



Bladder Cancer in North India: A Comprehensive Analysis of Risk Factor Determinants

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KEYWORDS

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Electromagnetic
radiation

ABSTRACT:

Objective:

To evaluate demographic, lifestyle, occupational, and environmental risk factors associated with bladder cancer and to assess their relationship with tumor grade and stage in a North Indian population.

Methods:

A prospective case-control study was conducted including 100 histopathologically confirmed bladder cancer patients and 100 matched controls. Data on demographic characteristics, lifestyle habits, and occupational and environmental exposures were collected. Tumor grade and stage were analyzed in relation to age and exogenous risk factors. Statistical analysis was performed using odds ratio, relative risk, and Fisher's exact test, with significance set at $p < 0.05$.

Results:

The mean age of patients was 61 ± 11 years, with a male predominance (82%). Low-grade (71%) and early-stage tumors (81%) were most prevalent. However, the proportion of high-grade and advanced-stage tumors increased with advancing age. Smoking, alcohol consumption, drug use, occupational exposure, pesticide exposure, and electromagnetic radiation exposure showed significant associations with bladder cancer risk. Case-only analysis demonstrated that occupational exposure and electromagnetic radiation exposure were significantly associated with high-grade tumors, whereas other exposures showed non-significant increasing trends.

Conclusion:

Bladder cancer in this North Indian cohort is strongly associated with modifiable lifestyle and occupational risk factors, with advancing age contributing to more aggressive disease characteristics. The significant association of occupational and electromagnetic radiation exposure with high-grade tumors highlights emerging risk determinants. These findings emphasize the importance of targeted preventive strategies, improved occupational safety measures, and age-specific surveillance to reduce disease burden.



Introduction

Bladder cancer represents a major global public health concern and is consistently ranked among the ten most frequently diagnosed malignancies of the urinary tract. Recent global estimates indicate that more than 490,000 new cases were diagnosed worldwide in 2022, with marked geographic variation in both incidence and mortality rates, reflecting differences in population demographics, environmental exposures, and healthcare access [1,2]. The disease predominantly affects older individuals and occurs substantially more often in men than in women, with painless hematuria being the most common presenting symptom [3]. Urothelial carcinoma, also referred to as transitional cell carcinoma, constitutes over 90% of bladder cancer cases globally. The development of this malignancy is widely recognized as multifactorial, arising from complex interactions between genetic susceptibility, host metabolic processes, and exogenous environmental exposures [4]. Among these factors, tobacco smoking remains the most firmly established and dominant risk factor, accounting for a substantial proportion of bladder cancer cases through urinary excretion of carcinogenic aromatic amines and related compounds [5,6]. Beyond tobacco exposure, occupational contact with carcinogenic substances has long been implicated in bladder carcinogenesis. Workers exposed to aromatic amines, dyes, solvents, metals, and petroleum derivatives demonstrate significantly elevated risks of developing bladder cancer, even decades after exposure cessation [7]. In parallel, growing attention has been directed toward environmental pollutants, including ambient air contamination. Epidemiological and meta-analytic evidence suggests that long-term exposure to fine particulate matter (PM_{2.5}) and nitrogen dioxide may be associated with modest but measurable increases in bladder cancer risk, highlighting the expanding role of environmental determinants in disease etiology [3]. Despite the extensive global literature, region-specific epidemiological data from Asian populations remain comparatively limited, particularly in contexts where occupational practices, environmental regulations, and lifestyle patterns differ substantially from those in high-income countries. Exposures such as pesticide use, long-term medication or drug intake, and electromagnetic radiation (EMR) have received relatively little attention in bladder cancer research,

especially with respect to their potential influence on tumour aggressiveness and disease progression. Understanding the contribution of these understudied factors within local populations is essential for developing targeted prevention strategies and context-appropriate public health interventions. In this context, the present case-control study evaluated six major exogenous risk factors—smoking, alcohol consumption, drug use, pesticide exposure, occupational exposure, and electromagnetic radiation exposure—in a cohort of bladder cancer patients and matched healthy controls from North India. Statistical analyses, including chi-square testing, relative risk estimation, odds ratio calculation, and 95% confidence interval assessment, were employed to quantify associations between exposures and disease occurrence. The primary objective was to compare exposure prevalence between cases and controls and to rank the relative contribution of these risk factors within the studied population.

Methods

Study design: A prospective study on the prevalence of exogenous and risk factors for bladder cancer was done in the Human Molecular and Cytogenetics Laboratory, Maharshi Dayanand University, Rohtak. All sample subjects were collected from the Department of Urology, Post-graduate Institute of Medical Sciences (PGIMS), Rohtak, Haryana, India from September 2021 to March 2025 of bladder cancer patients. Ethical clearance was obtained from institutional human ethical committees (MDU IHEC approved ref. letter no.-HEC/2021/282). The study was conducted after obtaining signed consent from each patient and healthy control groups who had no prior history of malignancy. The research was conducted in full compliance with the ethical standards outlined in the Declaration of Helsinki.

Study Population and Matching Criteria

The control group consisted of apparently healthy individuals with no prior history of malignancy. Controls were frequency-matched with cases based on age (± 5 years) and sex to minimize confounding effects. Participants in both groups were recruited from the same geographic region to ensure comparability.



Sampling Method

A hospital-based convenience sampling method was employed for the recruitment of both cases and controls. All eligible patients presenting during the study period and fulfilling the inclusion criteria were enrolled consecutively to reduce selection bias.

Selection criteria:

Inclusion criteria: Patients with reported cases of bladder cancer of any stage were included. Patients with recurrent bladder cancer were included.

Exclusion criteria: Patients reported to have any other disease like diabetes; cardiac disorder, arthritis etc. were excluded. Co-morbid disorders were excluded. Patients undergoing chemotherapy, radiotherapy were excluded.

Sample size: 100 patients diagnosed for bladder cancer and 100 normal healthy individuals as control groups were considered as sample size and examined as per ethical guidelines.

Sample Size Justification

The sample size was determined based on feasibility and the availability of eligible participants during the study period. A total of 100 cases and 100 controls were considered adequate to detect statistically significant associations between major risk factors and bladder cancer with acceptable power, as supported by previous epidemiological studies with similar designs.

Formulation of questionnaire

Data was collected by conducting face-to-face interviews with bladder cancer patients and recorded in a predesigned Performa /questionnaire. The questionnaire was formulated after an extensive review of relevant literature to capture demographic, lifestyle, clinical, and environmental exposures associated with bladder cancer. In addition, medical records and diagnostic charts were reviewed to ensure completeness and accuracy of information. The authenticity and reliability of the collected data was carefully ensured.

Contents of questionnaire

The contents of the questionnaire included the following:

General socio-demographic details such as patient's name, father's and mother's names, age at diagnosis,

sex, height, weight, education, address, occupation, parental occupation, socioeconomic status, caste/religion, and rural/urban background.

Associated medical details including history of complications, smoking and alcohol use, schistosomiasis, and presence of any other disease.

Environmental and lifestyle exposures such as occupational exposure to paints, dyes, metals, petroleum products, pesticide exposure, drug history, electromagnetic radiation (EMR) exposure, and other relevant environmental factors.

Clinical details including type of bladder cancer, early versus advanced cancer status, and tumor classification (T1: tumor spread to connective tissue of sub-epithelial cells, T2: muscle invasion, T3: perivesical tissue invasion, T4: invasion of adjacent organs such as prostate, vagina, uterus).

Diagnostic and treatment protocols such as surgical history, cytological findings, radiological evaluation (ultrasound, MRI/CT, tumor markers), and therapies received including chemotherapy, radiotherapy, and surgery. Additional information on medications (e.g., antifungal creams, talc), family history of bladder cancer, and other contributing factors was also documented.

Follow-up and recurrence details, including recurrence of bladder cancer after treatment, time of recurrence (in years or months), and the number of recurrence episodes.

Bias Control

Several measures were implemented to minimize potential biases. Selection bias was reduced by enrolling consecutive eligible participants and recruiting controls from the same source population. Recall bias was minimized by using a structured and pre-validated questionnaire administered through face-to-face interviews. Information bias was further controlled by cross-verification of patient data with medical records wherever available.

Statistical Analysis

Collected and recorded data was managed in Microsoft-Excel Worksheet (Microsoft Corp, Redmond, WA). GraphPad Prism 8.0.1 (244) and SPSS software version



29.0.2.0 (20) for Windows (SPSS Inc., Chicago, IL, USA) were used for all statistical analyses. Socio-demographic details, age of diagnosis, location, were represented in percentage. Pearson chi-square test (testing equality between observed and expected frequencies) was used to analyze the relationship between descriptive variables. The strength of association was assessed using odds ratios (OR) with 95% confidence intervals (CI). A level of significance (p -value) < 0.05 was considered statistically significant. All statistical tests were two-tailed.

Results and Discussion

The study analyzed 100 bladder cancer patients and 100 matched healthy individuals revealing a mean patient age of 61 ± 11 years with a marked male predominance (82%), and a predominantly rural background (70%). Most tumors presented at early-to-intermediate stages, with T2 (43%) and T1 (38%) comprising the majority, while T3 and T4 accounted for 19% of cases; low-grade tumors were more common (71%) than high-grade lesions (29%). Risk factor evaluation demonstrated highly significant associations for smoking (OR 22.67, RR 4.25, $p < 0.0001$), alcohol use (OR 12.00, RR 3.20, $p < 0.0001$), drug use (OR 15.81, RR 6.78, $p < 0.0001$), occupational exposure to chemicals such as dyes and petroleum products (OR 17.54, RR 9.60, $p < 0.0001$), and electromagnetic radiation (OR 9.94, RR 5.63, $p < 0.0001$), while pesticide exposure showed a moderate yet significant association (OR 2.33, RR 1.67, $p = 0.0059$). Peak incidence occurred in the 61–65-year age group, followed by 56–60 years and 51–55 years. Females constituted **18%**, yielding a **male-to-female ratio of approximately 4.5:1** (Table 1).

Table 1. Clinical Profile of Patients

Clinical Profile	Value
Age (years)	61 ± 11
Male	82 (82%)
Female	18 (18%)
Mean duration of	4.5 ± 2.1

symptoms (months)	
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The mean duration of presenting symptoms prior to diagnosis was **4.5 ± 2.1 months**, highlighting a relatively short clinical latency between onset and presentation (Figure 1). Overall, the findings highlight that bladder cancer in this region predominantly affects older rural males, with strong contributions from both traditional (smoking, occupational hazards) and emerging risk factors (drug use, EMR), underscoring critical targets for prevention, early detection, and public health intervention. Importantly, among the evaluated exposures, smoking demonstrated the strongest association with bladder cancer risk, followed by occupational exposure, drug use, electromagnetic radiation exposure, and alcohol consumption, while pesticide exposure showed a comparatively weaker yet statistically significant association. This hierarchical pattern highlights the dominant etiological role of tobacco exposure, alongside the substantial contribution of occupational and environmental risk factors in the studied population.

Tumor Stage and Grade Distribution

The age-wise distribution of tumor grade demonstrated that low-grade tumors constituted the majority across all age groups, accounting for 71% of total cases, while high-grade tumors represented 29% overall. The highest proportion of cases was observed in the 61–65-year age group (23%), comprising 16% low-grade and 7% high-grade tumors. Younger age groups, particularly 40–45 years (7%) and 46–50 years (9%), showed a predominance of low-grade tumors with minimal representation of high-grade lesions. In contrast, older age groups exhibited a relatively higher frequency of high-grade tumors, with notable proportions in the 66–70-year (4%), 71–75-year (4%), and ≥ 76 -year (4%) categories. Overall, the frequency distribution suggests an increasing contribution of high-grade tumors with advancing age, indicating a tendency toward more aggressive disease patterns among older bladder cancer patients (Figure 1).

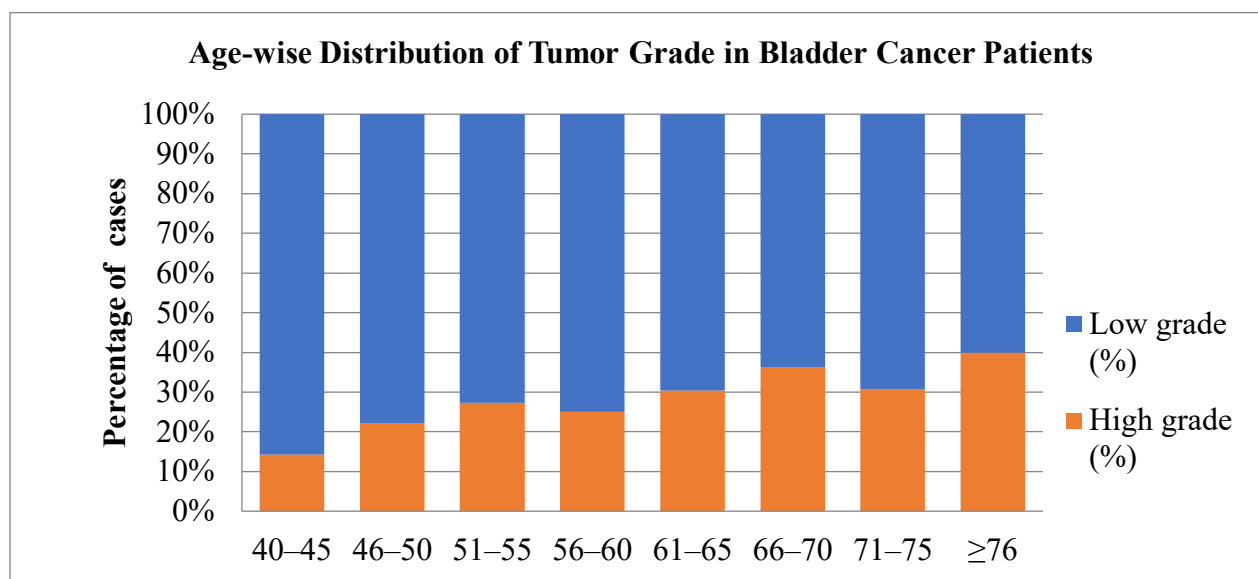


Figure 1. Age-wise distribution of tumor grade among bladder cancer patients.

Stage-wise classification of tumors demonstrated that **Stage T2 disease was most prevalent, observed in 43 patients (43%)**, followed by **Stage T1 in 38 patients (38%)**. Advanced stages were less frequent, with **Stage T3 in 13 patients (13%)** and **Stage T4 in only 6 patients (6%)**. The age-wise distribution of tumor stage showed that early-stage disease (T1–T2) predominated across all age groups, accounting for 81% of the total cases, while advanced-stage disease (T3–T4) constituted 19% overall (**Figure 2**). The highest proportion of cases was observed in the 61–65-year age group (23%), with early-stage tumors comprising 17% and advanced-stage tumors accounting for 6%. Younger

age groups, including 40–45 years (7%) and 46–50 years (9%), demonstrated almost exclusive representation of early-stage disease, with negligible or absent advanced-stage tumors. In contrast, a gradual increase in the frequency of advanced-stage tumors was noted with advancing age, particularly in the 56–60-year (4%), 61–65-year (6%), 66–70-year (3%), and 71–75-year (3%) age groups. Overall, this frequency distribution indicates a tendency toward more advanced-stage presentation among older patients, suggesting an age-related pattern in disease progression (**Figure 2**).

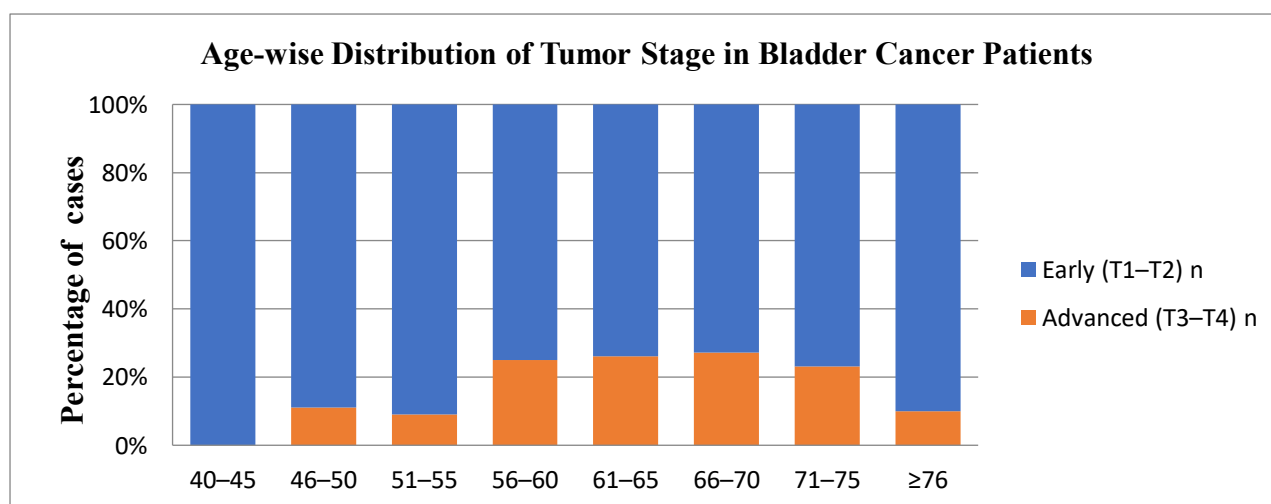




Figure 2. Age-wise distribution of tumor stage among bladder cancer patients.

Risk Factors in Cases and Control Group

The distribution of putative risk factors among cases and control groups is detailed (Table 2). **Cigarette smoking emerged as the most common exposure, present in 85% of patients compared to 20% of control groups.** Alcohol consumption was the second most frequent factor (80% of cases vs. 25% of control

groups), followed by drug use (61% vs. 9%), pesticide exposure (50% vs. 30%), occupational exposure to industrial chemicals such as paints, dyes, metals, and petroleum derivatives (48% vs. 5%), and exposure to electromagnetic radiation (EMR) (45% vs. 8%). Family history was reported in only two cases, precluding meaningful statistical evaluation.

Table 2. Risk Factors among Bladder Cancer Patients (n=100)

Risk Factor	Cases Exposed n (%)	Control groups Exposed n %	Chi-square	Relative Risk (RR)	95% CI RR	Odds Ratio (OR)	95% CI OR	p-value
Smoking	85 (85%)	20 (20%)	82.13	4.25	2.85–6.34	22.67	10.86–47.31	<0.0001
Alcohol	80 (80%)	25 (25%)	58.47	3.20	2.25–4.56	12.00	6.16–23.38	<0.0001
Drug	61 (61%)	9 (9%)	57.16	6.78	3.56–12.89	15.81	7.15–34.99	<0.0001
Pesticides	50 (50%)	30 (30%)	7.52	1.67	1.17–2.38	2.33	1.31–4.17	0.0059
Occupational	48 (48%)	5 (5%)	45.28	9.60	3.99–23.11	17.54	6.57–46.78	<0.0001
EMR	45 (45%)	8 (8%)	33.27	5.63	2.70–11.73	9.94	4.38–22.57	<0.0001

Statistical Analysis of Risk Factors

Pearson's chi-square test confirmed statistically significant associations for all major risk factors studied. The association was strongest for **smoking ($\chi^2 = 82.13$, $p < 0.0001$)**, followed by **alcohol consumption ($\chi^2 = 58.47$, $p < 0.0001$)**, **drug use ($\chi^2 = 57.16$, $p < 0.0001$)**, **occupational exposure ($\chi^2 = 45.28$, $p < 0.0001$)**, and **EMR exposure ($\chi^2 = 33.27$, $p < 0.0001$)**. Pesticide exposure, though less robust, remained statistically significant ($\chi^2 = 7.52$, $p = 0.0059$).

The **relative risk (RR)** and **odds ratio (OR)** calculations further substantiated these associations.

The highest risk magnitude was observed for **occupational exposure (RR = 9.60, 95% CI: 3.99–23.11; OR = 17.54, 95% CI: 6.57–46.78)**, underscoring the occupational hazard associated with bladder carcinogenesis. **Drug use (RR = 6.78, 95% CI: 3.56–12.89; OR = 15.81, 95% CI: 7.15–34.99)** and **EMR exposure (RR = 5.63, 95% CI: 2.70–11.73; OR = 9.94, 95% CI: 4.38–22.57)** also demonstrated strong associations. Smoking (RR = 4.25, 95% CI: 2.85–6.34; OR = 22.67, 95% CI: 10.86–47.31) and alcohol consumption (RR = 3.20, 95% CI: 2.25–4.56; OR = 12.00, 95% CI: 6.16–23.38) were also highly significant risk determinants. Pesticide exposure showed a comparatively lower risk magnitude (RR = 1.67, 95%



CI: 1.17–2.38; OR = 2.33, 95% CI: 1.31–4.17), though it retained statistical significance. The magnitude of association observed across risk factors suggests a gradient of risk contribution, with occupational exposure and smoking emerging as the most influential determinants. The notably high odds ratios associated with these exposures indicate a strong carcinogenic potential, likely reflecting prolonged and cumulative exposure to hazardous substances.

Association of Exogenous Risk Factors with High-Grade and Advanced-Stage Bladder Cancer

The association between exogenous risk factors and tumor aggressiveness, assessed in terms of high-grade and advanced-stage bladder cancer, is presented in **Table 3**. Among the evaluated exposures, smoking demonstrated higher risks for both high-grade tumors (RR = 2.39) and advanced-stage disease (RR = 3.17); however, these associations did not reach statistical significance. Similar trends were observed for alcohol consumption and drug use, where exposed patients showed increased relative risks for high-grade and advanced-stage tumors compared to unexposed patients,

though the differences were not statistically significant. In contrast, occupational exposure exhibited a significant association with high-grade bladder cancer, with exposed individuals showing a more than threefold increase in odds (OR = 3.43, $p = 0.011$). Electromagnetic radiation (EMR) exposure was also significantly associated with high-grade disease (OR = 2.67, $p = 0.033$).

Although elevated risks for advanced-stage tumors were noted across several exposure categories, none of these associations achieved statistical significance. Overall, the findings indicate that while multiple exogenous risk factors are associated with increased tumor aggressiveness, occupational and EMR exposures show the strongest and statistically significant relationships with high-grade bladder cancer (**Table 3**). From a biological perspective, the significant association of occupational and electromagnetic radiation exposure with high-grade tumors may reflect their potential role in promoting genomic instability, oxidative stress, and tumor progression pathways. These findings suggest that certain environmental exposures may influence not only cancer initiation but also tumor aggressiveness.

Table 3. Association of Exogenous Risk Factors with High-Grade and Advanced-Stage Bladder Cancer

Comparison	Outcome	Exposed (events / total)	Unexposed (events / total)	Risk (Exposed)	Risk (Unexposed)	RR	OR	95% CI (OR)	Fisher p-value
Smoking vs Grade	High grade	27 / 102	1 / 18	0.318	0.133	2.39	3.03	0.63–14.6	0.118
Smoking vs Stage	Advanced (T3–T4)	18 / 85	1 / 15	0.212	0.067	3.17	3.76	0.46–30.8	0.133
Alcohol vs Grade	High grade	26 / 80	3 / 20	0.325	0.150	2.17	2.73	0.73–10.2	0.129
Alcohol vs Stage	Advanced (T3–T4)	17 / 80	2 / 20	0.213	0.100	2.13	2.43	0.52–11.4	0.177
Drug use vs Grade	High grade	22 / 61	7 / 39	0.361	0.179	2.02	2.58	0.95–6.99	0.064
Drug use vs Stage	Advanced (T3–T4)	14 / 61	5 / 39	0.230	0.128	1.80	2.03	0.65–6.29	0.240



Occupational vs Grade	High grade	20 / 48	9 / 52	0.417	0.173	2.41	3.43	1.33–8.86	0.011
Occupational vs Stage	Advanced (T3–T4)	12 / 48	7 / 52	0.250	0.135	1.85	2.13	0.74–6.14	0.153
EMR vs Grade	High grade	18 / 45	11 / 55	0.400	0.200	2.00	2.67	1.08–6.60	0.033
EMR vs Stage	Advanced (T3–T4)	10 / 45	9 / 55	0.222	0.164	1.35	1.45	0.54–3.91	0.454

The present investigation offers a detailed and region-specific understanding of bladder cancer epidemiology in North India by integrating demographic characteristics, clinicopathological features, and a comprehensive evaluation of exogenous risk factors. In addition to reaffirming established etiological determinants, the study provides valuable insight into emerging environmental and occupational exposures that may influence both disease occurrence and tumor aggressiveness. This is particularly relevant in populations characterized by rural residence and heterogeneous occupational practices, which are increasingly recognized as important modifiers of cancer risk in low- and middle-income countries [2,8].

A key observation of this study is the marked concentration of bladder cancer cases in older age groups, with the highest incidence observed among individuals aged 61–65 years. Bladder cancer is widely recognized as an age-related malignancy, and large population-based studies have consistently demonstrated a progressive increase in incidence with advancing age [3]. The age-stratified analysis in the present cohort further revealed a shift toward higher tumor grade and more advanced stage among older patients, suggesting that aging is associated not only with increased disease risk but also with a tendency toward more aggressive tumor phenotypes. This pattern may reflect cumulative exposure to carcinogens over time, along with age-related changes in DNA repair capacity and immune surveillance [4].

The pronounced male predominance observed in this cohort is consistent with global epidemiological trends, wherein bladder cancer incidence among men exceeds

that in women by three- to five-fold [2]. In the present population, this disparity appears to coincide with a higher prevalence of smoking, alcohol consumption, occupational exposure, and environmental contact among males. These findings support earlier evidence indicating that gender differences in bladder cancer incidence are largely attributable to differential exposure patterns rather than intrinsic biological susceptibility alone [6].

From a clinicopathological standpoint, the predominance of early- to intermediate-stage disease and low-grade tumors suggests improved diagnostic access and heightened health-seeking behavior, paralleling trends reported in contemporary registry-based and guideline-driven studies [9]. Nonetheless, nearly one-fifth of patients in this study presented with advanced-stage disease, and older age groups showed a disproportionate burden of high-grade and advanced tumors. This observation reinforces prior reports indicating that delayed diagnosis, prolonged carcinogenic exposure, and age-related vulnerability contribute to more aggressive disease presentation in elderly individuals [3].

The analysis of risk factors represents a major strength of this study. Smoking emerged as the most prevalent exposure and demonstrated the strongest association with bladder cancer risk, reaffirming its dominant etiological role. Tobacco smoking is estimated to account for up to half of bladder cancer cases in men globally, primarily due to urinary excretion of carcinogenic aromatic amines derived from tobacco smoke [5,6]. The high magnitude of association observed in this cohort likely reflects cumulative



exposure and limited cessation practices within the studied population. Alcohol consumption and drug use also demonstrated strong associations, suggesting potential synergistic interactions with smoking, as previously reported in epidemiological investigations of combined lifestyle exposures [10].

Occupational exposure emerged as one of the most influential determinants in this study, exhibiting the highest relative risk among all evaluated factors. Occupational contact with industrial chemicals such as dyes, metals, solvents, and petroleum derivatives has been firmly established as a major contributor to bladder carcinogenesis [7]. Importantly, the case-only analysis revealed a significant association between occupational exposure and high-grade tumors, suggesting that such exposures may play a role not only in cancer initiation but also in tumor progression and aggressiveness.

Pesticide exposure showed a moderate yet statistically significant association with bladder cancer risk. This finding is consistent with reports from agricultural populations, where chronic exposure to pesticides has been linked to increased risk of urothelial malignancies [11]. Given the extensive use of pesticides in rural regions of North India, even a modest elevation in risk carries substantial public health implications.

One of the most notable and novel findings of this study is the association between electromagnetic radiation (EMR) exposure and bladder cancer risk, as well as its significant relationship with high-grade tumors. Although EMR exposure has been more extensively studied in relation to neurological and hematological cancers, emerging experimental and epidemiological evidence suggests that low-intensity EMR may induce oxidative stress, genomic instability, and DNA damage, providing biological plausibility for carcinogenic effects [12]. While causality cannot be inferred from the present data, this observation is hypothesis-generating and warrants further investigation in larger, well-characterized cohorts.

The case-only analysis highlights an important distinction between factors associated with disease occurrence and those influencing disease severity. While smoking, alcohol consumption, and drug use were associated with increased risks of aggressive tumor features, statistically significant associations

were primarily observed for occupational and EMR exposures. Similar divergence between etiological and prognostic determinants has been reported previously, underscoring the multifactorial and context-dependent nature of bladder cancer progression [4]. To place these findings in a broader context, key clinicopathological characteristics and exposure patterns observed in the present cohort were compared with published global data, as summarized in Table 4.

Table 4. Comparison of Bladder Cancer Characteristics and Risk Factors across Regions

Parameter	Present Study (North India)	Global / Published Data
Mean age at diagnosis	61 ± 11 years	65–70 years
Male predominance	82% (4.5:1)	70–75%
Early-stage disease	81%	70–75%
Low-grade tumors	71%	~65–70%
Smoking prevalence (cases)	85%	50–65%
Occupational exposure	48%	10–20%
Pesticide exposure	50%	Variable / limited
EMR exposure	45%	Rarely evaluated

Collectively, these findings underscore that bladder cancer in this population arises from the convergence of age, lifestyle behaviors, occupational hazards, and emerging environmental exposures. The study corroborates established global evidence while contributing region-specific insights of direct public health relevance. By contextualizing these findings against published international data, the present work strengthens the evidence base for targeted prevention strategies, improved occupational safety measures, and exposure-informed risk stratification in similar settings.



This study has certain limitations. The sample size was relatively modest, which may limit the generalizability of the findings. The case–control design is inherently susceptible to recall bias in exposure assessment. Additionally, the study was conducted at a single center, which may not fully represent broader population variability. Future multi-center studies with larger cohorts are warranted to validate these findings.

This investigation offers a robust and region-specific characterization of bladder cancer by integrating demographic patterns, clinicopathological features, and a comprehensive evaluation of exogenous risk factors within a North Indian population. The findings clearly demonstrate that bladder cancer in this cohort is not only a disease of advancing age and male predominance but also one that reflects cumulative environmental and occupational exposures characteristic of the regional socioeconomic landscape. The predominance of low-grade and early-stage tumors suggests that a substantial proportion of patients are being diagnosed at a potentially manageable stage; however, the consistent age-related increase in high-grade and advanced-stage disease highlights a critical transition toward aggressive tumor biology in older individuals. This age-associated shift underscores the importance of age-stratified risk assessment and reinforces the need for heightened clinical vigilance in elderly patients. The exposure analysis strengthens the evidence that lifestyle and occupational factors remain central to bladder cancer etiology in this population. The high prevalence of smoking and alcohol consumption among patients confirms their continued relevance as dominant modifiable risk factors. More importantly, occupational exposure demonstrated a statistically significant association with high-grade disease, emphasizing that workplace-related carcinogenic exposure not only contributes to cancer development but may also influence tumor aggressiveness. The significant association observed between electromagnetic radiation exposure and high-grade tumors further identifies EMR as a potential emerging modifier of tumor behavior, warranting focused attention in future epidemiological and mechanistic studies. The case-only analysis provides an important distinction between factors associated with disease occurrence and those influencing disease severity. While several exposures showed elevated relative risks for aggressive tumor

features, statistical significance was limited for some associations, reflecting the multifactorial nature of tumor progression and the influence of cumulative biological and environmental interactions. These findings reinforce the concept that bladder cancer progression cannot be attributed to a single determinant but rather arise from the convergence of age, exposure duration, and biological susceptibility. Collectively, the results of this study carry important implications for public health and clinical practice. They highlight the urgent need for strengthened tobacco control measures, stricter enforcement of occupational safety regulations, and increased awareness of emerging environmental exposures in high-risk populations. From a clinical perspective, the findings support the incorporation of exposure history and age-related risk stratification into diagnostic and surveillance strategies. By providing localized evidence on both established and emerging risk factors, this study contributes meaningful insight into bladder cancer epidemiology and lays a foundation for targeted prevention, early detection, and risk-adapted management strategies in similar settings. These findings provide important evidence for region-specific risk stratification and support the development of integrated public health strategies targeting modifiable environmental and occupational exposures.

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Ethical Approval

The study was approved by the Institutional Human Ethics Committee of Maharshi Dayanand University, Rohtak (Approval No.: HEC/2021/282). The study was conducted in accordance with the Declaration of Helsinki, and written informed consent was obtained from all participants.



Author Contribution

MV conceptualized and designed the study. RK collected the data and performed the statistical analysis. DP provided clinical inputs and facilitated patient recruitment. AS, GR, and SN contributed to literature review and data interpretation. All authors reviewed and approved the final version of the manuscript.

Conflict of Interest

The authors declare that there are no conflicts of interest related to the publication of this work. No financial or personal relationships could have inappropriately influenced this study.

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