

Etiological Assessment of Newly Diagnosed Bladder Cancer Patients Presenting to Hospital

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Abstract

Aim: The aim of the present study was to find out common causes of urinary bladder carcinoma in patients presenting to tertiary care centre.

Methods: The present study was conducted in the Department of General Surgery, Fort U Mediemergency hospital, Patna, Bihar, India on all newly diagnosed bladder cancer patients for the period of one year. There were 100 patients included in the present study.

Results: The mean age of presentation of carcinoma urinary bladder was 55.25 years (30-89 years) with the maximum number of patients being in the age group of 60-69 years followed by 30-39 years. 90% of the patients of carcinoma urinary bladder in our study were non-smokers. The history of UTI was present in only 25% of the patients of carcinoma urinary bladder. The maximum number of patients of carcinoma urinary bladder was Sikhs followed by Hindus. The maximum number of patients of carcinoma urinary bladder was farmers by occupation followed by labourers (mainly workers of dye, chemical, fertilizer industry and housewife in females' subset). 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.

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

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Introduction

The diseases of the urinary bladder are quite common and include both non-neoplastic and neoplastic lesions. Urothelial tumors represent about 90% of all bladder tumors. Urinary bladder cancer is the most common malignancy of the urinary tract, responsible for significant mortality and morbidity worldwide. [1]

Cancer of the urinary bladder accounts for about 3.2% of all cancers worldwide and is considerably more common in males than in females (ratio worldwide is about 3.5:1). Most cases of urothelial carcinoma of the bladder present in patients over the age of 50 years, but they can also occur in younger adults and children. [2]

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. [3] 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. [5] Of those, 5.4 million occurred in developed countries and 6.7 million in developing countries. [3,4] UBC ranks ninth in worldwide cancer incidence. It is the seventh most common malignancy in men and seventeenth in women. [3]

There are several risk factors connected to bladder carcinoma. The use of tobacco with its release of α -naphthalene and β -naphthalene into the urine is an important risk factor. [6] Another risk factor for development of bladder cancer is occupational exposure to aromatic amines (2-naphthylamine, 4-aminobiphenyl and benzidine) and 4,4'-methylenebis (2-chloroaniline), which can be found in the products of the chemical, dye and rubber industries as well as in hair dyes, paints, fungicides, cigarette smoke, plastics, metals and motor vehicle exhaust, drinking water contaminants and phenacetin-containing analgesics. [7] Among the various known risk factors, cigarette smoking is the most important and responsible for 48% cases of bladder cancer in men and 32% in female in USA. [8]

Until now few of the studies conducted in western countries have concluded that incidence of similar studies in India have concluded that NMIBC is most common in B blood group.^{9,10} Bladder carcinoma represents a type of cancer which has

many causes which are preventable and which vary in different parts of the world. It also presents with symptoms early on (hematuria) and if detected early on has a good prognosis. 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 Sri Guru Ram Das institute of medical sciences and research, Amritsar 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.

The aim of the present study was to find out common causes of urinary bladder carcinoma in patients presenting to tertiary care centre.

Materials and Methods

The present study was conducted in the Department of General Surgery, Fort U Mediemergency hospital, Patna, Bihar, India on all newly diagnosed bladder cancer patients for the period of one year. There were 100 patients included in the present study.

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.

After obtaining ethical approval from the institutional ethics committee, all newly diagnosed patients with urinary bladder carcinoma from March 2018 to December 2019 were included for their etiological analysis. 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

Table 1: Age distribution

Age (years)	Number	Percentage
30-39	20	20
40-49	15	15
50-59	17	17
60-69	25	25
70-79	20	20
80-89	3	3
Total	100	100
Mean±SD	55.25±15.19	

The mean age of presentation of carcinoma urinary bladder was 55.25 years (30-89 years) with the maximum number of patients being in the age group of 60-69 years followed by 30-39 years.

Table 2: Smoking history, Distribution according to UTI history and Religion wise distribution

Smoker/non-smoker	Number	Percentage
Non-smoker	90	90
Smoker	10	10
UTI history		
Absent	75	75
Present	25	25
Religion		
Christian	3	3
Hindu	20	20
Muslim	2	2
Sikh	75	75

90% of the patients of carcinoma urinary bladder in our study were non-smokers. The history of UTI was present in only 25% of the patients of carcinoma urinary bladder. The maximum number of patients of carcinoma urinary bladder was Sikhs followed by Hindus.

Table 3: Distribution according to occupation and blood group

Occupation	Number	Percentage
Businessman (owner)	5	5
Farmer	60	60
Housewife	12	12
Labourer	15	15
Others	8	8
Blood group		
A+	35	35

A-	3	3
AB+	7	7
B+	27	27
B-	2	2
O+	25	25
O-	1	1

The maximum number of patients of carcinoma urinary bladder was farmers by occupation followed by labourers (mainly workers of dye, chemical, fertilizer industry and housewife in females' subset). 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.

Discussion

Urothelial carcinoma of urinary bladder cancer is the fourth most common cancer in men and eighth most common malignancy in women in Western world. [11] In India, according to the recent reports of the National cancer registry programme, the overall incidence rate of the urinary bladder cancer is 2.25% (per 100,000 annually): 3.67% among males and 0.83% for females. [12] There are several risk factors connected to bladder carcinoma. The use of tobacco with its release of α -naphthalene and β -naphthalene into the urine is an important risk factor. [13]

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. History of tobacco smoking is present in 78.9% males and 25% females in the series. It depends on amount and duration as it is observed throughout the world. [14] 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. [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] 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 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. [18] We 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]

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]

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. [23,24]

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. The true natural history of bladder cancer is not yet fully known. Every effort has been made to explore epidemiological risk factors and for appropriate diagnosis. The study suggests that epidemiological survey should be incorporated in the evaluation of bladder cancer to formulate any disease control programme. However, large well designed prospective multicentre studies are needed to standardize the protocol.

References

1. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, Kiemeny L, Kriegmair M, Montironi R, Murphy WM, Sesterhenn IA. Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology*. 2005 Dec 1;66(6):4-34.
2. Benson Jr RC, Tomera KM, Kelalis PP. Transitional cell carcinoma of the bladder in children and adolescents. *The Journal of urology*. 1983 Jul 1;130(1):54-5.
3. Ploeg M, Aben KK, Kiemeny LA. The present and future burden of urinary bladder cancer in the world. *World journal of urology*. 2009 Jun; 27(3):289-93.
4. Garcia M, Jemal AW, Ward EM, Center MM, Hao Y, Siegel RL, Thun MJ. *Global cancer facts & figures 2007*. Atlanta, GA: American cancer society. 2007;1(3):52.
5. Longe JL. *The Gale encyclopedia of cancer: a guide to cancer and its treatments*. Gale; 2010.
6. Morrison AS. Advances in the etiology of urothelial cancer. *Urologic Clinics of North America*. 1984 Nov 1;11(4):557-66.
7. Le Pendu J, Marionneau S, CAILLEAU-THOMAS AN, Rocher J, LE MOULLAC-VAIDYE BÉ, Clément M. ABH and Lewis histo-blood group antigens in cancer. *Apmis*. 2001 Jan;109(1):9-26.
8. Kirkali Z, Chan T, Manoharan M, Algaba F, Busch C, Cheng L, Kiemeny L, Kriegmair M, Montironi R, Murphy WM, Sesterhenn IA. Bladder cancer: epidemiology, staging and grading, and diagnosis. *Urology*. 2005 Dec 1;66(6):4-34.
9. Biswas RR, Mangal S, Guha D, Basu K, Karmakar D. An epidemiological study of cases of urothelial carcinoma of urinary bladder in a tertiary care centre. *J Krishna Institute of Med Sci*. 2013 Jan 1;2(1):82.
10. Ferlay J, Soerjomataram I, Dikshit R, Eser S, Mathers C, Rebelo M, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136(5):359-86.
11. Parkin DM, Whelan SL, Ferlay J, Teppo L, Thomas DB. *Cancer incidence in five continents Volume VIII*. IARC scientific publication. 2002(155).
12. National Cancer Registry Program. *Consolidated report of population-based cancer registries*. 2006.
13. Morrison AS. Advances in the etiology of urothelial cancer. *Urologic Clinics*

- of North America. 1984 Nov 1;11 (4):557-66.
14. Schairer C, Hartge P, Hoover RN, Silverman DT. Racial differences in bladder cancer risk a case-control study. *Am J Epidemiol.* 1988; 128 (5):1027-37.
 15. Goldgar DE, Easton DF, Cannon-Albright LA, Skolnick MH. Systematic populationbased assessment of cancer risk in first degree relatives of cancer probands. *J Natl Cancer Inst.* 1994; 86 (21):160-8.
 16. Wesseling C, Antich D, Hogstedt C, Rodríguez AC, Ahlbom A. Geographical differences of cancer incidence in Costa Rica in relation to environmental and occupational pesticide exposure. *International journal of Epidemiology.* 1999 Jun 1;28(3):365-74.
 17. Kantor AF, Hartge P, Hoover RN, Narayana AS, Sullivan JW, Fraumeni JF. Urinary tract infection and risk of bladder cancer. *Am J Epidemiol.* 1984; 119(4):510-5.
 18. Hakomori SI. Antigen structure and genetic basis of histo-blood groups A, B and O: their changes associated with human cancer. *Biochimica et Biophysica Acta (BBA)-General Subjects.* 1999 Dec 17;1473(1):247-66.
 19. Orlow I, Lacombe L, Pellicer I, Rabbani F, Delgado R, Zhang ZF, et al. Genotypic and phenotypic characterization of the histoblood group ABO (H) in primary bladder tumors. *Int J Cancer.* 1998;75(6):819-24.
 20. Chihara Y, Sugano K, Kobayashi A, Kanai Y, Yamamoto H, Nakazono M, et al. Loss of blood group A antigen expression in bladder cancer caused by allelic loss and/or methylation of the ABO gene. *Lab Invest.* 2005; 85(7):895.
 21. Primdahl H, Von der Maase H, Sørensen F, Wolf H, Ørntoft T. Immunohistochemical study of the expression of cell cycle regulating proteins at different stages of bladder cancer. *J Cancer Res Clin Oncol.* 2002; 128(6):295-301.
 22. Primdahl H, Von der Maase H, Sørensen F, Wolf H, Ørntoft T. Immunohistochemical study of the expression of cell cycle regulating proteins at different stages of bladder cancer. *J Cancer Res Clin Oncol.* 2002; 128(6):295-301.
 23. Caygill CP, Royston C, Charlett A, Wall CM, Gatenby PA, Ramus JR, et al. Barrett's, blood groups and progression to oesophageal cancer: is nitric oxide the link? *Eur J Gastroenterol Hepatol.* 2011;23(9):801-6
 24. Muñoz A. F. D., Ibrahim T. M., Ortiz, C. T. N., Chávez Ángel F. L., Amaya, G. P. B., Galvis M. C. C., Pacheco, M. E. F., & Herrera, M. A. I. Typical Mri Findings of Ramsay Hunt Syndrome. *Journal of Medical Research and Health Sciences.* 2022; 5(4): 1899–1905.