Association of Metabolic Syndrome and its Components with Risk of Bladder Carcinoma: A Hospital-Based Study

Syed Atif Hussain[1], Rukhsana Tumrani[2], Mehvish Sana[3], Anber Rahim[4], Afsheen Nigar[5], Seerat Fatima Tu Zahra[6]

Abstract

Objective: The study aims to determine the association of metabolic syndrome and its components with the risk of bladder carcinoma.

Methods: The study was conducted in the Department of Urology, Sheikh Zayed Hospital, Rahim Yar Khan from August 2021 to November 2023. A total of 139 study subjects aged between 20 to 80 years, histopathologically confirmed cases of bladder carcinoma with documented grade were evaluated for presence and absence of metabolic syndrome by clinical and laboratory examination. Data related to blood pressure, waist circumference, lipid profile, and fasting blood glucose were collected. The association was evaluated between metabolic syndrome and individual components of metabolic syndrome with bladder carcinoma. Metabolic syndrome was diagnosed according to the guidelines of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III). Data was entered and analyzed by using SPSS version 25.

Results: Of the total 139 study subjects, 78 (56%) had low-grade bladder carcinoma, and 61 (44%) were diagnosed with high-grade bladder carcinoma. Metabolic syndrome was present in 16 (11.5%) and absent in 123 (88.48%) study subjects. The risk of bladder carcinoma in metabolic syndrome is shown by the odds ratio (OR=1.544, 95% CI: 0.198-1.859). The odds ratio with 95% CI for bladder carcinoma was 1.206 (0.379-2.781) for central obesity, 1.215 (0.619-2.385) for triglyceride, 0.769 (0.386-1.532) for hypertension, 0.539 (0.260-1.117) for blood glucose fasting and 2.028 (0.665-6.183) for High-Density Lipoprotein HDL-cholesterol.

Conclusion: On the basis of our study, it has been concluded that the frequency of metabolic syndrome is low (11.5%) in bladder carcinoma but the individual components of metabolic syndrome such as triglyceride and HDL-cholesterol have shown significant association with bladder carcinoma. The findings of our study highlight the significance of individualized metabolic syndrome management keeping in view the components of metabolic syndrome to prevent bladder carcinoma.

Key Words: Bladder Carcinoma, Metabolic syndrome

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Introduction

Urinary bladder carcinoma is one of the common tumors of the genitourinary tract and it is the 10th most common malignancy in the world[1,2]. Most prevalent malignancy affecting the urinary tract is bladder cancer (BC). Evidence from treatment trials, epidemiologic research, and pooled analyses points to a possible link between metabolic syndrome and an increased risk of bladder cancer mortality as well as recurrence. It is unclear how metabolic syndrome affects the carcinogenesis and prognosis of bladder carcinoma patients because the majority of primary research and pooled analyses only examined select individual metabolic syndrome components, such as diabetes and excessive body weight, rather than the entire disease. Many factors contribute to the development of bladder carcinoma and smoking is considered as one of the most common factors among all etiological factors[3,4,5].

[1] Department Urology, Sheikh Zayed Hospital, Rahim Yar Khan
[2] Department of Chemical Pathology, Shalamar Medical and Dental College, Lahore
[3] Department of Chemical Pathology, Children Hospital, Multan
[4] Department of Chemical Pathology, Sheikh Zayed Hospital, Rahim Yar Khan
[5] Department of Pathology, Shalamar Medical and Dental College, Lahore
[6] Department of Pathology, Shalamar Medical and Dental College, Lahore

Corresponding Author: Dr. Syed Atif Hussain
Department of Urology, Sheikh Zayed Hospital, Rahim Yar Khan.
Email: Dratifqmc@gmail.com
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Other risk factors reported for bladder carcinoma include age, sex, alcohol and tobacco use, nitrate or arsenic in potable water, family history, and workplace exposure to potential carcinogens[6].

A cluster of metabolic derangements are characteristic of metabolic syndrome such as central obesity (waist circumference > 40 inches in males and > 35 inches in females), hypertension (Blood pressure > 130/85mmHg), hypertriglyceridemia (Serum Triglyceride level > 150mg/dl), impaired fasting blood glucose (BGF > 100mg/dl), Low high-density lipoprotein (HDL cholesterol < 40mg/dl in male, HDL cholesterol < 50mg/dl in female)[7,8]. The relationship of metabolic syndrome has been evaluated with multiple malignancies[9]. It places a heavy cost of disease on communities since it is linked to serious consequences and mortality in many regions of the world. Metabolic syndrome may raise the risk, recurrence, and mortality of bladder cancer, a complex illness, according to data from clinical research. Additionally, a number of studies have demonstrated that obesity and aging are risk factors for bladder cancer. Thus, bladder cancer is more common in older adults with chronic conditions like metabolic syndrome. It has been found that there is an association of metabolic syndrome with an increased risk of bladder carcinoma[10,11]. Low HDL levels have been linked to an increased risk of bladder urothelial carcinoma, according to research. Moreover, metabolic syndrome may be linked to the malignant potential of bladder urothelial carcinoma due to increased insulin secretion. Additionally, a correlation has been documented between the risk of bladder cancer recurrence and being overweight, a component of the metabolic syndrome. Metabolic syndrome contributes to the elevation of inflammatory cytokines and reactive oxygen which damage the DNA and are responsible for the development of bladder carcinoma. Metabolic syndrome with a higher number of metabolic syndrome components greatly increases the risk of bladder carcinoma[12].

Based on the data that is now available, it is not yet clear enough how the metabolic syndrome which includes insulin resistance, high blood triglycerides, low HDL cholesterol, obesity, and hypertension and bladder cancer are related to one another to draw conclusions that are trustworthy. The study aims to determine the association between metabolic syndrome and individual components of metabolic syndrome with bladder carcinoma. Early diagnosis and intervention in patients with bladder carcinoma prolong survival in these patients and screening should be done properly in patients having risk factors for metabolic syndrome.

Methodology

After obtaining ethical approval from the Institutional Review Board, a cross-sectional study was conducted in the Urology department of Sheikh Zayed Hospital Rahim Yar Khan from August 2021 to November 2023. A total of 139 study subjects aged between 20 to 80 years, histopathologically confirmed cases of bladder carcinoma with documented grade were included. Sample size calculated by using formula ($n=z^2x\ p\ (1-p)/!^2$) where z is z score, p is the proportion of bladder cancer among all other tumors according to a study conducted in central Punjab, Pakistan (43%)[3] and ! is margin of error (9%). The confidence interval is taken as 95% and Z score value is 1.96 for a 95% confidence interval. After obtaining informed consent from study participants, clinical as well as laboratory examinations were performed to collect the data related to blood pressure, waist circumference, lipid profile, and, blood glucose fasting. Data was recorded on predesigned proforma for individual metabolic syndrome components (hypertension, blood glucose fasting, central obesity, triglyceride level, and HDL). Metabolic syndrome was diagnosed according to the guidelines of the National Cholesterol Education Program-Adult Treatment Panel III (NCEP-ATP III) as patients fulfilling three or more of the following five criteria: central obesity (waist circumference > 102cm (40 inches) in men and > 88cm (35 inches) in women; Serum triglyceride level >150mg/dl; blood glucose fasting >100mg/dl; hypertension (Blood pressure > 130/85mmHg); HDL-c <40mg/dl in male and < 50mg/dl in female[13].

Data was analyzed using SPSS version 25. Frequency and percentages are used to present categorical variables and numerical variables presented in terms of (m ± SD) mean and standard deviation. Fisher's exact test was applied to compare independent proportions. Odds ratios with corresponding 95% confidence interval for metabolic syndrome and its components were estimated by applying multiple logistic regression analysis. All variables were stratified and post-stratification, an independent sample t-test was applied to see the significant difference between subgroups. A two-tailed *p*-value < 0.05 was taken as statistically significant.

Results

Of the total 139 study subjects, 78 (56%) had low-grade bladder carcinoma and 61 (44%) were diagnosed with high-grade bladder carcinoma (Table 1). 80 (57.5%) patients were d"60 years of age and 59 (42.44%) were >60 years of age with a mean age of 57 ± 9.833 years (Table 1). In the age subgroup ≤60years, 43 subjects had low-grade bladder carcinoma and 37 individuals had high-grade carcinoma (Table 1). While in the age subgroup >60 years, 35 individuals had low-grade carcinoma and 24 had high-grade bladder carcinoma (Table 1). Of the total 139 study subjects, 106 (76.25%) were male while 33 (23.74%) were female (Table 1). Among males, 64 had low-grade bladder carcinoma while 42 had high-grade bladder carcinoma (Table1). Among females, 14 had low-grade carcinoma while 19 had high-grade bladder carcinoma (Table 1). Among individuals with central obesity, 10 had low-grade bladder carcinoma while 8 had high-grade bladder carcinoma (Table 1). Among individuals with triglyceride levels >150mg/dl, 37 had low-grade carcinoma while 26 had high-grade bladder carcinoma (Table 1). Among all individuals with hypertension, 33 had low-grade carcinoma, while 22 were diagnosed with high-grade bladder carcinoma (Table 1). Among individuals with blood glucose fasting >100 mg/dl, 31 were diagnosed with low-grade carcinoma and 16 were diagnosed with high-grade bladder carcinoma (Table-1). Metabolic syndrome was present in 16 (11.5%) and absent in 123 (88.48%) study subjects (Table 1). Central obesity was present in 18 (12.94%) study subjects while absent in 121 (87.05%) study subjects (Table 1). Of the total 139 study subjects, 76 (54.67%) had serum triglyceride levels d"150 while 63 (45.32%) had triglyceride levels >150mg/dl (Table 1). Hypertension was pre-sent in 55 (39.56%) patients while absent in 84 (60.43%) patients (Table 1). Of the total 139 study subjects, blood glucose fasting was >100mg/dl in 47 (33.81%) study subjects while less than 100mg/dl in 92 (66.18%) study subjects (Table 1). HDL cholesterol was ≤40mg/dl in 64 (46.04%) study sub jects while >40mg/dl in 75 (53.95%) study subjects (Table 1). The risk of bladder carcinoma in metabolic syndrome is shown by the odds ratio (OR=1.544, 95% CI: 0.198-1.859) (Table 1). The odds ratio with 95% CI for bladder carcinoma was 1.206 (0.379-2.781) for central obesity, 1.215 (0.619 -2.385) for triglyceride, 0.769 (0.386-1.532) for hypertension, 0.539 (0.260-1.117) for blood glucose fasting and 2.028 (0.665-6.183) for HDL-cholesterol (Table 1). A significant association of bladder carcinoma was found with respect to triglyceride and HDL cholesterol. The association was found statistically significant (*p*-value 0.010) between metabolic syndrome and risk of bladder carcinoma. (Table 1).

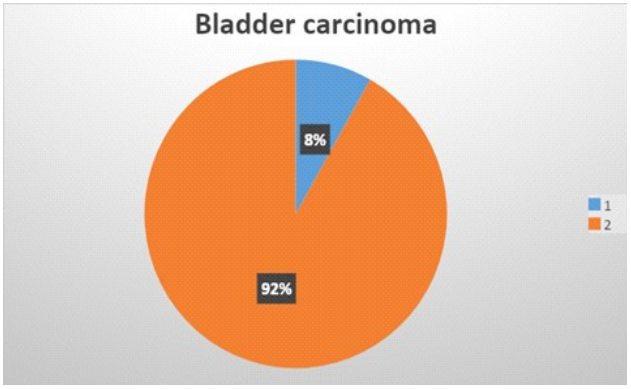

Fig 1. Frequency of Metabolic syndrome in high-grade bladder carcinoma.

Table 1. Multivariate logistic analysis of patients with low-grade and high-grade bladder carcinoma along with odds ratio and p-value.

Variables	Subgroups	Tumor Grade		OR (95% CI)	P value
		Low Grade	High Grade		
Age (Years)	≤60	43	37	1.255(0.635-2.478)	0.516
57±9.833	>60	35	24		
Gender	Male	64	42	0.484 (0.219-1.068)	0.070
	Female	14	19		
Central Obesity	Present	10	8	1.206 (0.379-2.781)	0.959
	Absent	68	53		
Triglyceride (mg/dl)	≤150	41	35	1.215 (0.619-2.385)	0.001
154±41.656	>150	37	26		
Hypertension	Present	33	22	0.769 (0.386-1.532)	0.459
	Absent	45	39		
Blood glucose fasting	≤100	47	45	0.539 (0.260-1.117)	0.096
(mg/dl)99±14.281	>100	31	16		
HDL (mg/dl)41±6.937	≤40	34	30	1.798 (0.408-1.564)	0.035
	>40	44	31		
Metabolic syndrome	Present	11	5	1.544 (0.198-1.859)	0.010
	Absent	67	56		

Table 2. Multivariate logistic analysis of patients with metabolic syndrome and without metabolic syndrome along with odds ratio and p-value.

Variables	Subgroups	Metabolic Syndrome		OR (95% CI)	P value
		Present	Absent		
Age (Years)	≤60	7	73	0.533 (0.186-1.524)	0.238
	>60	9	50		
Gender	Male	13	93	1.398 (0.373-5.239)	0.621
	Female	3	30		
Central Obesity	Present	7	11	7.919 (2.468-25.409)	0.001
	Absent	9	112		
Triglyceride (mg/dl)	≤150	1	75	0.043 (0.005-0.334)	0.050
154±41.656	>150	15	48		
Hypertension	Present	15	40	31.125 (3.971-243.985)	0.001
	Absent	1	83		
Blood glucose fasting	≤100	3	89	11.343 (3.042-42.297)	0.070
(mg/dl)99±14.281	>100	13	34		
HDL (mg/dl)41±6.937	≤40	5	59	2.028 (0.665-6.183)	0.210
	>40	11	64		
Bladder Carcinoma	Low Grade	11	67	1.544 (0.198-1.859)	0.010
	High Grade	5	56		

Discussion

On the basis of our study, it has been found that the frequency of metabolic syndrome is low in bladder carcinoma. The association was found statistically significant with a p-value of 0.010. By evaluating the association of components of metabolic syndrome with bladder carcinoma, triglyceride level and, HDL-cholesterol have shown significant association with bladder carcinoma. No association between hypertension and central obesity and blood glucose fasting has been established with bladder carcinoma risk. The association of bladder carcinoma with individual components of metabolic syndrome shows a statistically significant difference for triglyceride (p-value 0.001) and HDL-cholesterol (p-value 0.035). No statistically significant association of bladder carcinoma with respect to hypertension, central obesity, and blood glucose fasting has been found with a p-value >0.05. The bulk of research c-oncurs with our findings, which show a distinct and

direct correlation between triglycerides and cholesterol and bladder urothelial cancer. It's unclear what exactly causes the link between low HDL and bladder cancer. Therefore, doctors ought to check these patients for tumor development. A study was conducted by Ahmadinezhad M. et al. to see the association between metabolic syndrome and bladder carcinoma and it was demonstrated that there was a statistically significant association of bladder carcinoma with metabolic syndrome and the findings are consistent with our study findings. However, the association of individual components of metabolic syndrome with the risk of bladder carcinoma was found inconsistent as we have found no association between hypertension and blood glucose fasting with the risk of bladder carcinoma but on the basis of a meta-analysis conducted by Ahmadinezhad M. et al, the findings showed that diabetes, as well as hypertension, had a significant association with risk of bladder carcinoma[14].

Mondal et al. found a strong positive association between metabolic syndrome and the risk of bladder carcinoma. Individual components of metabolic syndrome that were found to have strong positive association were triglyceride level >150mg/dl, HDL-cholesterol <40mg/dl, and BMI (body mass index) >307. Dong Y. et al demonstrated in their study that patients with obesity and other metabolic abnormalities lead to poor prognosis in patients with bladder carcinoma [hyperglycemia: aHR=1.11, 95% Confidence Interval: 1.05–1.17; hypertension: aHR= 1.09, 95% CI: 1.03–1.15) obesity: adjusted hazard ratio (aHR)=1.08, 95% confidence interval (CI): 1.01–1.16]. It was concluded that management should be focused on reducing obesity and other metabolic abnormalities for better prognosis[15].

Another meta-analysis conducted by Lotan Y. demonstrates the strong association of metabolic syndrome with bladder carcinoma but the findings related to the components of metabolic syndrome had been found inconsistent as the strong association was demonstrated with diabetes in their study, but in our study, no association has been demonstrated with blood glucose fasting individually. There is a need to define further the relationship of metabolic syndrome and its individual components with bladder carcinoma risk[16,17].

A case-control study conducted by M Montella et al of 690 patients diagnosed with urothelial carcinoma of the bladder and 665 study subjects were cancer free and both groups were subjected to the estimation of metabolic syndrome and bladder carcinoma association. The odds ratio was found 2.20 for subjects with metabolic syndrome and thus data was strongly suggestive of a strong positive association between metabolic syndrome and bladder carcinoma[18]. Fang S. et al. demonstrated in their study that an association has been found between metabolic syndrome and its components with bladder carcinoma risk and they found the following hazard ratio for metabolic syndrome and components of metabolic syndrome. MetS (OR = 1.32, 95% CI = 1.08–1.61), for HDL cholesterol (OR = 1.31 & 95% CI = 1.04–1.66), central obesity (OR = 1.39, 95% CI = 1.15–1.68), hyperglycemia (OR = 1.44, 95% CI = 1.16–1.79) were positively associated with bladder carcinoma risk[19]. On the basis of previous studies conducted by Bae WJ. et al and Choi JB. et al, a positive association was demonstrated for central obesity with bladder carcinoma and these findings are consistent with our study[20, 21]. Our study findings are inconsistent with a study conducted by Nagase et al. In which they have found a positive association between urothelial carcinoma of the bladder and metabolic syndrome. In their study, the degree of bladder malignancy as well as the stage of bladder carcinoma was evaluated and the relationship was studied with metabolic syndrome. Individual components were also investigated and it was concluded that low HDL-c level was found to have a significant association with the stage and no association was established with other components of metabolic syndrome such as blood pressure, central obesity, triglyceride, and fasting blood glucose level[22].

The effect of body composition and body size has been studied by Sanchez A et al. and it has been demonstrated that the association is inconsistent for the risk of bladder carcinoma[23].

On the basis of our study, metabolic syndrome was found in 14% of cases of low-grade bladder carcinoma and 8% of cases of high-grade bladder carcinoma. However, the findings are inconsistent with the previous studies[24]. Further studies should be conducted and it should be explored further with a large sample size in order to establish the relationship between different stages and grades of bladder carcinoma in association with metabolic syndrome and its individual components. On the basis of our study, it has been found that there is an association between central obesity and the risk of bladder carcinoma which is consistent with a study conducted by Xu et al. In their study, they have also established a strong positive association between this individual component and a risk of bladder carcinoma[25].

Our study had certain limitations. It was a single-centered study. The outcome of patients was not studied in the bladder carcinoma with and without metabolic syndrome[17-25]. However, no such study has been conducted in that area for establishing the association of metabolic syndrome with a risk of bladder carcinoma as the prevalence of metabolic syndrome is much increased in our country.

Conclusion

On the basis of our study, it has been concluded that the frequency of metabolic syndrome is low (11.5%) in bladder carcinoma but the individual components of metabolic syndrome such as triglyceride and HDL-cholesterol have shown significant association with bladder carcinoma. The findings of our study highlight the significance of individualized metabolic syndrome management keeping in view the components of metabolic syndrome to prevent bladder carcinoma.

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