer, Immunohistochemistry, Proliferation Marker, Predictive Marker, India.

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Introduction

Bladder cancer is the 10th most common cancer worldwide, with an estimated 573,000 new cases and 212,000 deaths annually (Sung et al., 2021). In India, it ranks among the top 20 cancers in males, with tobacco use being the predominant risk factor. Jharkhand, an eastern Indian state with significant industrial and mining activity, lacks region-specific data on bladder cancer biomarkers.

Histopathological staging and grading remain the gold standards for prognostication, but interobserver variability and biological heterogeneity limit their accuracy. Ki-67 is a nuclear protein expressed in all active phases of the cell cycle (G1, S, G2, M) but absent in G0, making it a reliable proliferation marker.

Meta-analyses have shown that high Ki-67 expression correlates with poor survival in bladder cancer (Tian et al., 2016), but results vary due to non-standardized cut-offs, scoring methods, and population differences. There is a paucity of Ki-67 data from eastern India. This study aimed to evaluate Ki-67 expression in histologically confirmed UBC and correlate it with clinicopathological parameters in a tertiary care centre in Jharkhand.

Materials and Methods

Study design and setting: Cross-sectional, observational study conducted over 18 months (2023–2025) in the Department of Pathology, Rajendra Institute of Medical Sciences (RIMS), Ranchi, in collaboration with the Department of Urology.

Participants: Fifty-four adult patients with histologically confirmed primary urinary bladder carcinoma were included. Exclusion criteria: pediatric patients, prior chemotherapy/ radiotherapy, other primary malignancies, inadequate tissue, incomplete clinical records.

Tissue processing and IHC: Formalin-fixed, paraffin-embedded (FFPE) tissue sections (3–4 µm) were stained with H&E for histopathological evaluation. Ki-67 immunostaining was performed using the Novolink™ Polymer Detection System (Leica Microsystems) with MIB-1 antibody.

Antigen retrieval was done using Tris-EDTA buffer (pH 9.0) in a pressure cooker.

Ki-67 Scoring: Ki-67 labeling index (LI) was calculated as the percentage of positively stained tumor cell nuclei among at least 200 tumor cells in high-power fields (×400). A cut-off of ≥20% was used to define "high" Ki-67 expression, based on previous literature.

Statistical Analysis: Data were analyzed using SPSS version 27.0. Associations between Ki-67 categories and categorical variables were tested using Chi-square test. $P < 0.05$ was considered statistically significant.

Results

Tables 1: Demographic and clinical profile

Parameter	**N (%)**
Gender	
Male	38 (70)
Female	16 (30)
Tobacco use	
Yes	36 (67)
No	18 (33)
Cancer type	
NMIBC	35 (65)
MIBC	19 (35)
Tumor grade	
Low grade	15 (28)
High grade	39 (72)
Multicentricity	Multiple: 33 (61)
CIS present	13 (24)
Lymph node positive	9 (17)
Prior BCG	38 (70)
TURBT (vs radical cystectomy)	52 (96)

Mean age: 60.8 ± 12.09 years.

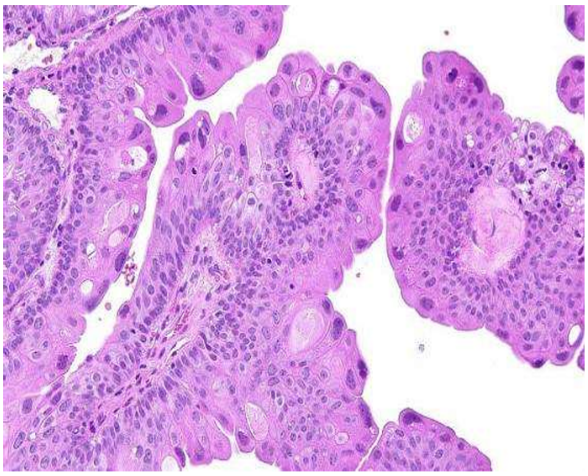
Ki-67 expression

- Mean Ki-67 LI: 33.5% (SD 23.47, range 5–85%)
- High Ki-67 (≥20%): 31 patients (57%)
- Low Ki-67 (<20%): 23 patients (43%)

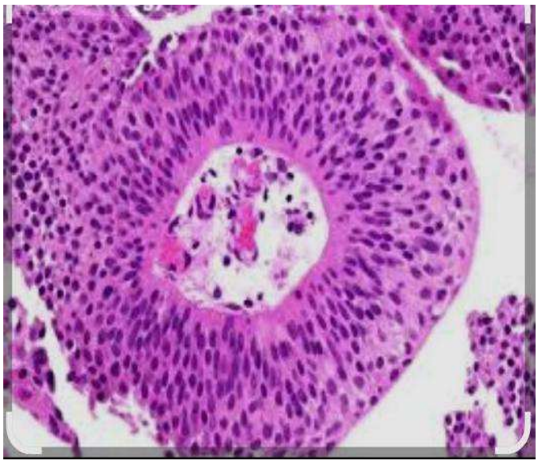
Tables 2: Association between Ki-67 and clinicopathological variables (Table 3)

Variable	**p-value (Chi-square)**
Gender	0.623
Tobacco use	0.846
Cancer type (NMIBC vs MIBC)	0.957
Tumor grade (low vs high)	0.322
Multicentricity	0.551
CIS	0.322
Lymph node status	0.902
Prior BCG	0.090
Surgery type	0.214

No variable showed a statistically significant association with Ki-67 expression (all p > 0.05).



Urothelial papilloma with umbrella cells showing degenerative atypia.



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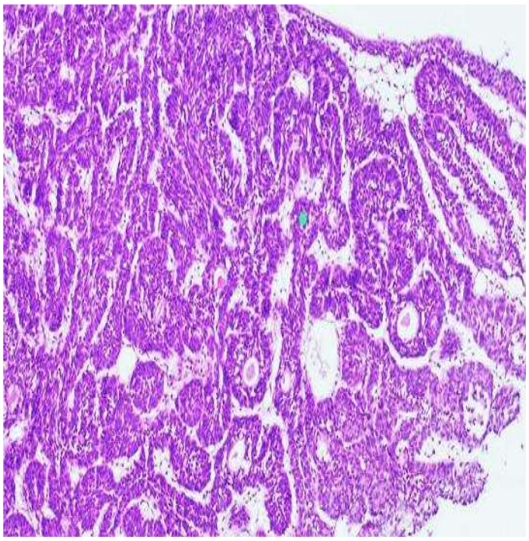
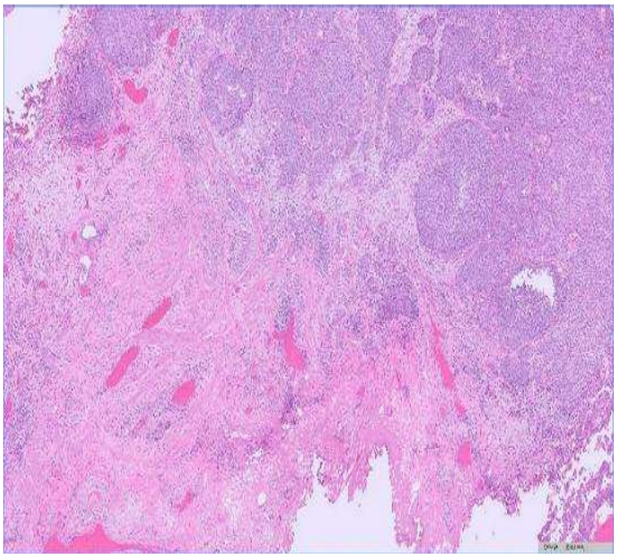
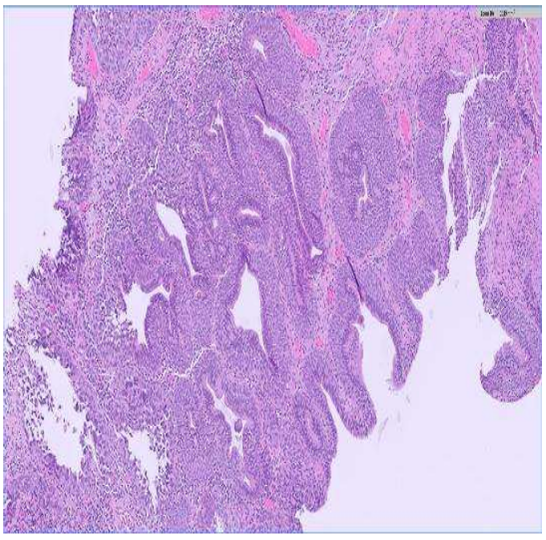


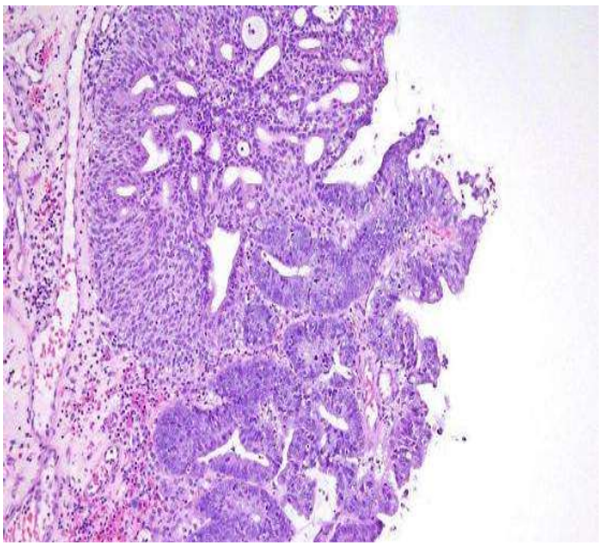
Inverted urothelial papilloma



High Grade Urothelial Ca, Invading Lamina Propria



Urothelial carcinoma in situ (CIS) colonizing cystitis cystica glandularis



Adenocarcinoma ,in situ bladde

Figure 1: Representative H&E images – low-grade and high-grade urothelial carcinoma.

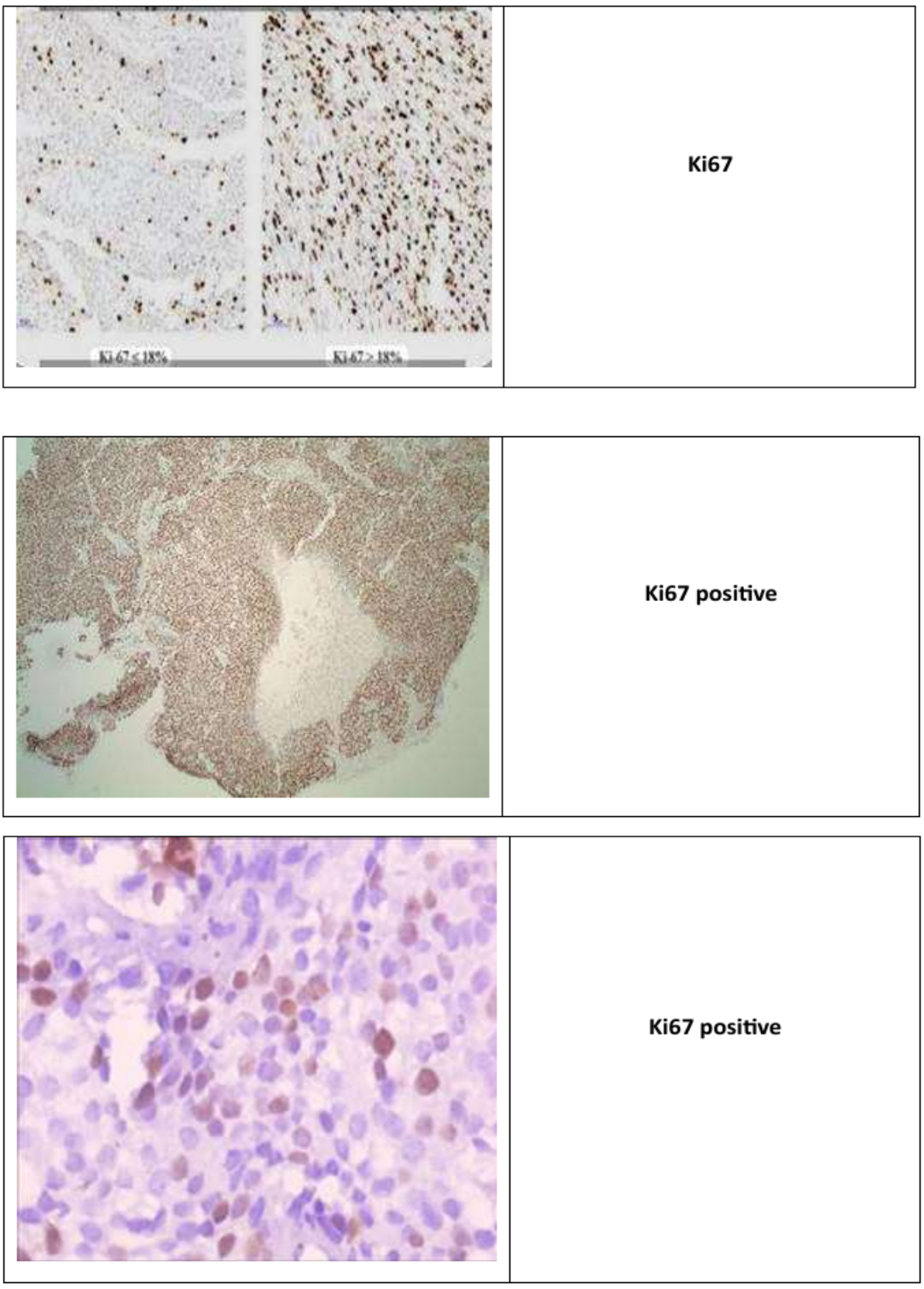


Figure 2: Ki-67 immunohistochemistry – low expression vs high expression

Discussion

This is one of the first studies from Jharkhand, eastern India, evaluating Ki-67 expression in urinary bladder carcinoma and its correlation with standard clinicopathological parameters. Our cohort's demographic profile (older males, high tobacco use) mirrors global and Indian bladder cancer epidemiology. The predominance of NMIBC (65%) and high-grade tumors (72%) suggests that despite early diagnosis in many, aggressive biology exists in a significant proportion.

The mean Ki-67 LI (33.5%) and proportion with high Ki-67 (57%) are comparable with previous Indian studies (Gupta et al., 2018; Singh et al., 2017) and meta-analyses (Tian et al., 2016).

However, contrary to several published reports, we found no statistically significant association between Ki-67 expression and tumor grade, stage (NMIBC vs MIBC), lymph node status, or other variables.

Possible explanations for lack of association:

1. **Sample size (n=54)** – limited statistical power to detect modest differences.
2. **Cross-sectional design** – captures only a snapshot; no longitudinal follow-up for recurrence/progression.
3. **Cut-off variability** – lack of universally accepted Ki-67 threshold (used ≥20% here; others use 10%, 15%, or 25%).
4. **Tumor heterogeneity** – manual scoring in hotspot areas may not reflect whole tumor biology.
5. **High prevalence of high-grade tumors (72%)** – may have reduced discriminatory power between grade categories.
6. **Prior BCG therapy (70%)** – might have altered Ki-67 expression at the time of sampling.

Our findings align with some cohort studies (Stec et al., 2019) and meta-analyses that note significant heterogeneity and lack of independent predictive value for Ki-67 when adjusted for grade and stage (Tian et al., 2016; Ko et al., 2017).

Clinical implication: Ki-67 alone should not be used as a standalone predictive marker in routine practice without standardization.

It may be more useful as part of a multimarker panel (e.g., Ki-67 + p53) or in combination with digital pathology/AI-based scoring.

Strengths and Limitations

Strengths:

- First tertiary care centre study on Ki-67 in bladder cancer from Jharkhand.
- Strict histopathological confirmation and standardized IHC protocol.
- Systematic evaluation of multiple clinicopathological parameters.

Limitations:

- Small sample size (n=54).
- Short follow-up (max 6 months) – no survival/recurrence analysis.
- Single centre, limits generalizability.
- Manual counting (observer variability).
- Non-standardized Ki-67 cut-off.

Conclusion

In this cohort of 54 urinary bladder cancer patients from Jharkhand, Ki-67 expression was elevated in the majority (57%), but it did not show statistically significant associations with tumor grade, stage, or other clinicopathological variables. While Ki-67 remains a biologically informative proliferation marker, its standalone use as a predictive marker in routine pathology practice requires caution. Larger, prospective, multicentre studies with standardized methodology and long-term follow-up are needed to define its clinical utility in Indian populations.

References

1. Sung H, Ferlay J, Siegel RL, et al. CA Cancer J Clin. 2021;71(3):209-249.
2. Tian Y, Ma Z, Chen Z, et al. PLoS One. 2016;11(7):e0158891.
3. Ko K, Jeong CW, Kwak C, et al. Oncotarget. 2017;8(59):100614-100630.
4. Gupta P, Jain M, Kapoor R, et al. Indian J Pathol Microbiol. 2018;61(4):521-526.
5. Singh V, Sinha RJ, Mehrotra S, et al. J Cancer Res Ther. 2017;13(2):281-286.
6. Margulis V, Lotan Y, Karakiewicz PI, et al. J Natl Cancer Inst. 2009;101(2):114-119.
7. Stec R, Cierniak S, Lubas A, et al. Pathol Oncol Res. 2019;26:1211-1219.
8. Downes MR, van der Kwast TH, Lopez-Beltran A, Cheng L. Histopathology. 2026; 88(1):86-107.