

Prevalence and survival in patients with bladder cancer: a study in high cancer incidence zone

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ABSTRACT

Background: Bladder cancer (BC) is the most common malignancy of the urinary tract caused by the uncontrollable division of cells lining the bladder. The clinicopathological characteristics of BC determine largely the prognosis and aid in the treatment and management of disease.

Aim: The aim of the study was to analyze the incidence of BC in our region. **Materials and methods:** The study prospectively screened all the patients who were diagnosed with BC between 2018 and 2020. Detailed history of 235 patients was taken and Kaplan-Meier survival analysis of 137 BC patients was also performed to evaluate any possible association between various clinico-pathological characteristics, with respect to overall survival (OS) and recurrence in terms of disease free survival (DFS). **Results:** Among BC cases, 78.72% (185) patients were males and 21.27% (50) were females with a male: female ratio of 3.7:1. The frequency of BC was observed to be 36.17% (85) in cases that belonged to the age group of <50 years whereas 63.82% (150) cases belonged to ≥50 years. Of all cases 67.65% (159) patients were active smokers. The pathological characteristics of BC cases included 59.14% (139) cases of low stage (pTa/pT1) versus 40.86% (96) of the high stage (pT2/higher). Moreover, non-smokers, females and patients exhibiting low grade and stage had significant and better OS and DFS than the rest (Log rank $P < 0.05$). **Conclusion:** BC remains one of the leading cancers in our region despite absence of many occupational exposures except smoking.

Keywords: Bladder cancer, Disease free survival, Incidence, Overall survival, Stage

Asian Pac. J. Health Sci., (2022); DOI: 10.21276/apjhs.2022.9.4.48

INTRODUCTION

The urinary bladder is a storage and discharge organ for urine that is found in the pelvic cavity. The inner lining of the urinary tract, known as urothelium, is one of the slowest cycling epithelia in the human body.^[1] It is constantly exposed to a range of potential carcinogens that are discharged by the kidneys and remain in urine for a few hours before urination which makes bladder a high-risk organ for cancer development, and its neoplasms are among the most frequent malignancies worldwide. Because of the differences in oncological natural histories, bladder cancer (BC) is typically regarded as three disease entities: Low grade non-muscle invasive (LG-NMIBC, the most indolent), high grade non-muscle invasive (HG-NMIBC, grade 3 pTis, pTa, or pT1 tumors), and muscle invasive BC (MIBC, T2).^[2] At the time of diagnosis, 70–80% of BC patients possess NMIBC. Because such tumors lack aggressive histological characteristics, they recur, and a subgroup of high-risk lesions frequently progress to invasive forms. MIBC is seen in about 25–30% of patients at the time of diagnosis that further portends frequent progression to metastasis. Despite the fact that MIBC is treated with cystectomy, radical radiotherapy, or palliation, the 5-year overall survival (OS) rate is <50%, owing to chemotherapy resistance and patient fragility.^[3–6] Because of the frequent relapses and progression, BC is the most expensive malignancy to treat from diagnosis to death.^[6] BC is the second most prevalent kind of urological tumor, with a high recurrence rate and a poor prognosis. BC is the 10th most prevalent kind of cancer globally, affecting more men than women, with incidence and death rates of 9.6 and 3.2/100,000 in men, respectively, about four times those of women worldwide. As a result, the disease is more frequent in males, who have BC as the 6th most common cancer and 9th primary cause of death from cancer.^[7] Cigarette smoking is the major risk factor for BC, besides certain occupational exposures to chemical and water pollutants.^[8] With the growing frequency of smoking among women, the attributable risk has surpassed that of males in the United States, with 50% of BC cases in both sexes due

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How to cite this article: Anwar I, Pandith AA, Wani MS, Godha M, Manzoor U, Amin I, *et al.* Prevalence and Survival in Patients with Bladder Cancer: A Study in High Cancer Incidence Zone. *Asian Pac. J. Health Sci.*, 2022;9(4):243–247.

Source of support: Nil.

Conflicts of interest: None.

Received: 01/03/2022 **Revised:** 04/04/2022 **Accepted:** 08/05/2022

to smoking.^[9,10] BC is said to rise with age, and it is more frequent in countries with more resources.^[11–13] This also reflects the incidence of tobacco smoking and environmental carcinogens. Arshad *et al.* (2012) conducted a thorough hospital-based investigation in the Kashmir area and revealed that urinary tract cancers accounted for 9.1% of all prevalent cancer types. BC was found to be the most prevalent cancer in Kashmir, affecting 5.9% of the population, and was rated as the seventh most common cancer overall.^[14] Due to the high prevalence of BC in Kashmir, the goal of our study was to look into the epidemiology of BC in the region in order to assess the incidence, numerous risk factors (such as age, smoking status, and gender), and their influence on BC OS and disease free survival (DFS).

MATERIALS AND METHODS

The current study is the observational prospective study that was conducted in a tertiary care hospital. The records were screened for all patients who were diagnosed with BC and the study was conducted between 2018 and 2020. Emphasis was laid to determine the various factors which included age, gender, smoking status, dwelling, exposure to pesticides, grade, and stage of the disease. Patients from outside the valley were excluded from the study. The patient's history was evaluated thoroughly and a written informed consent was obtained from each recruited subject, and the study was approved by the local Institutional Ethical Committee. The admission records available were scrutinized and reviewed for detailed history. An in-house developed pro forma was used to collect information on demographic data and risk factors. Further, using Kaplan–Meier survival analysis, 137 BC patients were examined to evaluate any possible association between various clinico-pathological characteristics, with respect to OS and recurrence in terms of DFS of patients. Comparison of survival between patient groups was based on the log-rank test.

RESULTS

In our study, age group was considered as a factor, wherein 36.17% (85) BC cases belonged to age group <50 years and 63.82% (150) to ≥50 years. Among 235 BC cases, 78.72% (185) patients were males and 21.27% (50) were females with a male: female ratio of 3.7:1. BC cases that belonged to rural population were 75.74% (178). Smoking status was considered as a risk factor of BC, wherein 67.65% (159) patients were active smokers as compared to 32.34% (76) non-smokers. The pathological characteristics of BC cases included 57.44% (135) cases of low grade (GI/GII) versus 42.56% (100) of the high (GIII/GIV) grade disease. Histopathological pTa/pT1 of low stages included 59.14% (139) cases and 40.86% (96) cases belonged to higher stage (pT2/higher) of the disease. Mostly BC cases belonged to transitional cell carcinoma type 99.57% (234), but there was only one case that belonged to adenocarcinoma type (0.42%). In the current study, we also examined that 18.3% (43) bladder cancer cases had exposure to pesticides whereas 81.7% (192) cases were not exposed. The detailed information is given in Table 1.

Patients were followed for a mean duration of 25.1 months ranging from 0 to 30 months and Kaplan–Meier survival analysis was performed to assess the OS and the DFS of patients and details are given in Table 2.

A marked difference in both OS and DFS was observed in histological types of BC wherein low stage of the disease accounted for significantly high OS of 29.65 (95%; 29.2–30.08) months (log rank $P = 0.02$) and high DFS of 27.71 (95%; 26.67–28.74) months (log rank $P = 0.03$) as compared to high stage with less OS and DFS of 29.19 (95%; 28.7–29.6) and 25.42 (95%; 23.80–27.04) months, respectively [Figure 1a and b]. BC grade also acquired a significant difference in OS wherein low grade observed a slightly better OS of 29.65 (95%; 29.2–30.09) months in contrast to the high grade with OS of 29.23 (95%; 28.7–29.7) months (log rank $P = 0.046$) [Figure 2a and b]. Similarly, patients with different smoking statuses showed significant differences in both OS and DFS ($P < 0.05$) in which smokers accounted for less OS of 29.13 (95%; 28.6–29.5) months (log rank $P = 0.009$) and less DFS of 26.24 (95%; 24.98–27.51) months (log rank $P = 0.04$) as compared to non-smokers with higher OS and DFS of 30.00 (95%; 30.0–30.0) and 27.96 (95%; 26.82–29.11) months, respectively [Figure 3a and b]. Similarly females were

also found to have significantly better OS of 30.0 (95%; 30.0–30.0) months as compared to males with the OS of 29.26 (95%; 28.8–29.6) months (log rank $P = 0.041$) [Figure 4a and b].

Statistical Analysis

Recurrence of bladder tumor is defined as the time starting from diagnosis to the established recurrence in the bladder after earlier intervention. Kaplan–Meier analysis was used to measure differences in OS and DFS using the log-rank test.

DISCUSSION

There are significant variations in the prevalence and incidence of urinary bladder tumors amongst the different regions of world and globally it varies around 10-fold. Most often bladder tumors are reported from most of the European, western and to some extent from Asian descent. Over the last few decades proper management and timely diagnosis has caused a steady decline in incidence and mortality in West in particular European belt.^[15] In our region, Kashmir (North India), a study conducted a decade ago where BC ranks as the 7th among all commonly occurring cancers. The overall incidence rates noted was around 3.5/cases/105. It ranks sixth among men (9%) and tenth in women (2.2%) in Kashmir giving a male: female ratio of 5:1. The current study found gender differences of 4:1 (male: female) and is in accordance with most of the regions of the world. As per global cancer incidence (2018), BC occurs more commonly in males than in females where incidence rate is 3.2/10^[5] in men and account for 4 times as against the women globally as seen in our report. On the basis of this scenario BC ranks more in men where it sites as 6th most common cancer.^[7,14] Smoking of tobacco is the most ingrained cause and a risk factor for BC, that accounts for >50% of cases in men and >20 in women.^[9] A fundamental connection has been recognized irrefutably in many cancers in particular BC due to tobacco exposure in several studies

Table 1: Clinico-pathological features of bladder cancer patients

Clinico-pathological features	Number (%)
Age Group	
<50 year	85 (36.17)
≥50 year	150 (63.82)
Gender	
Male	185 (78.72)
Female	50 (21.27)
Dwelling	
Rural	178 (75.74)
Urban	57 (24.25)
Smoking status	
Ever	159 (67.65)
Never	76 (32.34)
Family history	
Yes	6 (2.55)
No	229 (97.45)
Grade	
GI/GII	135 (57.44)
GIII/GIV	100 (42.56)
Stage	
pTa/pT1	139 (59.14)
pT2/higher	96 (40.86)
Bladder cancer type	
Transitional cell carcinoma	234 (99.57)
Adenocarcinoma	1 (0.42)
Exposure to pesticides	
Yes	43 (18.3)
No	192 (81.7)

Table 2: Relation of various variables of BC patients with respect to OS and DFS

Parameter	Mean OS	95% CI	P value	Mean DFS	95% CI	P value
Age						
<50	29.74	29.4–30.05	0.4	26.825	25.25–28.39	0.999
≥50	29.27	28.8–29.7		26.892	25.76–28.02	
Gender						
Male	29.26	28.8–29.6	0.041	26.632	25.55–27.71	0.307
Female	30.00	30.0–30.0		27.876	26.36–29.38	
Smoking Status						
Smoker	29.13	28.6–29.5	0.009	26.249	24.98–27.51	0.044
Non-Smoker	30.00	30.0–30.0		27.968	26.82–29.11	
Dwelling						
Urban	29.03	28.4–29.6	0.07	26.676	24.76–28.59	0.741
Rural	29.57	29.2–29.9		26.976	25.9–28.008	
Grade						
I/II (Low)	29.65	29.2–30.09	0.046	27.384	26.29–28.47	0.187
III/IV (High)	29.23	28.7–29.7		26.134	24.59–27.67	
Stage						
I/II (Low)	29.67	29.2–30.08	0.02	27.711	26.67–28.74	0.036
III/IV (High)	29.19	28.7–29.6		25.424	23.80–27.04	
Exposure to pesticides						
Yes	28.429	27.3–29.4	0.840	26.318	24.22–28.41	0.819
No	29.419	29.08–29.7		27.001	26.04–27.95	

BC: Bladder cancer, OS: Overall survival, DFS: Disease free survival, CI: Confidence interval

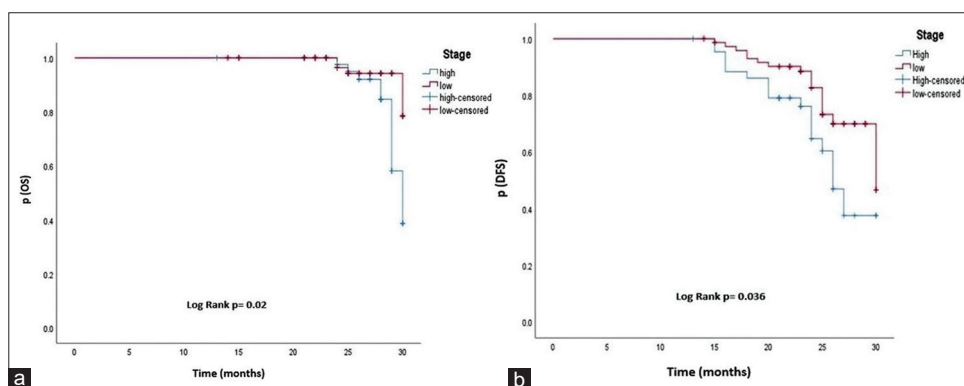


Figure 1: (a) Kaplan–Meier survival curves showing correlation of overall survival with respect to stage (low and high). p(OS): Probability of overall survival. (b) Kaplan–Meier survival curves showing correlation of disease free survival with respect to stage (low and high). p(DFS): Probability of disease free survival

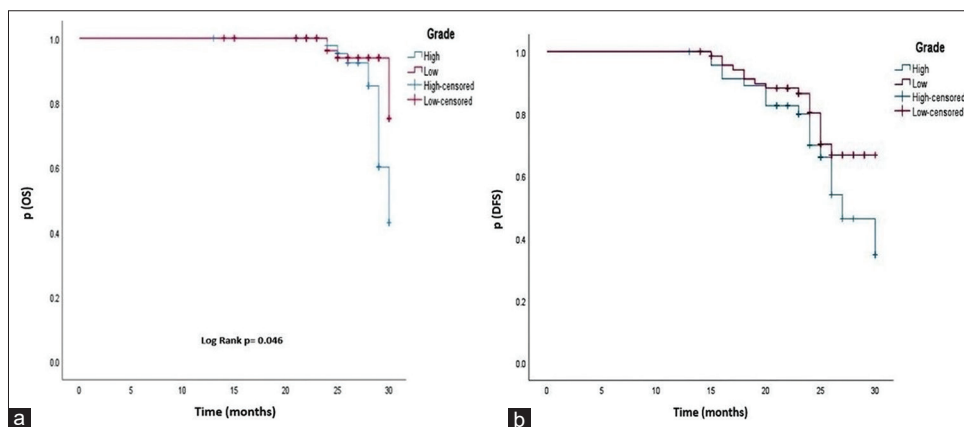


Figure 2: (a) Kaplan Meier survival curves showing correlation of overall survival with respect to grade (low and high). (b): Kaplan–Meier survival curves showing correlation of disease free survival with respect to grade (low and high)

wherein partiality and perplexing factors can be discounted with rational confidence.^[16] This study found 67.65% BC patients as active

smokers than 32.34% non-smokers. Cigarette smoke exposure is the leading risk factor for BC^[8] and emerging higher occurrence

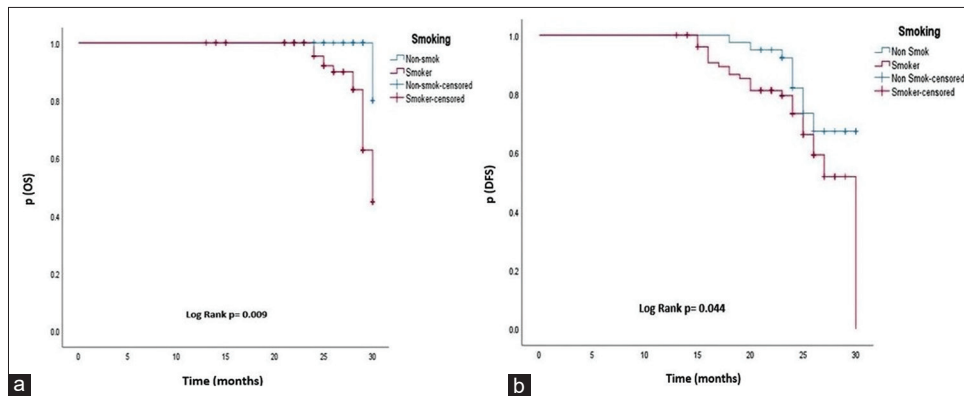


Figure 3: (a) Kaplan–Meier survival curves showing correlation of overall survival with respect to smoking status (smokers and non-smokers). (b) Kaplan–Meier survival curves showing correlation of disease free survival with respect to smoking status (smokers and non-smokers)

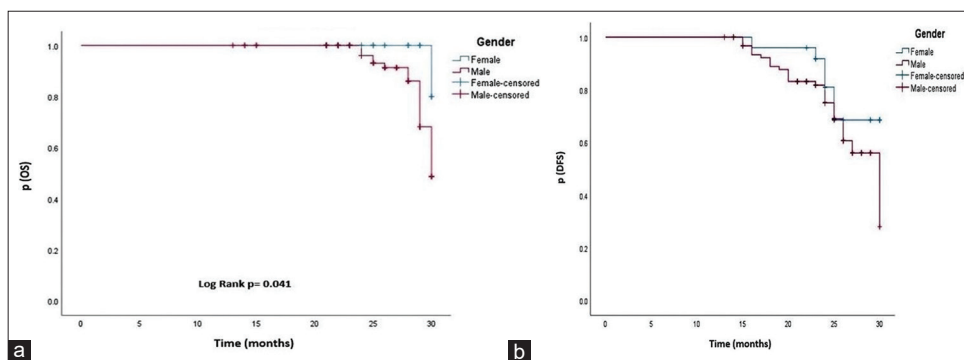


Figure 4: (a) Kaplan–Meier survival curves showing correlation of overall survival with respect to gender (male and female). (b) Kaplan–Meier survival curves showing correlation of disease free survival with respect to gender (male and female)

of smoking amid women complicated the situation more. In our study although patients with history of smoking comprise more of men than women but due to passive smoking women are also get affected. The attributable risk is not globally but at least in the USA has become comparable among men and women with 50% of BC cases linked to smoking among both sexes.^[9,10] Further, our region has moderate reduced risk of workplace exposure and active smoking accounts for the maximum environmental risk that contributes to overall incidence of BC cases in our population.^[17]

Mostly BC cases in our study were of urothelial (Transitional) cell carcinoma type 99.57% followed by one case of Adenocarcinoma (AC) 0.42%. In accordance with this, urothelial carcinoma is the most frequent among BC pathology (~90%) as found in west followed by SCC (2-5%), AC (2%), and other uncommon bladder tumors (<1%).^[18]

The study found 57.44% cases of low grade and 42.56% high grade cases with BC while as low stages (pTa/pT1) were 59.14% cases. The scenario slightly differs among the western region where high grade and stage tumors are less compared to our study possibly due to robust and immediate diagnostic evaluation. The conventional clinico-pathological characteristics such as pathological cancer stage or grade^[19] and lymph node metastasis NM,^[20] are established as vital factors with prognostic and predictive importance that contributes to disease management and treatment.

The study found a marked difference in survival wherein low stage of the disease accounted for significantly better OS and DFS (log rank $P < 0.05$). Low grade significantly showed slightly better

OS in contrast to the high grade (log rank $P = 0.046$). The scenario is universally accepted norm where low grade and stage show good survival irrespective of recurrences. Similarly smokers accounted for less OS (log rank $P = 0.009$) and less DFS (log rank $P = 0.04$) as compared to non-smokers respectively. Also females were found to have significantly better OS of as compared to males (log rank $P = 0.041$). Like our finding, study by Zaitso,^[21] showed both OS and cancer-specific survival significantly worse in female compared with male patients.

CONCLUSION

The study shows that BC exists in a very sizeable portion of population in our region with presence of all the histological types despite the fact that except smoking other occupational exposures are very least common here. Further, we conclude that smokers had poorer OS while females had better survival than men.

CONFLICT OF INTEREST

There are no conflicts of interest.

ETHICAL APPROVAL AND PATIENT CONSENT

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki

declaration and its later amendments or comparable ethical standards. A written informed consent was obtained from each recruited patient in the language they fully understood.

ACKNOWLEDGMENTS

We thank the Department of Advanced Centre for Human Genetics, SKIMS for their selfless help and support. We acknowledge the support and help from the staff of the Department of Urology and kidney transplant, SKIMS in keeping track of the patients.

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