

Original research article

Clinico-etiological profile patients with urinary bladder carcinoma presenting to tertiary care centre: an observational studyDr. Santosh Kumar¹, Dr. Shri Krishna Ranjan²¹Assistant Professor, Department of Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India²Associate Professor, Department of Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India.

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Abstract

Background: Bladder cancer (BC) is one of the most common urological malignancies. It is the fourth most common cancer in men and eighth most common malignancy in women of the western world. As per the Indian cancer registry, BC constitutes the ninth most common malignancy and accounts for an overall 3.9% of all cancer cases.

Aim: to determine the etiological of urinary bladder carcinoma patients.

Material and methods: This Prospective observational study was done in the Department of Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar for 24 months. 200 patients with a diagnosis of bladder cancer were included in the study. Clinical details including history of hematuria, smoking, daily fluid intake, dietary history, symptoms of urinary tract infection (UTI), loss of weight/appetite, past medical history and blood tests including hemogram, renal function tests, liver function tests, imaging like ultrasonography of kidney, ureter, urinary bladder (USG KUB), Cystoscopy and guided biopsy, contrast enhanced computed tomography of kidney, ureter, urinary bladder (CECT KUB) (if needed) and chest X-ray (CXR) was done in all the patients as per the standard protocol in the department of surgery.

Results: The mean age of presentation of carcinoma urinary bladder was 54.26 years. The male to female ratio was 4:1. The mean age of presentation of carcinoma urinary bladder was 54.26 years (29-84 years) with the maximum number of patients being in the age group of 60-70 years followed by below 40 years. 90% of the patients of carcinoma urinary bladder in our study were non-smokers. History of UTI was present in only 25.5% of the patients of carcinoma urinary bladder. Maximum number of patients of carcinoma urinary bladder belonged to A+ blood group followed by B+ and the least number of patients belonged to O- blood group. The maximum number of patients of carcinoma urinary bladder was labourers by occupation followed by farmers and housewife in females' subset. As shown in the table the maximum number of patients of carcinoma urinary bladder was Hindus followed by Muslim.

Conclusion: the majority of the patients turned out to be non-smokers and A +ve blood group in contrast to the strong predilection of smoking and bladder cancer.

Keywords: Carcinoma bladder, Etiology, Non-smoker

Introduction

The most common type of bladder cancer occurs in cells lining, inside of the bladder, which is called transitional cell carcinoma (urothelial carcinoma). Another type of UBC is squamous cell carcinomas that originated from the thin, flat cells that result in the

inflammation or irritation for many months or years. The third type is adenocarcinoma that forms in glands, specialized structures that produce and release fluids such as mucus. In the United States, urothelial transitional cell carcinomas account for more than 90 percent of all bladder cancers. The remaining 10% are squamous cell carcinomas (3% to 8%) and adenocarcinomas (1%). Other sarcoma, small cell carcinoma, and other cancers can also occur in the bladder. Recurrence of cancer can happen in the urinary bladder or another nearby organ after having been treated.¹ Bladder cancers are classified (staged or graded) by how deeply the bladder wall is invaded. Superficial bladder cancer is limited to the innermost lining of the bladder known as the mucosa and lamina propria. Invasive bladder cancer has at least penetrated the muscular layer of the bladder wall. Nearly all wall cell cancers are invasive. Most urothelial cell carcinomas are not invasive. More than 90% of case of UBC occur in people older than 55, and 50% of cases occur in people older than 73. Ploeg et al.² reported in 2009 that more than 2.7 million people have a history of UBC, and more than 12 million new cases occurred worldwide in 2003.¹ Of those, 5.4 million occurred in developed countries and 6.7 million in developing countries.^{2,3} UBC ranks ninth in worldwide cancer incidence. It is the seventh most common malignancy in men and seventeenth in women.² An estimated 386,300 new bladder cases and 150,200 deaths from bladder cancer were diagnosed worldwide in 2008.⁴ It is predicted that the burden of UBC will increase in less developed areas of the world because of smoking prevalence that goes along with economic development.² In the United States, UBC is the fifth most common type of cancer with an estimated 68,000 newly diagnosed cases and 14,000 deaths in 2008.⁵ There are multiple factors involved with the etiology of UBC. Many studies have been done on its etiology the world over which further show that different regions have a different etiological profile. So an etiological study at Anugrah Narayan Magadh Medical college and hospital, Gaya, Bihar, India, was done to understand the disease etiology in our region with objective for early identification of high risk groups and also identifying remedial measures which would enable us to eradicate the preventable causes.

Material and methods

This Prospective observational study was done in the Department of Surgery, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India, for 24 months, after taking the approval of the protocol review committee and institutional ethics committee.

Inclusion criteria

All patients with a diagnosis of bladder cancer presenting during the study period were included in the study.

Exclusion criteria

Patients unwilling or unable to give consent were excluded from the study.

Methodology

Clinical details including history of hematuria, smoking, daily fluid intake, dietary history, symptoms of urinary tract infection (UTI), loss of weight/appetite, past medical history and blood tests including hemogram, renal function tests, liver function tests, imaging like ultrasonography of kidney, ureter, urinary bladder (USG KUB), contrast enhanced computed tomography of kidney, ureter, urinary bladder (CECT KUB) (if needed) and chest X-ray (CXR) was done in all the patients as per the standard protocol in the department of surgery. In addition, blood grouping of every patient was done and recorded. All patients underwent treatment in the form of transurethral resection of bladder tumor as per the standard protocol in the department.

Results

The mean age of presentation of carcinoma urinary bladder was 54.26 years. The male to female ratio was 4:1

Table1: Age distribution.

Age (years)	Number	Percentage
Below 40	41	20.5
40-50	31	15.5
50-60	30	15
60-70	51	25.5
70-80	40	20
Above 80	7	3.5
Total	200	100
Mean±SD	54.26 ±16.32	

As shown in the table, the mean age of presentation of carcinoma urinary bladder was 54.26 years (29-84 years) with the maximum number of patients being in the age group of 60-70 years followed by below 40 years.

Table 2: Smoking history.

Smoker/non-smoker	Number	Percentage
Non-smoker	180	90
Smoker	20	10
Total	200	100

As shown in the table and figure 90% of the patients of carcinoma urinary bladder in our study were non-smokers.

Table 3: Distribution according to UTI history

UTI history	Number	Percentage
Absent	149	74.5
Present	51	25.5
Total	200	100

As shown by the table, history of UTI was present in only 25.5% of the patients of carcinoma urinary bladder.

Table 4: Distribution according to blood group

Blood group	Number	Percentage
A+	65	32.5
A-	4	2
AB+	16	8
B+	57	28.5
B-	5	2.5
O+	52	26
O-	1	0.5
Total	200	100.0

As shown by the table the maximum number of patients of carcinoma urinary bladder belonged to A+ blood group followed by B+ and the least number of patients belonged to O- blood group.

Table 5: Distribution according to occupation

Occupation	Number	Percentage
Businessman (owner)	10	5
Farmer	61	30.5
Housewife	22	11
Labourer	90	45
Others	17	8.5
Total	200	100

As shown by the table, the maximum number of patients of carcinoma urinary bladder were labourers by occupation followed by farmers and housewife in females' subset.

Table 6: Religion wise distribution

Religion	Number	Percentage
Christian	4	2
Hindu	170	85
Muslim	17	8.5
Sikh	9	4.5
Total	200	100

As shown in the table the maximum number of patients of carcinoma urinary bladder was Hindus followed by Muslim.

Discussion

Bladder cancer is the ninth most common cancer in the world and one of the most common urological malignancies.⁶ 200 patients with a primary diagnosis of carcinoma urinary bladder were included in our study. These included newly diagnosed cases as well as previously operated patients who were under follow up in the Department of Surgery, anugrah narayan magadh medical college and hospital, Gaya, Bihar, India. Etiological parameters of these patients were recorded and these patients were followed up for the duration of the study period. Median follow up of the patients included in the study was 2 years. The median age of patients in our study was 54.26 years. The ratio of males to females is 4:1. Cigarette smoking is the most important risk factor for bladder cancer on a population basis, additional factors play a role in modifying the risk posed by the smoking. 90% of the patients of carcinoma urinary bladder in our study were non-smokers. It depends on amount and duration as it is observed throughout the world.⁷ There are populations with high smoking rates but low bladder cancer rates.⁸ This suggests differences in the metabolism of smoking-related carcinogens. For example, individuals with N-acetyltransferase-2 slow acetylators as compared to rapid acetylators are known to have a higher risk of bladder cancer.⁹ Exogenous agents (such as vitamins C and E intake) may modify the susceptibility to smoking induced bladder cancer as well. Familial bladder cancer is a fairly rare phenomenon compared with the familial occurrence of cancer in many other tumor sites. Numerous case reports describe familial clustering of urothelial carcinoma and early age of onset suggesting a genetic component.¹⁰ Only a few epidemiologic studies specifically address familial bladder cancer, Goldgar et al.¹⁰ We therefore tried to explore the relationship between blood group and TCC with familial background but it remains inconclusive due to small sample size for a familial type of TCC.

It has been estimated that occupational exposures may account for as much as 20% of all bladder cancer.¹¹ Exposure to α -naphthylamine, 4-aminobiphenyl (ABP), and benzidine, principally among workers in the textile dye and rubber industries are the only specific agents that have been unequivocally associated with bladder cancer.¹² In fact, many occupations have

been marked as potentially high risk. The authors observed maximum number (45%) of bladder cancer among labourers and industry workers including employees of leather and textile factories, hair-dye handlers (barber) and shoe-makers. But the limited sample size does not give any significant epidemiological clue. Carcinogenesis in these cases thought to be a result of exposure to possible carcinogenic constituents of paints and solvents. The risk of bladder cancer among workers, especially in industries should therefore be monitored continuously. Though the present study did not find any occupational relationship since the subjects were not exposed to typical jobs. Study used data from the Agricultural Health Study, a prospective cohort study which includes 57,310 pesticide applicators with detailed information on pesticide use, to evaluate the association between pesticides and bladder cancer. Results found associations with bladder cancer risk for two imidazolinone herbicides, imazethapyr and imazaquin, which are aromatic amines. Ever use of imazaquin was associated with increased risk whereas the excess risk among users of imazethapyr was evident among never smokers. Study also observed increased risks overall and among never smokers for use of several chlorinated pesticides including chlorophenoxy herbicides and organochlorine insecticides. Several associations between specific pesticides and bladder cancer risk were observed, many of which were stronger among never smokers, suggesting that possible risk factors for bladder cancer may be more readily detectable in those unexposed to potent risk factors like tobacco smoke.¹³

A study was conducted by Sharma et al carried out in urinary bladder cancer (UBC) subjects and healthy control subjects with an aim to determine the role of GST and GSTT1 polymorphism and its implication on the organophosphate compounds (OPC) detoxification or bioaccumulation which may increase the risk of UBC in humans.¹⁴ This study was also designed to identify the "gene-environment interaction" specifically between gene polymorphism in xenobiotic metabolizing genetic enzyme (s) and blood OPC levels. The results demonstrated a significant increase in frequency of glutathione S- transferase GSTM1/GSTT1 (null) genotype in UBC cases without interfering the distribution of other GSTT1/GSTM1 genotypes. Findings indicate that "gene-environment interaction" may play a key role in increasing the risk for UBC in individuals who are genetically more susceptible due to presence of GSTM1/GSTT1 null deletion during their routine encounter with or exposure to OPCs. A study in Costa Rica finds heavy pesticide use in rural counties is associated with an increased risk for bladder cancer in males (OR 1.71).¹⁵

People having non-vegetarian diet (3/4th of cases) and poor water intake (almost half of the cases) are the victims of TCC. This can be explained by their poor socio- economic status (82% of the study population) who cannot afford balanced diet lacking anti-oxidants like fruits and vegetables. High heavy metal level in water may be one of the risk factors which could be included in the study. Chronic UTI is associated with the development of bladder cancer, especially invasive squamous cell carcinoma.¹⁶

Genes for ABO blood group antigens are located on chromosome 9q34.¹⁷ This area of chromosome 9 has been seen to be frequently affected by gene deletions in carcinoma urinary bladder. It has been seen that these deletions might lead to loss of ABO antigen expression in about 25% of the cases.¹⁸ It has been hypothesized that loss of ABO antigen expression may cause resistance to immune mediated apoptosis, altered adhesion /aggregation. Moreover, single nucleotide polymorphisms of the ABO gene are associated with increased plasma levels of soluble ICAM-1 and TNF, leading to altered immune response and possibly cancer growth. In the study by Chihara et al loss of heterozygosity of ABO gene or hypermethylation in the promoter region of the ABO gene showed significant reduction of A antigen expression in UBC, while the expression of the A antigen is maintained in concomitant dysplasia or

normal urothelium, suggesting that loss of the ABO gene and/or its promoter hypermethylation is a specific marker for TCC.¹⁹

Most common blood group among patients with NMIBC in our study was A positive (32.5%). In a study by Biswas et al it was seen that urothelial cancer was most commonly seen in B blood group. However they did not comment on the statistical significance of that finding.

The Rhesus factor gene is located on the short arm of chromosome 1, a region of tumor suppressor genes and the proto-oncogene L-Myc, which is down-regulated in UBC.²⁰ The Rhesus factor proteins are expressed on erythrocyte membranes as well as various epithelial tissues, facilitating the oxygenation of tissue and removal of deoxyribonucleic acid (DNA)-damaging agents.²¹ Thus, the risk of development of various malignancies may be increased in Rhesus factor-negative patients, as shown in skin, esophageal, breast, lung and endometrial cancer.

Conclusion

We concluded that the majority of the patients turned out to be non-smokers and A +ve blood group in contrast to the strong predilection of smoking and bladder cancer.

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