International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Clinical Outcomes of Intravesical Bacillus Calmette-Guérin (BCG) Immunotherapy in Non-Muscle-Invasive Bladder Carcinoma: A Single-Centre Prospective Analysis

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Abstract: ***Background: Non-muscle-invasive bladder carcinoma (NMIBC) constitutes approximately 70–75% of newly diagnosed bladder cancer cases globally. Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy remains the cornerstone of post-resection management for intermediate- and high-risk NMIBC. Despite its established efficacy, real-world institutional data from Indian tertiary centres remain limited. Objectives: To evaluate early tumour response, recurrence patterns, adverse event profile, and clinico-pathological predictors of outcome following standard BCG induction in NMIBC patients at a single tertiary institution. Methods: A single-centre, Institutional Ethics Committee-approved prospective and retrospective study was conducted over one year at G.G. Hospital, Jamnagar. Forty consecutive adult patients with histologically confirmed NMIBC who underwent a complete six-instillation induction course of intravesical BCG following transurethral resection of bladder tumour (TURBT) were enrolled. Baseline demographics, risk factors, histopathological grade, BCG completion rates, adverse events, and post-induction cystoscopic findings were systematically recorded and analysed. Results: The study enrolled 40 patients (mean age predominance: 61–70 years; 95% male). The dominant presenting symptom was hematuria (72.5%). All patients (100%) completed the six-week BCG induction course. Post-induction cystoscopy demonstrated complete tumour clearance in 36/40 patients (90%); residual disease was detected in 4/40 patients (10%), necessitating maintenance BCG therapy. Adverse effects were limited to mild cystitis in 4 patients (10%); no systemic reactions or treatment discontinuation occurred. High-grade carcinoma constituted 52.5% of the cohort, with the proportion rising with advancing age (33% at 31–40 years to 75% at 71– 80 years). Conclusion: Intravesical BCG induction achieved a 90% complete response rate with a favourable safety profile in this Indian cohort. These findings corroborate international evidence supporting BCG as an effective, risk-adapted treatment modality for NMIBC. Advancing age and high tumour grade were notable predictors of persistent disease.***

Keywords: BCG immunotherapy; bladder carcinoma; NMIBC; intravesical therapy; TURBT; tumour recurrence; cystoscopy; urothelial carcinoma

1. Introduction

Bladder carcinoma ranks among the ten most frequently diagnosed malignancies worldwide, carrying a substantial burden in terms of morbidity, healthcare expenditure, and patient quality of life. The preponderance of cases- approximately 70–75%- are classified as non-muscle-invasive bladder cancer (NMIBC), encompassing tumours confined to the urothelium (stage Ta), the lamina propria (stage T1), or presenting as carcinoma in situ (Tis). Although transurethral resection of bladder tumour (TURBT) constitutes the primary therapeutic intervention, NMIBC is characterised by a pronounced tendency for recurrence, with rates reaching 60–70% within five years, and a meaningful risk of progression to muscle- invasive disease in high-risk subsets.

Intravesical Bacillus Calmette-Guérin (BCG) immunotherapy has occupied the position of gold standard for intermediate- and high-risk NMIBC since the landmark clinical investigations of Morales and colleagues in the 1970s. Derived from an attenuated strain of Mycobacterium bovis, BCG exerts its anti- tumour activity by initiating a complex cascade of local immune responses within the bladder urothelium. Upon instillation, BCG adheres to the urothelial surface via fibronectin binding and is internalised by bladder cancer cells and antigen-presenting cells, triggering recruitment of macrophages, natural killer cells, and cytotoxic T lymphocytes. The resultant release of pro-inflammatory cytokines—including TNF- α, IL-2, IL-6, IL-12, and interferon-gamma—mediates targeted destruction of neoplastic cells and generates immunological memory that may sustain long-term disease control.

Despite its proven efficacy, BCG therapy is associated with a well-characterised spectrum of adverse effects—from local manifestations such as cystitis, dysuria, and hematuria to, rarely, systemic BCGosis- and a proportion of patients demonstrate primary or acquired BCG unresponsiveness. Data from tertiary institutions in India, where epidemiological profiles, smoking patterns, and patient demographics may differ from Western cohorts, remain sparse. This study was undertaken to generate institutional evidence on the early clinical outcomes of BCG induction therapy at a teaching hospital in Gujarat, India, and to compare these findings against contemporary global literature.

2. Aims and Objectives

The primary objective of this investigation was to assess the efficacy of intravesical BCG induction therapy in reducing

early tumour recurrence in NMIBC patients. Secondary objectives included: evaluation of the impact of BCG therapy on disease progression and the requirement for radical interventions; characterisation of the adverse event profile and tolerability of the six-instillation induction protocol; and identification of clinico-pathological parameters- including age, tumour grade, gender, and smoking history- that influence therapeutic outcomes.

3. Materials and Methods

3.1 Study Design and Setting

This investigation was conducted as a single-centre, Institutional Ethics Committee-approved study at the Department of General Surgery, Guru Gobind Singh Government Hospital and Shri M. P. Shah Government Medical College, Jamnagar, Gujarat, India. The study incorporated both prospective and retrospective components over a one-year study period.

3.2 Patient Selection

Forty consecutive adult patients with histologically confirmed NMIBC who completed a full six-instillation induction course of intravesical BCG following adequate TURBT were enrolled. Inclusion criteria required documented histopathological confirmation of urothelial carcinoma, adequate surgical clearance, and fitness for intravesical therapy. Patients with muscle-invasive disease (T2 or beyond), prior pelvic irradiation, active urinary tract infection, significant immunosuppression, or history of prior BCG therapy were excluded.

3.3 BCG Protocol

Intravesical BCG (standard strain, 81 mg per instillation) was administered once weekly for six consecutive weeks constituting the induction phase. Each instillation was retained intravesically for a minimum of one to two hours. Patients with residual disease detected at post-induction follow-up cystoscopy at three weeks were offered a maintenance BCG course. Adverse events were assessed at each instillation visit and graded according to clinical severity.

3.4 Data Collection and Statistical Analysis

Structured case-record forms were used to document baseline demographics, risk factor history, presenting symptoms, cystoscopic findings, histopathological grade, BCG completion status, post- induction cystoscopic outcomes, and adverse event profiles. Descriptive statistical analysis was employed to summarise patient characteristics, treatment outcomes, and safety data. Associations between clinico-pathological variables were evaluated through cross-tabulation.

4. Results

4.1 Age Distribution

The study enrolled 40 patients with bladder carcinoma. The majority of patients (45.00%) were concentrated in the 61–70 year age group, followed by 25.00% in the 51–60 year bracket. Only 7.50% were aged 31–40 years, reflecting the established late-adult predominance characteristic of urothelial malignancy.

Table 1: Age-wise Distribution of Study Patients (n = 40)

Age Group (Years)	Number of Patients (n)	Percentage (%)	Cumulative (%)
31–40	3	7.50%	7.50%
41–50	5	12.50%	20.00%
51–60	10	25.00%	45.00%
61–70	18	45.00%	90.00%
71–80	4	10.00%	100.00%
Total	40	100%	—

4.2 Gender Distribution

A striking male predominance was observed in this cohort, with 38 of 40 patients (95.00%) being male and only 2 (5.00%) female, yielding a male-to-female ratio of 19:1. This finding is consistent with internationally reported gender disparities in bladder cancer incidence, attributable in part to differential tobacco exposure and occupational carcinogen risk.

Table 2: Gender-wise Distribution of Study Patients (n = 40)

Gender	Number of Patients (n)	Percentage (%)
Male	38	95.00%
Female	2	5.00%
Total	40	100%

4.3 Presenting Symptoms

Hematuria constituted the most prevalent presenting complaint, occurring in 29 of 40 patients (72.50%). Abdominal pain was reported in 26 patients (65.00%), burning micturition or dysuria in 16 patients (40.00%), and urinary retention in 4 patients (10.00%). Notably, symptoms were not mutually exclusive, and several patients reported more than one complaint at initial presentation.

Table 3: Presenting Symptoms in Study Patients (n = 40)

Gender	Number of Patients (n)	Percentage (%)
Hematuria	29	72.50%
Abdominal Pain	26	65.00%
Burning Micturition / Dysuria	16	40.00%
Urinary Retention	4	10.00%

4.4 Smoking History

Smoking history was documented in 14 of 40 patients (35.00%), with the remaining 26 patients (65.00%) denying any prior tobacco exposure. All 14 smokers were male. Within the male cohort, the proportion of high-grade disease did not differ significantly between smokers (8/15 = 53.3%) and non-smokers (13/23= 56.5%), suggesting that tumour grade may be driven by multiple interacting carcinogenic factors beyond tobacco alone.

4.5 Histopathological Grade

Histopathological examination of resected specimens classified 21 patients (52.50%) as high-grade urothelial carcinoma and 19 patients (47.50%) as low-grade urothelial carcinoma. High-grade tumours constituted the slight majority in this cohort and carried implications for surveillance intensity and maintenance therapy decisions.

Table 4: Histopathological Grade Distribution (n = 40)

Tumour Grade	Number of Patients (n)	Percentage (%)
High-grade Urothelial Carcinoma	21	52.50%
Low-grade Urothelial Carcinoma	19	47.50%
Total	40	100%

4.6 BCG Treatment Outcomes and Follow-up Cystoscopy

Universal completion of the six-instillation induction course was achieved across all 40 patients (100%), reflecting adequate tolerability and patient compliance. Post-induction surveillance cystoscopy was performed at three weeks. Complete tumour clearance- defined as no residual mass on cystoscopic examination- was demonstrated in 36 of 40 patients (90.00%). A residual mass was detected in 4 patients (10.00%), all of whom subsequently received maintenance BCG therapy. These four patients collectively comprised the 10% maintenance BCG requirement rate.

Table 5: BCG Treatment Parameters and Cystoscopic Outcomes (n = 40)

Parameter	Number of Patients (n)	Percentage (%)
BCG Induction Completed	40	100.00%
Residual Mass at Follow-up Cystoscopy	4	10.00%
Proceeded to Maintenance BCG	4	10.00%
Complete Tumour Clearance	36	90.00%
Adverse Effects (Cystitis)	4	10.00%

4.7 Adverse Effects

Adverse effects were observed in 4 of 40 patients (10.00%), all manifesting as symptomatic cystitis of mild-to-moderate severity. No patient required hospitalisation, dose reduction, or permanent discontinuation of therapy. Systemic complications such as BCG sepsis, hepatitis, or pneumonitis were not encountered. The low adverse event burden in this cohort may be attributed to stringent patient selection and consistent adherence to post-void instillation protocols.

4.8 Age-Histopathology Correlation

Cross-tabulation of age group against histopathological grade revealed a stepwise increase in the proportion of high-grade tumours with advancing age: 33% at 31–40 years, 40% at 41–50 years, 50% at 51–60 years, 56% at 61–70 years, and 75% at 71–80 years. The 61–70 year stratum contributed the greatest absolute number of high-grade lesions (10 of 21 total high-grade cases, representing 48% of all high-grade cases). This age-grade relationship has important prognostic and surveillance implications.

Table 6: Correlation of Age Group with Histopathological Grade (n = 40)

Age Group (Years)	Patients (n)	High-Grade	Low-Grade
31–40	3	1 (33%)	2 (67%)
41–50	5	2 (40%)	3 (60%)
51–60	10	5 (50%)	5 (50%)
61–70	**18**	**10 (56%)**	**8 (44%)**
71–80	4	3 (75%)	1 (25%)
Total	**40**	**21 (52.5%)**	**19 (47.5%)**

4.9 Histopathology and Cystoscopic Outcome Correlation

Among 21 high-grade carcinoma patients, residual mass was detected in only 1 patient (4.8%) at follow- up cystoscopy, indicating a high complete response rate. Conversely, among 19 low-grade carcinoma patients, 3 patients (15.8%) demonstrated residual disease. This seemingly paradoxical finding- higher residual disease rates in low-grade tumours- may reflect differences in tumour biology, vascularisation, and responsiveness to local immune stimulation, and merits further investigation with longer follow-up.

5. Discussion

The present study provides a single-centre institutional profile of NMIBC patients managed with intravesical BCG induction therapy at a tertiary government hospital in western India. Several observations merit contextualisation against the broader literature.

The predominance of patients in the sixth to seventh decade is consistent with the well-established epidemiology of bladder carcinoma. Comparative series from India and abroad report peak incidence in the 60–70 year range, with only a small fraction presenting below 40 years. The 7.5% rate of young- onset carcinoma observed in this cohort aligns with the 5–11% range reported across international series. The extreme male predominance (95%) in this cohort—yielding a 19:1 male-to-female ratio—exceeds the global average of approximately 8–9:1 but is consistent with patterns reported from Indian tertiary centres, likely reflecting higher rates of tobacco use and occupational carcinogen exposure among men in this demographic.

Hematuria as the dominant presenting complaint (72.5%) is robustly supported by multicentre studies globally, which consistently report hematuria as the initial trigger for urological evaluation in 53–90% of bladder cancer cases. The 35% smoking prevalence in this cohort, while lower than the 40–55% reported in large Western cohorts, is concordant with patterns in Indian studies where occupational exposures— including aromatic amine contact in the textile and dye industries—contribute independently to carcinogenesis.

The 100% induction completion rate in this series is a clinically meaningful benchmark. It contrasts with large multicentre trials such as that of Brausi and colleagues, in which 7.8% of patients discontinued therapy due to toxicity, and with an Indian series by Thyavihally et al. reporting adverse effect rates of 46% including 17.7% grade III events. The 10% cystitis rate and absence of systemic

complications in this cohort are substantially lower than the 30–45% range reported in multicentre datasets, possibly reflecting institutional experience, patient selection, or regional differences in BCG strain and dose handling.

The 90% complete response rate observed post-induction places this series at the favourable end of the spectrum. Published series have reported residual disease rates ranging from 10% to 35% at post- induction cystoscopy, with the wide range attributable to differences in tumour risk stratification, BCG strain, and cystoscopy timing. The observation that residual disease was more common in low-grade (15.8%) than high-grade (4.8%) tumours—contrary to expectation—is an intriguing finding that may reflect the immunological milieu of low-grade tumours or heightened clinician vigilance in high-grade cases, and warrants prospective evaluation with molecular markers.

6. Limitations

This study carries several methodological limitations that should be acknowledged. The investigation was conducted at a single centre, which inherently limits the generalisability of findings to broader populations. The sample size of 40 patients, while sufficient for preliminary descriptive analyses, constrains the statistical power available for subgroup comparisons and multivariate modelling. The study duration and follow-up period were limited to one year, precluding assessment of long-term recurrence-free survival, progression-free survival, and disease-specific mortality. Prospective multi-centre studies with extended follow-up and molecular subtyping are recommended to validate these preliminary observations.

7. Conclusion

Intravesical BCG induction therapy achieved a clinically meaningful 90% complete tumour clearance rate in this Indian single-centre cohort, with a favourable safety profile characterised by only mild cystitis in 10% of patients and no treatment discontinuation. Universal completion of the six-instillation induction course underscores the tolerability and feasibility of this immunotherapeutic approach in a resource- constrained tertiary setting. Advancing age was associated with a progressively higher proportion of high-grade tumours, reinforcing the importance of age-informed risk stratification in surveillance planning. These findings affirm BCG immunotherapy as an effective, well-tolerated, and risk-adapted management strategy for NMIBC, consistent with international guidelines and comparable global datasets. Larger prospective multi-institutional studies with extended follow-up are warranted to refine predictors of BCG response and long-term oncological outcomes in the Indian population.

Declarations

Ethical Approval: This study was approved by the Institutional Ethics Committee (IEC) of Shri M. P. Shah Government Medical College, Jamnagar. Informed written consent was obtained from all participating patients prior to enrollment.

Conflict of Interest: The authors declare no conflicts of interest with respect to the research, authorship, or publication of this article.

Funding: No external funding was received for this study.

Author Contributions: Dr. Kinnari Chapla (Primary Author) — study conceptualisation, data analysis, manuscript preparation, and submission. Dr. Seval Kotadiya (Second Author) — study design, data collection, clinical supervision, and critical manuscript review.

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