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Original Research Article

Assessment of Clinico-Etiological Profile of Urinary Bladder Carcinoma in Patients Presenting to Tertiary Care Centre

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Abstract

Aim: The aim of this study was to determine the etiological of urinary bladder carcinoma patients. **Methods:** This Prospective observational study was done in the Department of General Surgery, Madhubani Medical College and Hospital, Madhubani, Bihar, India, for 13 months. 100 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), 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 53.16 years. The male to female ratio was 3:1. The mean age of presentation of carcinoma urinary bladder was 53.16 years (27-81 years) with the maximum number of patients being in the age group of 60-70 years followed by below 40 years. 88% of the patients of carcinoma urinary bladder in our study were non-smokers. History of UTI was present in only 27% 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. **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.

Keywords: Carcinoma bladder, Etiology, Non-smoker.

Introduction

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 India of the western world[1]. As per the Indian cancer

registry, BC constitutes the ninth most common malignancy and accounts for an overall 3.9% of all cancer cases[2]. With increasing use of tobacco in various forms and with an ever-increasing risk of exposure to occupational hazards, more and more of these BCs are being diagnosed nowadays. In spite of various stringent measures taken by various authorities with respect to manufacturing and legislative changes to workplace hygiene, many BCs still do rise through a risk of exposure to occupational carcinogens[3]. Smoking has been recognized as a very strong independent risk factor for bladder tumor occurrence and recurrence. Refraining from smoking for more than 15 years has been identified to reduce the risk of tumor recurrence as well[4]. In general, the risk increases as the frequency and duration of smoking levels increase and the risk typically decreases in former smokers than in current smokers[5]. Gender has been found to affect the overall survival prognosis of patients with BC. Men have a three-fold greater risk of developing BC than women, but female gender is identified as an independent adverse prognostic factor in terms of both recurrence and progression of the disease. Women with BC are more often diagnosed with a higher tumor stage than men[6]. Traditionally, BC is usually seen as a disease of advanced age. Nowadays, with an increased use of various diagnostic techniques and increased health awareness among the common public, many new cases of BCs are being diagnosed at a relatively younger age[7]. 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, the present study 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 General Surgery, Madhubani Medical College and Hospital, Madhubani, Bihar, India, for 13 months, after taking the approval of the protocol review committee and institutional ethics committee. 100 patients with a diagnosis of bladder cancer were included in the study. 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 53.16 years. The male to female ratio was 3:1

Table 1: Age distribution

Age (years)	Number	Percentage
Below 40	20	20
40-50	15	15
50-60	14	14
60-70	26	26
70-80	21	21
Above 80	4	4
Total	100	100
Mean±SD	53.16 ±15.32	

As shown in the table, the mean age of presentation of carcinoma urinary bladder was 53.16 years (27-81 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	88	88
Smoker	12	12
Total	100	100

As shown in the table and figure 88% 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	73	73
Present	27	27
Total	100	100

As shown by the table, history of UTI was present in only 27% of the patients of carcinoma urinary bladder.

Table 4: Distribution according to blood group

Blood group	Number	Percentage
A+	34	34
A-	2	2
AB+	7	7
B+	28	28
B-	3	3
O+	25	25
O-	1	1
Total	100	100

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)	4	4
Farmer	32	32
Housewife	10	10
Labourer	47	47
Others	7	7
Total	100	100

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

Table 6: Religion wise distribution

Religion	Number	Percentage
Christian	3	3
Hindu	84	84
Muslim	9	9
Sikh	4	4
Total	100	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[8]. 100 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. 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 1 years. The median age of patients in our study was 53.16 years. The ratio of males to females is 3:1. 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. 88% 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[9]. 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[11]. 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[12]. Only a few epidemiologic studies specifically address familial bladder cancer, Goldgar et al.[12] 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[13]. 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[14]. In fact, many occupations have been marked as potentially high risk. The authors observed maximum number (47%) of bladder cancer among labourers and industry workers including employees of leather and textile factories, hair-dye handlers (barber) and shoemakers. 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[15].

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[16]. 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)[17].

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 antioxidants 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[18]. In the present study it was observed in 27% cases.

Genes for ABO blood group antigens are located on chromosome 9q34[19]. 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[20]. 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[21].

Most common blood group among patients with NMIBC in our study was A positive (34%). 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[22]. 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[23]. 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

The present study 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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