



Diagnostic utility of Serum biochemical parameters in early detection of bladder cancer

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Abstract

Bladder cancer ranks ninth in frequency worldwide and is the most prevalent cancer in the urinary tract. Significant risk factors include smoking, occupational exposures, and environmental exposures. Hematuria without discomfort is one of the common symptoms. Examine the following risk factors for bladder cancer: age, gender, occupation, BMI, smoking, and place of residence. The majority of patients (66.15%) were men between the ages of 50 and 60. Examine biochemical factors, including: blood urea, creatinine, AST, ALT, cholesterol, and triglycerides (TG). Thirty healthy people served as the study's control group, while 70 bladder cancer patients participated. Standard methods were used to measure the samples, and SPSS software was used for statistical analysis. Patients with bladder cancer had significantly higher levels of creatinine and urea than healthy controls ($P < 0.05$). AST levels did not differ considerably, whereas ALT levels were significantly lower ($P = 0.016$). While the patients' cholesterol levels were not statistically significant, their triglycerides were considerably higher ($P = 0.017$). Changes in creatinine, urea, ALT, and triglycerides indicate metabolic and renal disturbances associated with bladder cancer. Risk factors include age, gender, smoking, and occupation, highlighting the importance of early detection.

Keywords: Bladder cancer, Biochemical parameters , Urea , Creatinine , cholesterol, Triglycerides, AST, ALT, Early detection.

1-Introduction

In terms of malignant tumor frequency (BC), urinary bladder cancer is the most prevalent

malignant tumor in the urinary tract and ranks tenth worldwide. It is expected that there would be a 4:1 male-to-female ratio, with a male preponderance. Bladder cancer was one of the top 10 malignant

tumors worldwide in 2020, with around 570,000 new cases [1]. More than 90% of newly diagnosed instances of bladder cancer occur in those over the age of 55. People can get bladder cancer early in life [2]. Primary and secondary bladder cancer are the two primary types. Those that begin inside the bladder. The bladder is affected by subsequent malignancies that start in another organ. Some cancers can escape from a closed organ like the prostate or cervix, or they can enter the bladder through the lymphatic or circulatory systems. Malignancies that spread to the bladder. Transitional cell carcinoma (TCC), squamous cell carcinoma (SCC), adenocarcinoma, and mixed carcinoma type are among the bladder cancers that fall under the urothelial category [3]. Urothelial cell carcinoma accounts for around 90% of bladder cancer cases; the remaining instances are primarily neuroendocrine, adenocarcinoma, or squamous cell carcinoma [4]. According to the International Agency for Research on Cancer (IARC), there is enough evidence to support the following risk factors in British Columbia: smoking tobacco, being exposed to various occupational exposures (such as aluminum, rubber, painting, firefighting,

and occupational exposure to dyes [such as magenta and auramine] or dye intermediates [such as 4-aminobiphenyl]), being exposed to environmental exposures (such as X radiation gamma radiation and arsenic), taking medications (such as cyclophosphamide and chlornaphazine), using opium, and having Schistosoma infection [5]. 85% of patients present with painless visible hematuria, the most frequent presenting symptom. Symptoms of the lower urinary system include discomfort in the suprapubic area or urgency. Microscopic or macroscopic hematuria is nearly always present. Lower limb edema from lymphatic/venous blockage,

Bone pain, weight loss, anorexia, disorientation, and anuria are some of the symptoms of more severe instances. Pallor on a general examination may be a sign of anemia brought on by blood loss or long-term renal failure [6]. The study aimed to evaluate the risk factors of bladder Cancer among patients, which include: age group, gender, smoking, occupation, residency, and BMI. Measure some biochemical parameters such as: creatinine, urea, TG, Cholesterol, ALT, and AST.

2-Materials and Methods

2-1 Methods

This study was conducted at the Al-Furat Al-Awsat Center in Al-Najaf Al-Ashraf Governorate, where patients diagnosed with bladder cancer visited the center for diagnosis and treatment during this period. Samples were collected from

these patients between 17/11/2024 and 17/2/2025 for the purpose of studying and analyzing the disease-related markers.

2-2 Experimental design

This study involved a group of Iraqi patients, both male and female, who were diagnosed with bladder cancer and whose diagnosis was

confirmed by pathology reports. The study included seventy (70) bladder cancer patients and thirty (30) healthy individuals. The participants were fully informed about the details of the study, and their voluntary consent was obtained. The project was approved by the scientific ethics committee. Additionally, data were collected regarding several factors that may influence the study results, such as gender, age, BMI, smoking, area of residence, and occupation.

2-3 Diagnosis of Bladder Cancer

A specialized urologist examined and diagnosed all patients. In order to diagnose bladder cancer, doctors use various tests during a physical examination to confirm the presence of the disease. All patients were in the diagnostic stage. Therefore, this study approves medical reports based on various techniques such as blood tests, biochemical analysis, cystoscopy, biopsy, and imaging techniques like computed tomography (CT) scan and (MRI).

2-4 Collection of blood samples

To perform hematological and biochemical analyses, both bladder cancer patients and healthy controls provided five milliliters of venous blood drawn from the antecubital vein using a sterile syringe. For the assessment of specific hematological parameters, one milliliter of each blood sample was transferred into a tube containing ethylenediaminetetraacetic acid

(EDTA) as an anticoagulant. To measure the levels of various biochemical markers in the blood serum, four milliliters of blood were placed into plain glass tubes without anticoagulants and left at room temperature for one hour to allow clotting. After coagulation, the serum was separated through centrifugation and transferred into Eppendorf tubes using a micropipette. The samples were then stored at -20°C until further analysis.

Statistical Analysis.

Statistical analyses were performed using three software programs: Excel of Microsoft Office 2013, SPSS version 27, and MedCalc version 14.25. Descriptive statistics for the study variables were presented as means $\pm$ standard deviation (SD). The independent t-test was employed to compare parameters between the patient and healthy groups. A p-value of <0.05 was considered statistically significant.

3-Results:

3.1:Distribution in respect to the demographic features

In this study, we examined bladder cancer patients and compared them with a healthy control group in terms of demographic characteristics. Each characteristic had a specific distribution of values based on the results, as shown in the table (3-1).

Table (1): Distribution of the patients and control according to demographic features

Demographical features	Control		Patients	
	F	%	F	%
Residency				
Central	16	64	35	53.85
Peripheral	9	36	30	46.15
Smoking				
Yes	8	32	35	53.85
No	17	68	30	46.15
Occupation				
Housewife	3	12	12	18.46
Employee	15	60	16	24.62
Earnar	3	12	17	26.15
Retired	4	16	20	30.77
BMI				
<18.5	1	4	17	26.15
18.5 - 24.9	20	80	26	40.00
25.0 - 29.9	4	16	18	27.69
30.0-39.9	0	0	4	6.15
>40	0	0	0	0.00
Age				
<30y	7	28.00	0	0.00
31-40	6	24.00	4	6.15
41-50	5	20.00	10	15.38
51-60	3	12.00	21	32.31
61-70	3	12.00	17	26.15
>70	1	4.00	13	20.00
Gender				
Male	17	68	43	66.15
Female	8	32	22	33.85

3-1-1 Residency

Table (3-1) shows the distribution of residency in the patient with bladder cancer and the control groups. The analysis of residency did not reveal a significant difference between patients and the control group ($P = 0.174$). The proportions were similar between those living in central areas (53.85% for patients vs.

64% for controls) and peripheral areas (46.15% for patients vs. 36% for controls).

3-1-2 Smoking status

Table (3-1) shows a significantly higher proportion of smokers among patients (53.85%) compared to controls (32%) ($p = 0.04$). Non-smokers were more

common in the control group (68%) than among patients (46.15%).

3-1-3 Occupation

The analysis of occupational distribution in Table (3-1) showed significant differences between patients and controls ($p=0.017$). Housewives and retirees were more prevalent among patients (18.46% and 30.77%, respectively) compared to controls (12% and 16%). Conversely, employees were less common among patients (24.62%) than controls (60%). Farmers also showed a higher prevalence among patients (26.15%) compared to controls (12%).

3-1-4 Body mass index

Table (3-1) shows significant differences in BMI distribution between bladder cancer patients and controls ($p < 0.001$). Underweight individuals were more common among patients (26.15%) than controls (4%), while normal weight was lower in patients (40%) compared to controls (80%). Overweight and obesity were higher in patients (27.69% and 6.15%, respectively) than in controls (16% and 0%). Severe obesity ($BMI \geq 40$) was absent in both groups.

3-1-5 Age

Table (3-1) illustrates age distribution among bladder cancer patients and control groups, revealing

significant differences ($p < 0.00001$). Healthy individuals were predominantly under 50 years old (72%), while most patients were over 50 (78.64%). Notably, no patients were under 30 years old, compared to 28% of healthy individuals. The highest patient percentages were in the 51–60 (32.31%) and 61–70 (26.15%) age groups, emphasizing an age-related pattern.

3-1-6 Gender (sex)

Table (3-1) shows the gender distribution in bladder cancer patients and controls, with males comprising 66.2% of patients and 68% of healthy individuals, and females 33.8% of patients and 32% of healthy individuals. No statistically significant difference was observed ($p = 0.823$).

3.2: Kidney function indicators.

3-2-1 Urea

Figure (3-1) shows the results of comparing blood urea levels between two groups, bladder cancer patients (BC) and healthy individuals (the control group). For the patient group (BC) was mean urea level(39.93 ± 18.41) mg/dL, compared to the healthy group was mean urea level(23.90 ± 6.36) mg/dL, we found an increase in patients by 66.7%. Thus, this confirms the presence of a statistically significant difference between the two groups ($P < 0.05$).

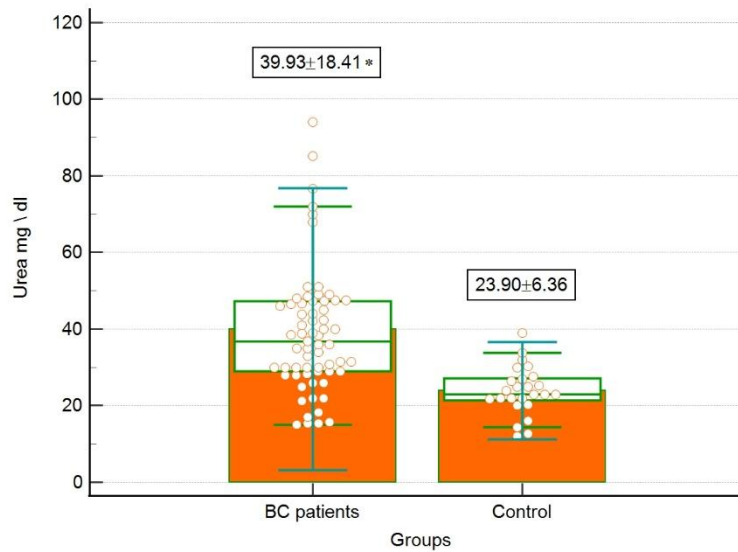


Figure (1): The urea of BC patients and control group.

- (*) =Significant differences ($p < 0.05$).

3-2-2 Creatinine

Figure (3-2) compares serum creatinine levels between bladder cancer patients (BC patients) and the control group. The results demonstrate a statistically significant increase ($P < 0.05$) in creatinine levels among BC patients. Since the mean creatinine level in bladder cancer patients

was (0.94 ± 0.43), while the mean creatinine level in healthy individuals was (0.68 ± 0.25), an increase in creatinine levels was observed in the patients (0.94) compared to the healthy group (0.68). Therefore, it was indicated that there was a significant difference.

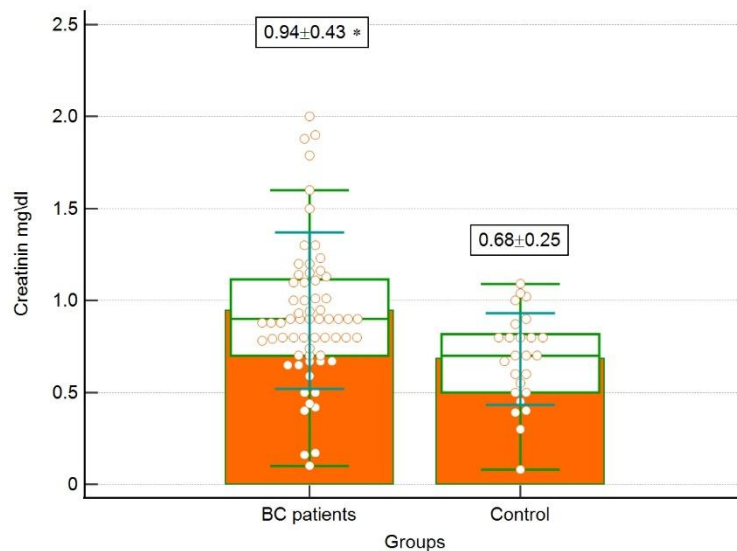


Figure (2): The creatinine of BC patients and control groups.

.* Significant differences (P<0.05).

3.3: Liver function indicators

3-3-1 Alanine aminotransferase

Figure(3-3) presents a comparison of Alanine Aminotransferase (ALT) enzyme levels between two groups. The bladder cancer (BC) patients group had a level of (25.25±9.99), compared to the control group (healthy individuals) with a level of

(32.75 ± 18.60). The results showed a statistically significant difference between the two groups, with a (p= 0.016), which is below the commonly used significance threshold (p > 0.05). This indicates the difference in ALT levels between the two groups.

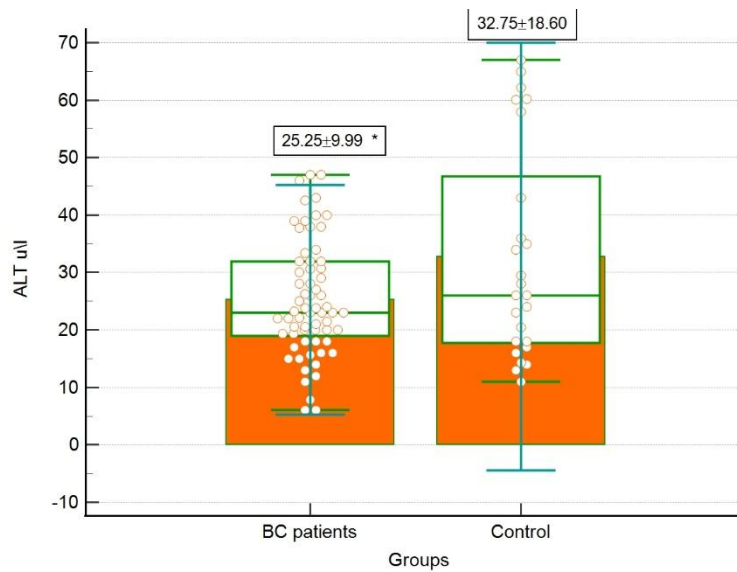


Figure (3): The ALT of BC patients and control groups.

-* Significant differences (P=0.016).

3-3-2 Aspartate aminotransferase

Figure (3-4) presents a comparative analysis of aspartate aminotransferase (AST) enzyme levels between two groups, bladder cancer (BC) patients and healthy individuals. AST levels in the blood serum of both groups were measured using

standardized techniques. The bladder cancer patient group recorded an average AST level of (21.75 ± 0.65) U/L, while the control group showed an average AST level of (24.44 ± 10.38) U/L. Statistical analysis yielded a p-value = 0.136 (denoted by 'ns,' indicating no statistical significance).

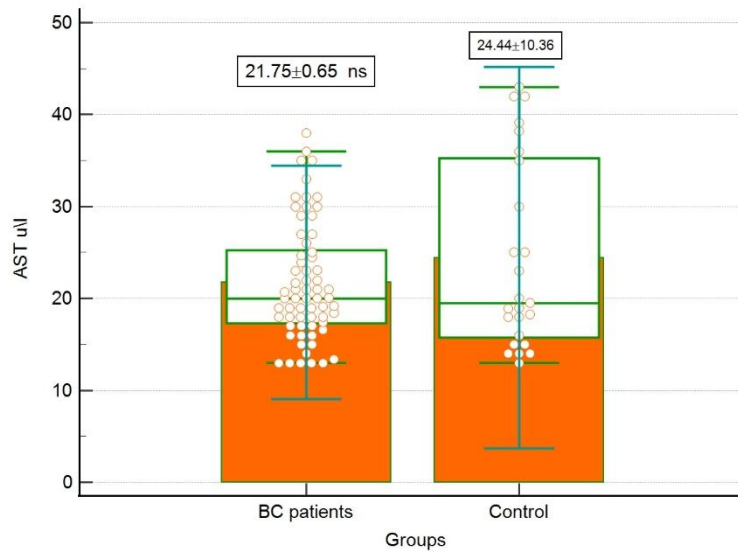


Figure (4): The AST of BC patients and control groups.

-ns non-Significant differences (P=0.136).

3.4: Lipid profile

3-4-1Total cholesterol

Figure (3-5) shows a comparison of cholesterol levels between two main groups, bladder cancer patients (BC patients) and control groups. The mean cholesterol level in bladder cancer patients

was (175.52 ± 63.15) mg/dL, while the mean cholesterol level in healthy individuals was (166.83 ± 41.66) mg/dL. Therefore, it was observed that the results of cholesterol levels were similar between the two groups, meaning they were not statistically significant, as the ($P=0.526$), which is greater than ($P>0.05$). Thus, it is considered non-significant.

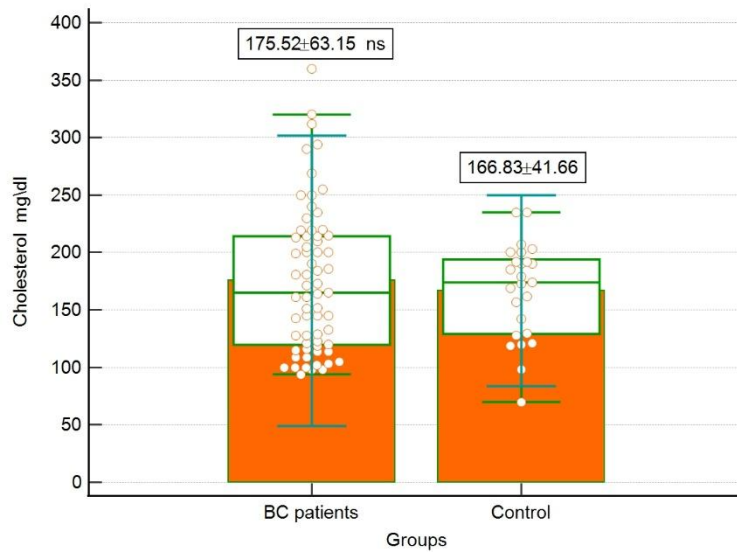


Figure (5): The cholesterol of BC patients and control groups.

-ns non-Significant differences (P=0.526).

3-4-2 Triglycerides

Figure (3-6) explains and analyzes the levels of triglycerides (TG) in bladder cancer (BC) patients compared to the control group. Bladder cancer patients (BC patients) had a triglyceride level of $(239.98 \pm 94.61^*)$ (mg/dL). The control group (healthy individuals) mean triglyceride level was $= (182.96 \pm 110.91)$ (mg/dL). The P-value (0.017),

indicated in the figure with an asterisk (*), signifies a statistically significant difference. Since $P < 0.05$, the difference in triglyceride levels between patients and healthy individuals is statistically significant. The elevated triglyceride levels in patients suggest that bladder cancer patients have significantly higher triglyceride levels compared to healthy individuals.

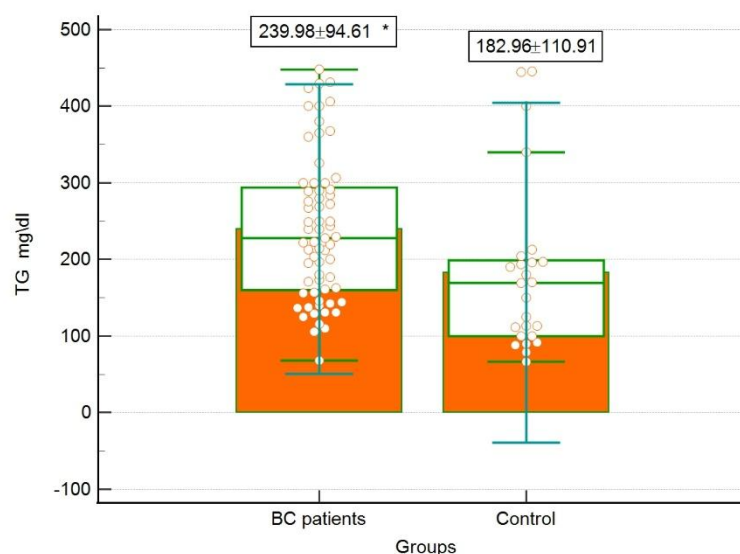


Figure (6): The TG of BC patients and control groups.

-* Significant differences (P=0.017).

4-Discussion

The findings presented in Table (3-1) indicate that the majority of patients (53.85%) originate from central urban areas, while a smaller proportion (46.15%) comes from peripheral regions. This aligns with the study by [2], which highlighted the influence of environmental and industrial factors in urban areas on bladder cancer risk, primarily due to exposure to carcinogens such as industrial dyes and heavy metals. Similarly, [7] confirmed that urban areas are more likely to expose individuals to environmental pollutants like asbestos and arsenic, further contributing to bladder cancer incidence. The table also shows that 53.85% of patients were smokers compared to only 32% in the control group. A study by [3] identified smoking as a primary risk factor for bladder cancer, given the presence of carcinogens in tobacco that directly damage urinary tract cells. This is corroborated by

[6], which found that smokers are three times more likely to develop bladder cancer than non-smokers due to the accumulation of toxins in the urine. Occupational factors were another.

Notable finding, as retirees (30.77%) and workers (26.15%) constituted the largest patient groups. This suggests a link between occupational exposure to chemicals and bladder cancer risk. For instance, a study by [8] in Iran reported an increased bladder cancer risk among metal industry workers exposed to aromatic amines, with an odds ratio (OR) of 2.2 (95% CI: 1.2–4.0). Another study by [9] demonstrated a dose-response relationship between exposure to organic solvents such as benzene, toluene, and xylene (BTX) and bladder cancer risk. Regarding nutritional status, 26.15% of patients had a BMI <18.5, indicating potential

malnutrition or weight loss associated with disease progression. [10] suggested that low BMI may result from cancer-induced metabolic changes. However, 40% of patients had a BMI within the normal range (18.5–24.9), underscoring that bladder cancer can occur irrespective of baseline weight. Age distribution revealed that 32.31% of patients were aged 51–60 years, followed by 26.15% in the 61–70 age group. These results are consistent with [11], which reported that approximately 90% of bladder cancer cases occur in individuals over 55 years, with a median diagnosis age of 73. Furthermore, a study by [12] highlighted higher recurrence, progression rates, and cancer-specific mortality among patients aged ≥ 81 years. Another study by [13] found that patients over 75 years had lower survival rates, confirming age as a critical prognostic factor for bladder cancer. Sex differences were also evident, with 66.15% of patients being male compared to 33.85% female. [14] attributed this disparity to greater exposure among men to smoking, environmental carcinogens, and occupational hazards. Additionally, [6] suggested that sex hormones like testosterone might contribute to the higher incidence of bladder cancer in men. Biochemical alterations associated with bladder cancer were highlighted in the study. Elevated blood urea and creatinine levels in bladder cancer patients, as noted in [15] and [16], suggest cancer-induced kidney dysfunction. An Iraqi study further revealed declining eGFR and increasing creatinine levels in patients undergoing bladder or prostate

surgeries, regardless of urinary diversion type [17]. Moreover, alterations in alanine aminotransferase (ALT) levels were linked to metabolic

Changes induced by cancer. According to [18], low ALT levels might reflect tumor-driven metabolic disturbances rather than direct liver damage. A recent study by [19] emphasized the potential of ALT levels as an indicator of cancer-related metabolic shifts. A recent study indicates that cancer cells reprogram metabolic pathways to utilize fats as an energy source for their growth, leading to triglyceride accumulation in the body [20]. Research has demonstrated a genetic association between elevated triglyceride levels and increased risk of bladder cancer, suggesting a potential role of triglycerides in the development of this cancer type [21].

Conclusion

Elevated creatinine and urea levels can serve as indicators of kidney dysfunction associated with bladder cancer. Decreased ALT and increased triglycerides may relate to tumor-induced metabolic changes. Age, gender, smoking, and occupation are prominent risk factors, highlighting the need for targeted early detection efforts in high-risk populations.

Ethical approval: The study was approved by the Scientific Ethics Committee, and informed consent was obtained from all participants.

Reference

1. Afonso J, Gonçalves C, Costa M, Ferreira D, Santos L, Longatto-Filho A, Baltazar F. Glucose metabolism reprogramming in bladder cancer: hexokinase 2 (HK2) as prognostic biomarker and target for bladder cancer therapy. *Cancer*. 2023;15(3):982. doi: 10.3390/cancers15030982
2. Saginala K, Barsouk A, Aluru JS, Rawla P, Padala SA, Barsouk A. Epidemiology of bladder cancer. *Med Sci*. 2020;8(1):15. doi: 10.3390/medsci8010015.
3. Richters A, Aben KK, Kiemeny LA. The global burden of urinary bladder cancer: an update. *World J Urol*. 2020;38:1895-904. doi: 10.1007/s00345-019-02984-4.
4. Mohanty SK, Lobo A, Mishra SK, Cheng L. Precision medicine in bladder cancer: present challenges and future directions. *JPersMed* 2023;13:756. doi:10.3390/jpm13050756
5. International Agency for Research on Cancer. List of classifications by cancer sites with sufficient or limited evidence in humans. IARC monographs volumes 1–132. July 1, 2022. https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf.
6. Choo, Min Soo. “Symptoms.” *Bladder Cancer*, 2018, pp. 45–55., doi:10.1016/b978-0-12-809939-1.00004-7.
7. International Agency for Research on Cancer (IARC). List of classifications by cancer sites with sufficient or limited evidence in humans. IARC Monographs Volumes 1–132, July 2022. URL: https://monographs.iarc.who.int/wp-content/uploads/2019/07/Classifications_by_cancer_site.pdf.
8. Hosseini, B., Zendehdel, K., Bouaoun, L., et al. (2023). Bladder cancer risk in relation to occupations held in a nationwide case-control study in Iran. *International Journal of Cancer*, 153(4), 765–774. DOI: 10.1002/ijc.34560 (<https://doi.org/10.1002/ijc.34560>).
9. Xie, S., Friesen, M. C., Baris, D., et al. (2024). Occupational exposure to organic solvents and risk of bladder cancer. *Journal of Exposure Science & Environmental Epidemiology*, 34(3), 546–553. DOI: 10.1038/s41370-024-00651-4 (<https://doi.org/10.1038/s41370-024-00651-4>).
10. Luo J, Chen Y, Chen L. Triglyceride levels and risk of cancer development: A meta-analysis. *Medicine*, 2019; 98(18): e14954. DOI: 10.1097/MD.00000000000014954 (<https://doi.org/10.1097/MD.00000000000014954>).
11. American Cancer Society. (2024). Key Statistics for Bladder Cancer. Retrieved from <https://www.cancer.org/cancer/types/bladder-cancer/about/key-statistics.html>.
12. European Urology Oncology. (2024). Association of Age with Non-muscle-invasive Bladder Cancer: Unearthing a Biological Basis for

Epidemiological Disparities? Retrieved from <https://pubmed.ncbi.nlm.nih.gov/38302322/>.

13. Cancer Control. (2023). Impact of Age at Diagnosis of Bladder Cancer on Survival: A Surveillance, Epidemiology, and End Results-Based Study 2004-2015. Retrieved from <https://pmc.ncbi.nlm.nih.gov/articles/PMC9903028/>.

14. Mohanty SK, Lobo A, Mishra SK, Cheng L. Precision medicine in bladder cancer: present challenges and future directions. *J Pers Med*, 2023; 13: 756. DOI: 10.3390/jpm13050756 (<https://doi.org/10.3390/jpm13050756>).

15. Oxidative Stress Markers in Urine and Serum of Patients with Bladder Cancer. *PMC*. 2023. <https://pmc.ncbi.nlm.nih.gov/articles/PMC9952604/>.

16. DGK α Enhances Tumorigenic Activity in Bladder Cancer Patients. *PMC*. 2023. <https://pmc.ncbi.nlm.nih.gov/articles/PMC11865707/>.

17. Kidney Function After Prostate and Urinary Bladder Cancer Surgery in Iraqi People. *Turkish*

Journal of Nephrology. 2025. <https://turkjnephrol.org/Content/files/sayilar/440/37-41.pdf>.

18. Liver function indicators and risk of hepatocellular carcinoma. *Frontiers in Genetics*. 2023. <https://www.frontiersin.org/journals/genetics/articles/10.3389/fgene.2023.1260352/full>.

19. Diagnostic significance of alanine aminotransferase isoenzymes in alcoholic and non-alcoholic fatty liver cancers. *Bioscience Reports*. 2023. <https://pubmed.ncbi.nlm.nih.gov/37883219/>.

20. Deciphering how lipid metabolism in cancer interfaces with the tumor microenvironment, *Molecular Cancer*, 2024 (<https://pmc.ncbi.nlm.nih.gov/articles/PMC11423921/>).

21. Higher genetically predicted triglyceride level increases the bladder cancer risk, *Scientific Reports*, 2024 (<https://www.nature.com/articles/s41598-024-69737-1>).