REVIEW ARTICLE

Journal of Pre-Clinical and Clinical Research
www.jpccr.eu

Microbiome and oncogenesis – role of the urobiome and its differentiation in the etiology of urinary bladder cancer

Wiktoria Śliwa[1,A-D], **Karol Olszak**[1,C-D], **Mateusz Pakosiński**[1,C-D], **Karolina Pidek**[1,C-D], **Iga Kuliniec**[2,E-F]

[1] *Student Scientific Society at the Department of Urology and Urological Oncology, Medical University, Lublin, Poland*
[2] *Department of Urology and Urological Oncology, Medical University, Lublin, Poland*
A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article

Śliwa W, Olszak K, Pakosiński M, Pidek K, Kuliniec I. Microbiome and oncogenesis – role of the urobiome and its differentiation in the etiology of urinary bladder cancer. J Pre-Clin Clin Res. doi:10.26444/jpccr/225060

Abstract

Introduction and Objective. Over the past few years, there has been growing interest among researchers in exploring the role of the microbiome in the human body. In the field of oncology, as knowledge about cancer and its treatment expands, new reports are emerging regarding the microbiome and its potential impact on the etiology of bladder cancer. The aim of the study is to analyze the available literature on the relationship between microbiome and bladder cancer.
Review Methods. A search of the PubMed and Scopus databases was conducted from inception to 20 December 2025. Original articles written in English and open access from 2018–2025, focusing on the analysis of urine samples from patients with and without bladder cancer, were included in the review. Review articles, case reports, letters to the editor, commentaries, and conference abstracts were excluded from the analysis.
Brief description of the state of knowledge. Significant differences in urinary microbiome composition were observed between healthy individuals and bladder cancer patients, as well as between urine samples obtained from women and men. A different microbiota composition was also observed in patients with cancer recurrence.
Summary. There is a correlation between urinary bladder cancer and changes in the urobiome in patients, which could be used in the future as panels combined with other factors as a helpful diagnostic tool. Microbiota testing may also be useful in predicting cancer recurrence. However, further large-scale studies are necessary to confirm these relationships for specific bacterial strains, as the currently available data are heterogeneous and subject to significant error due to the population and methodological bias of the study group. It is advisable to sensitize patients to the presence of symptoms that may suggest bladder cancer and to develop effective preventive measures.

Key words
microbiota, urinary bladder neoplasms, urine, diagnostic techniques

INTRODUCTION AND OBJECTIVE

Interest in the human microbiome has been growing for several years. Recent literature in this field enhances our understanding of disease pathogenesis, underlying causes, and associated symptomatic changes, focusing particularly on the role of the microbiome in oncogenesis. This review focuses on the urinary tract microbiota, the alterations observed in bladder cancer patients, and their potential role in the etiopathogenesis of the disease.

MATERIALS AND METHOD

Pubmed and Scopus databases were used to identify scientific articles. The database search was carried out between 1 December 2025 – 20 December 2025. Articles were searched using the following key words: 'urobiome' OR 'urinary microbiome' OR 'urinary microbiota' OR 'bladder microbiota' OR 'dysbiosis' AND 'bladder cancer' OR 'bladder neoplasm' AND 'oncogenesis' OR 'carcinogenesis' OR 'inflammation' OR 'inflammatory cytokines' OR 'toll-like receptors'. Original papers from 2018 – 2025 that included individuals with confirmed bladder cancer and a control group without cancer were analyzed; these papers then analyzed the composition of the urinary microbiota. Papers with free access and written only in English were selected. Exclusion criteria included reviews, case reports, letters to the editor, commentaries, and conference abstracts. Studies conducted exclusively *in vitro* or exclusively on animal models were also excluded. Studies whose subject matter was unrelated to the topic discussed in this paper and lacked clear information about the sampling method and bioinformatics analysis were not considered. Scopus limited the search to the following areas: Medicine; Biochemistry, Genetics, and Molecular Biology; Immunology and Microbiology; Pharmacology, Toxicology, and Pharmaceutics. Thirty-five articles were retrieved from PubMed, and 416 articles from Scopus. Duplicates were subsequently eliminated. The Rayyan software was used to analyze the articles. Articles were included or excluded based on abstracts in the first phase, and full texts were analyzed in the second phase. To further explore the topic, the bibliographies of the included articles and systematic reviews that contained the key words we used were analyzed. Subsequently, those with content

✉ Address for correspondence: Wiktoria Śliwa, Student Scientific Society, Department of Urology and Urological Oncology, Medical University, Doktora K. Jaczewskiego 8, 20-090 Lublin, Poland
E-mail: wiktoria.weronika.sliwa@gmail.com

Received: 21.05.2026; accepted: 25.06.2026; first published: 10.07.2026

deemed essential to provide a broader contextualization of the article were selected.

Ethical approval for the study was not required. This study is a narrative review summarizing studies that have already been published. It does not include any new data collection from human subjects or animals, and all data analyzed were obtained from publicly accessible sources.

Informed Consent was not relevant. The study reviews current literature and does not include direct engagement with human participants, or the use of any identifiable patient information.

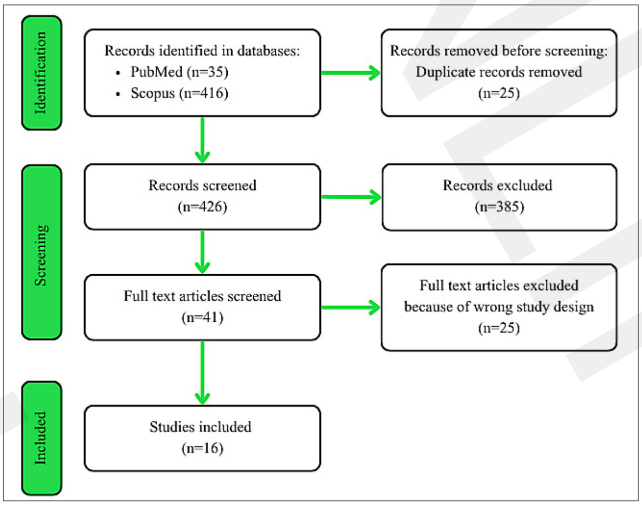

Figure 1. Study selection process

BLADDER CANCER AND UROBIOME – INTRODUCTION

Growing evidence indicates that specific microbial species are directly implicated in the etiopathogenesis of various malignancies. One of the best-known examples is *Helicobacter pylori*, which is associated with gastric cancer; another example is the HPV virus, which causes a significant proportion of cervical cancers [1]. The mechanisms linking the presence of specific pathogens to cancer are complex but can be grouped into three main categories: 1) the induction of inflammation, which can directly lead to cancer; 2) focuses on how microorganisms process nutrients and the toxic materials they release, which can lead to tumour development in remote areas of the body; 3) the body's immune response, which interferes with the proper elimination of cancer cells. These three mechanisms intertwine and complement each other in the pathogenesis of cancer [2,3].

Bladder cancer is a cancer that is becoming increasingly prominent, especially in Europe. According to GLOBOCAN 2022, the incidence of bladder cancer has increased to 614,298 new cases worldwide, ranking it ninth in the global incidence ranking – 225,596 deaths have also been recorded, making bladder cancer the 13th most lethal cancer. The etiology of this cancer is still not fully understood, and treatment is challenging for both the medical team and the patient. The highest incidence and prevalence of this cancer occur in the European population, which necessitates the development of new solutions and faster bladder cancer detection, perhaps in the future based on changes in the urobiome [4]. This is likely due to the fact that, although urine was considered microorganism-free for many years, today's scientific knowledge suggests otherwise. Recent microbiological and molecular techniques, such as 16S ribosomal RNA (16S rRNA) sequencing, have confirmed the presence of the urinary tract microbiome, also referred to as the urobiome [5]. Its composition can change throughout life, particularly under the influence of infection, smoking, antibiotic therapy, or diet. Gender also plays a key role in the composition of the urobiome [6,7]. Furthermore, the urobiome can significantly influence the induction of inflammation within the urinary tract and the clinical course of various urological disorders, such as interstitial cystitis and overactive bladder [8].

Therefore, there is a need to observe and study changes occurring in the urobiome, which may lead to chronic inflammation, and these subsequently predispose to the development of bladder cancer. Notably, established risk factors for bladder cancer, including smoking, obesity, and recurrent infections, have been shown to disrupt urobiome homeostasis, which may further influence disease progression [9, 10].

RISK FACTORS FOR URINARY TRACT CHANGES

Urinary tract infection is one of the most important factors contributing to urinary tract changes. It is usually triggered by *Escherichia coli*. Research has demonstrated that an *E. coli* infection can stimulate the NF-κB pathway, which subsequently prevents cell death, leading to the persistence and worsening of inflammation. Furthermore, this same bacterium can induce the progression of bladder cancer [6]. However, although women experience urinary tract infections more frequently, men are more likely to develop bladder cancer. Women, on the other hand, generally have a poorer prognosis. It is also possible that in women, frequent urinary tract infections stimulate the immune system, allowing the body to eliminate cancer cells more quickly and effectively [11].

Acinetobacter, among other known bacteria that activate the NF-κB pathway, may be involved in oncogenesis, as its growth has been observed in the urine of individuals with bladder cancer, as well as in tumour-affected tissues [11,12]. This correlation is particularly noticeable in patients diagnosed with high-grade urothelial carcinoma [11].

Another documented environmental factor that increases the risk of bladder cancer is exposure to chemicals, including polycyclic aromatic hydrocarbons and heavy metals. This exposure affects not only individuals working in harsh environments, but also smokers or passive smokers. The bacterium that metabolizes these substances is *Sphingomonas*, whose growth has been observed in patients with bladder cancer. Exposure to these substances can cause changes in the urobiome, in this case, the growth of *Sphingomonas*. Therefore, an interaction between heavy metal metabolism and oncogenesis is possible [11,13].

Other risk factors for bladder cancer include excess body weight, which itself causes many diseases. The strong association between obesity and urinary tract cancers remains a subject of ongoing investigation. However, a certain association has been observed between obesity and an increased risk of bladder cancer, as a 5 kg/m^2 increase in BMI alone corresponded to a 3.1%–4.2% increase in bladder cancer risk [10]. Given the increasing obesity rate in the population, this is another reason for appropriate preventive measures being essential, especially among paediatric patients.

REVIEW OF ORIGINAL STUDIES EXAMINING CHANGES IN THE UROBIOME

Table 1 presents a summary of 16 original studies in which urine samples were collected from patients with bladder cancer and healthy individuals, and analyzed for the presence of specific bacterial strains. The studies included patients categorized according to gender at birth.

According to the studies included in the current review, the microbiota in bladder cancer is altered. Ginwala R. et al. demonstrated that *Prevotella* was more prevalent in subtypes III and IV of bladder cancer (0%, 3%, 16%, and 18% in subtypes I, II, III, and IV, respectively (p=0.045, Fisher's test). It was also noted that the urine of bladder cancer patients contained numerous gammaproteobacteria, which detoxified gemcitabine in cell cultures [14].

Kang C. et al. investigated both urine and the impact of medical device materials on the proliferation of particular bacteria. In the study, non-sterile instruments exhibited a more diverse microbiome than other instruments. In male patients,

Table 1. Changes in the urobiome in patients with urinary bladder cancer

Author and year of investigation	Type of investigation	Participants of the investigation	Intervention	Control group of the investigation	Results and outcomes
Ginwala R., 2025 [7]	prospective cohort	76 patients with urothelial carcinoma (62 men, 14 women), median age – 70; outpatients	whole genome sequencing and 16S rRNA gene sequencing from urine samples	Archival diagnostic tumour samples from 21 bladder cancer patients	In women with bladder cancer: – increase in *Lactobacillus* and *Prevotella*. In patients with bladder cancer of both sexes: an increase in *Enterobacteriales*, *Flavobacterium*, *Varicubaculum*, and *Facklamia*. Patients: – who did not respond to neoadjuvant chemotherapy – increase in *Granulicatella* and *Proteus*; – who responded to treatment – presence of *E. faecalis*.
Moynihan M., 2019 [14]	cross-sectional observational	43 male patients with hematuria undergoing bladder cancer diagnostics (two excluded), including: 24 non-smokers (median age 61 years), 17 smokers (median age 67 years)	bacterial DNA isolation, PCR amplification, purification, 16S rRNA gene sequencing	35 patients without bladder cancer	No statistically significant change.
Kang C., 2025 [15]	observational case-control	35 patients with bladder cancer (6 women, 29 men), mean age – 67.6 years; 15 patients without cancer (2 women, 13 men), mean age – 67.2 years	DNA extraction, 16S rRNA gene sequencing	30 negative control samples (disposable instruments – catheters, consumables and laboratory reagents)	Latex materials: *Stenotrophomonas* dominance. Surgical instruments: *Escherichia* dominance. Mucosal tissue: *Rhodococcus*, *Rhizobium*, and *Pseudomonas* growth. Midstream urine: *Proteus* and *Providencia* growth. Catheter urine: *Comamonas* and *Fusimonas* growth.
Parra-Grande M., 2021 [12]	retrospective	32 patients (27 men, 5 women), average age – 67 years	DNA sequencing from samples	No typical control group was used. Paired samples from 26 patients with tumours and normal bladder tissue samples were included in the analysis. An additional 6 patients had only tumour tissue samples collected.	Healthy tissues: *Actinobacteria* predominate. In bladder cancer tissues decrease: *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, and *Actinobacteria*. Low-stage cancer: *Enterococcus* predominates.
Sheng Z., 2025 [11]	prospective, observational, case-control	Discovery cohort: 104 patients with bladder cancer (89 men, 15 women); mean age – 68.89 years; 56 with other malignant urinary tract tumours (43 men, 16 women); mean age – 63.95 years; 98 with benign urinary tract diseases (55 men, 43 women); mean age – 53.62 years Validation cohort: 66 patients with bladder cancer (49 men, 17 women); mean age – 65.27 years; 5 with other malignant urinary tract tumours (3 men, 2 women), mean age – 69 years; 51 with benign urinary tract diseases (31 men, 20 women), mean age – 52.82 years	DNA extraction and 16S rRNA gene sequencing from urine samples	Discovery cohort – 42 healthy controls; Validation cohort – 22 healthy controls	In patients with bladder cancer: – decreased numbers of *Firmicutes*, *Actinobacteria*, *Lactobacillales*, and *Bifidobacteriales*; – increased *Proteobacteria*, *Bacteroidetes*, *Sphingomonadales*, *Bacteroidales*, and *Clostridiales*; – The presence of *Sphingomonadaceae* and *Prevotellaceae* was observed. In patients with mild urinary tract disease: – dominance of *Lactobacillaceae*. Control group: – decreased numbers of *Sphingomonadales*; – increased numbers of *Lactobacillales*, *Bifidobacteriales*.

Author and year of investigation	Type of investigation	Participants of the investigation	Intervention	Control group of the investigation	Results and outcomes
Sheng Z., 2025 [13]	observational case-control with propensity score matching	170 patients – 125 with primary bladder cancer (108 men, 18 women); mean age – 67.62 years; 45 with recurrent bladder cancer during follow-up (31 men, 14 women), mean age – 67.13 years	DNA extraction and 16S rRNA gene sequencing from urine samples	Comparative analysis performed between two matched groups of patients: 39 patients with primary bladder cancer and 39 patients with recurrent bladder cancer (matching analysis is 1:1)	In both groups: *Firmicutes*, *Proteobacteria*, *Bacteroidetes* and *Actinobacteria*, *Prevotella*, *Streptococcus*, *Corynebacterium*, and *Escherichia/Shigella*. In patients with bladder cancer: increase in *Sphingomonas*, *Prevotella*, and *Corynebacterium*. In patients with recurrent bladder cancer: increase in *Veillonella*, *Escherichia/Shigella*, and *Lactobacillus*.
Li N., 2025 [16]	observational case-control	64 patients with bladder cancer (58 men, 6 women); mean age of men: 67 years, mean age of women: 68.5 years. 45 cases were primary tumours, and 19 were recurrent tumours.	DNA extraction and 16S rRNA gene sequencing from urine samples	94 healthy participants	In patients with bladder cancer: increase in *Firmicutes, Actinobacteria*, *Bacteroidetes*, *Proteobacteria*, *Fusobacteria*, *Tenericutes*, *Staphylococcus*, *Stenotrophomonas*, *Acinetobacter*, and *Propionibacterium*. In healthy women: increase in *Acinetobacter*, *Chryseobacterium*, and *Lactobacillus*. In healthy men: increase in *Corynebacterium*, *Staphylococcus*, *Veillonella*, *Gardnerella*, *Gemella*, *Helcococcus*, *Lactobacillus*, and *Sneathia*.
Nardelli C., 2024 [17]	observational case-control	48 patients (13 females, 35 males) who underwent transurethral resection of bladder tumour (TURBT), 30 patients with bladder cancer (BCa) (all >50 years old), including 5 women and 18 with benign bladder tumours	Analysis of 16S rRNA and urobiome diversity from urine samples	43 patients without cancer and 17 patients with prostate cancer	In patients with bladder cancer: increase in *Porphyromonas* and *Porphyromonas somerae*. In patients after TURBT: – increase in *Actinobaculum schaalii*, *Mobilincus*, *Peptoniphilus*, *Porphyromonas somerae*, and *Propionimicrobium lymphophilum*; – decrease in *Lactobacillus iners*. In the control group: – dominance of *Lactobacillus* and *Streptococcus*.
Wu P, 2018 [18]	observational case-control	31 men with bladder cancer (26 without muscle invasion and 5 with muscle invasion, mean age – 64 years)	16S rRNA gene sequencing from urine samples	18 men without bladder cancer, mean age 55.5	In patients with bladder cancer: – Increase in *Acinetobacter*, *Anaerococcus*, and *Sphingobacterium*; – Decrease in *Serratia*, *Proteus*, and *Roseomonas*. In the group at increased risk of recurrence and progression: – Increase in *Herbaspirillum*, *Porphyrobacter*, and *Bacteroides*.
Wu C, 2024 [19]	observational case-control	23 patients before bladder cancer treatment (20 men and 3 women), age 64.30 ± 11.18	16S RNA sequencing, flow cytometry and targeted metabolic profiling (mass spectrometry) from urine samples	9 cancer-free patients (8 men, 1 woman), age 56.44 ± 12.89	The *Actinomycetaceae* + arachidonic acid + IL-6 panel had satisfactory performance in diagnosing cancer (sensitivity 0.94, specificity 1.00). In the control group: increase in *Firmicutes* and *Proteobacteria*. In patients before therapy: increase in *Deinococcota*, *Bacteroidota*, *Actinobacteriota*, and *Fusobacteriota*.
LI J.K.M., 2025 [20]	cross-sectional observational	13 patients who recovered without intravesical Bacillus Calmette–Guérin (BCG) treatment (10 men, 3 women), mean age 70 years. 12 patients, 1–2 years after intravesical BCG treatment (10 men, 2 women), mean age 71 years.	DNA extraction and 16S rRNA gene sequencing from urine samples	9 patients without bladder cancer	In the observation group: presence of *Novosphingobium*, *Eubacterium xylanophilum*, *Ruminococcus*, *Alloscardovia*, *Roseburia*, *Capnocytophaga*, and *Akkermansia*. In the BCG vaccination group: increase in *Pseudomonas*, *Lactococcus*, and *Bacillus*. In the control group: presence of *Rubellimicrobium*, *Beijerinckiaceae*, *Microvirga*, *Oxalobacteraceae*, *Acidobacteriota*, *Vicinamibacteria*, *Luteitalea*, *Peptostreptococcus*, *Erysipelotrichaceae*, *Actinobacullum*, *Allobacullum*, *Solirubrobacteraceae*, *Blastocatella*, *Thermoleophilia*, and *Parviterribacter*. After BCG vaccination, increase in *Pseudomonas*, *Lactococcus*, and *Bacillus*.
Liu, Y., 2023 [21]	cross-sectional observational	32 patients with bladder cancer after radical cystectomy with various types of urinary diversion (including 13 patients with Studer neobladder, 10 patients with Bricker ileal conduit, 9 patients with cutaneous ureterostomy (CU))	DNA extraction and 16S rRNA gene sequencing from urine samples	5 patients without urinary tract diseases	In patients with Struder neobladder, the microbiota was most similar to that of healthy individuals, with an increase in *Barnesiella*. In patients with cutaneous ureterostomy: the microbiota was most disturbed. *Escherichia-Shigella* was frequently present in the three urinary diversion groups but was almost absent in healthy individuals. In healthy patients: the increase in *Barnesiella*.

Author and year of investigation	Type of investigation	Participants of the investigation	Intervention	Control group of the investigation	Results and outcomes
Mingdong, W., 2023 [22]	observational	Patients from GWAS databases: – Bladder cancer (BCa) – 951 patients, – Kidney cancer (KCa) – 1,631 patients, – Prostate cancer (PCa) – 79,148 patients	SNP analysis	Control group: cancer-free individuals from the same databases: – for bladder cancer – 307,092 controls, – for kidney cancer – 238,678 controls, – for prostate cancer – 61,106 controls.	Increased risk of bladder cancer (BCa) has been associated with: – *Bifidobacterium*, – *Actinobacteria*, – *Ruminococcus torques*. Reduced risk of bladder cancer (BCa) and prostate cancer (PCa) has been associated with: -*Allisonella*.
Uzelac, M., 2024 [23]	observational case-cont rol	In the main analysis: 18 patients with bladder cancer. In the validation set: 62 patients with bladder cancer.	16S rRNA gene sequencing from urine samples	In the main analysis: 12 healthy individuals In the validation set: 19 healthy individuals	*Escherichia*, *Acinetobacter*, and *Enterobacter* were consistently present in altered abundances. *Caldanaerobacter subterraneus* was significantly more abundant in urine samples from patients with bladder cancer. In contrast, the abundance of *Burkholderia ambifaria*, *Staphylococcus xylosus*, and *Klebsiella pneumoniae* was significantly lower in these samples.
Russo, F.,2024 [24]	observational case-control	102 men over 50 years of age, 37 patients with bladder cancer.	ddPCR	24 cancer-free patients – healthy control group, 41 oncology patients with prostate cancer – unhealthy control group	In patients with bladder cancer: Increase in *Porphyromonas somerae*. In the control group, the prevalence of *Porphyromonas somerae* was: – in healthy individuals – 20.8% – in patients with prostate cancer – 14.6%.
Zeng, J., 2020 [25]	observational case-control	62 patients with bladder cancer. This included 51 patients with non-muscle-invasive bladder cancer (NMIBC) and 11 patients with muscle-invasive bladder cancer (MIBC). The median age of patients was 65 years, and of smokers, 31.	16S rRNA sequencing from urine samples	19 men without cancer	Bacterial richness scores were significantly higher in the bladder cancer group than in the control group. Microbial diversity scores did not differ between groups. In patients with bladder cancer: Presence of *Streptococcus*, *Pseudomonas*, *Anaerococcus*, *Fusobacterium*, and *Acinetobacter*.

beta-diversity analysis revealed significant differences among the three sample types tested; however, when comparing two urine samples, no statistically significant difference was found ($p = 0.1449$). This suggests that mucosal tissue samples exhibit a different microbiome composition compared to urine samples. A similar trend was observed in female patients, with tissue samples from the urinary bladder mucosa showing a significant difference compared with urine samples, whereas the dominant bacterial taxa remained unchanged [15].

Some studies also examined microbial diversity. In the study by Parra-Grande M. et al., increased microbial diversity was observed in tumour-free tissues. Altered microbial composition was also noted in different tumour grades ($p = 0.03$ and 0.04 at the type and genus levels) [12].

Sheng Z. et al. demonstrated that the microbiota in patients with primary and recurrent bladder cancer exhibitd distinct functional profiles, which demonstrate diverse metabolic needs and ecological adaptations of the microbiota. It was shown that in patients with primary bladder cancer, the microbiota was significantly enriched in functional pathways related to metabolic adaptation, including carbon fixation pathways, tricarboxylic acid cycle, and prokaryotic cell cycle regulation pathways, whereas the microbiota in patients with recurrent bladder cancer presented significant contributions from functional pathways related to glucose metabolism and oxidative stress, such as amino sugar and nucleotide metabolism, pentose phosphate pathway, and starch and sucrose metabolism [13].

As changes occur in the urinary bladder caused by cancer, its biofilm also changes. In the study by Nardelli C. et al., it was observed that in patients diagnosed with BCa after TURBT, the microbiota was enriched in the genera *Aerococcus*, *Anaerococcus*, and *Porphyromonas*, and depleted in the genus *Gardnerella*. Enrichment in the species *Aerococcus urinae*, *Porphyromonas asaccharolytica*, *P. somerae*, and *Porphyromonas sp. 2007b* was also observed [17].

Functional pathways of urinary bacteria were also analyzed in the work of LI J.K.M. et al. In the observational group, the *de novo* biosynthesis pathways of various nucleotides, the biosynthesis of amino acids – threonine, and the biosynthesis of bacterial cell wall – peptidoglycan were enriched. In the BCG group, on the other hand, a significant intensification of the following pathways was found: the L-phenylalanine biosynthesis superpathway, the L-tyrosine biosynthesis superpathway, the biosynthesis of ubiquinol-7, 8, 9, 10, the lipopolysaccharide biosynthesis superpathway, the oxidative degradation of glucose, and the degradation of 4-hydroxyphenylacetate [20].

OVERVIEW OF STUDY RESULTS BY SAMPLE SIZE, GENDER DISTRIBUTION AND METHODOLOGICAL HETEROGENEITY

The study results presented in Table 1 demonstrate significant discrepancies in the microbiome diversity of patients with urinary bladder cancer, both in the general population and in gender-stratified analyses. The bacterial species that increase in abundance in urinary bladder cancer differ between studies, which may be influenced by such factors as small sample sizes, gender imbalance (a predominance of men), disease stage, and previous urological or cancer-related procedures. For example, Ginwala et al. reported an increased abundance of *Enterobacteriales*, *Flavobacterium*, *Varicubaculum*, and *Facklamia* in patients with bladder cancer, whereas Parra-Grande et al. identified a predominance of *Firmicutes*, *Bacteroidetes*, *Proteobacteria*, and *Actinobacteria* in these patients [7,12]. In most of the studies presented in Table 1, the sample size is too small, which limits the ability to draw more comprehensive and clinically reliable conclusions. Furthermore, the small proportion of women limits the ability to conduct comparative analysis between the two genders in terms of microbiome diversity.

Another limitation is the significant heterogeneity of the study populations. Some studies include patients who underwent specific types of procedures, making the results highly specific to these subgroups of patients and preventing the generalization of conclusions to the broader population. Furthermore, comparative analysis of studies may be complicated by methodological heterogeneity. The studies presented in Table 1 are mostly observational case-control or observational cross-sectional studies, which differ in sampling methods and inclusion criteria. Some studies do not present results stratified by gender, which may further contribute to discrepancies between the analyzed studies.

To enable the formulation of more objective conclusions, it is necessary to increase the number of available studies, include larger and more diverse study groups in terms of gender and age, and standardize methods for assessing the microbiome in patients with urinary bladder cancer.

DISCUSSION

This review included 16 studies that examined differences in the microbiome of urine/bladder tissue samples in oncology patients with bladder cancer, once in a control group – only one in the control group – whereas the other 15 demonstrated a significant association between alterations in the urinary microbiome and bladder cancer. Only one study did not find statistically significant differences (Moynihan M. et al. [14]).

Based on these findings, it is concluded that there is a correlation between changes in the urinary bladder microbiome and tumourigenesis in the urinary bladder. The most frequently observed shifts in the microbiome include an increase in the number of *Proteobacteria, Bacteroidetes,* and some bacteria belonging to the *Actinobacteria* and *Firmicutes*. Other systematic reviews (Yacouba A. et al. [26], Surber J. et al. [27], Ghabousian A. et al. [28]) also found such a correlation. This is important information that opens up further research opportunities to better understand the etiopathogenesis of bladder cancer.

However, study results are inconsistent regarding the increase or decrease of specific types of bacteria and gender. Different bacteria often predominated in patients with bladder cancer compared to healthy controls, depending on the specific cohort and the type of study, most of which were observational: case-control or cross-sectional. The study material included midstream urine samples, urine catheter samples, tissue samples from bladder tumours, and normal bladder mucosa tissue. Patient samples were analyzed by DNA extraction and 16S rRNA gene sequencing to assess the urinary tract. Unfortunately, the methodologies of these studies varied in terms of patient selection, sampling procedures, and gender stratification. Further studies should include larger, more homogeneous cohorts in terms of age and gender, while standardizing sampling techniques. A review by Wu C. et al. [19] indicated that in the future, certain bacterial strains, such as *Actinomycetaceae*, could be used in the diagnosis of bladder cancer, for example, in combination with arachidonic acid and IL-6 in the form of panels. It has also been noted that bacteria, such as gammaproteobacteria, can reduce the effectiveness of chemotherapy. Furthermore, the composition of the microbiota may predispose to cancer recurrence.

CONCLUSIONS AND OUTLOOKS

While still under investigation, 15 independent studies point to shifts in the urinary tract microbiome composition that may predispose to its development. Studies show that there is a distinct link in activities taking place between cancer-affected bladders and healthy controls. Additionally, a correlation exists between gender-based variations in the urinary microbiome (Fig. 2). Consideration should also be given to using urobiome bacteria for diagnosing and predicting bladder cancer.

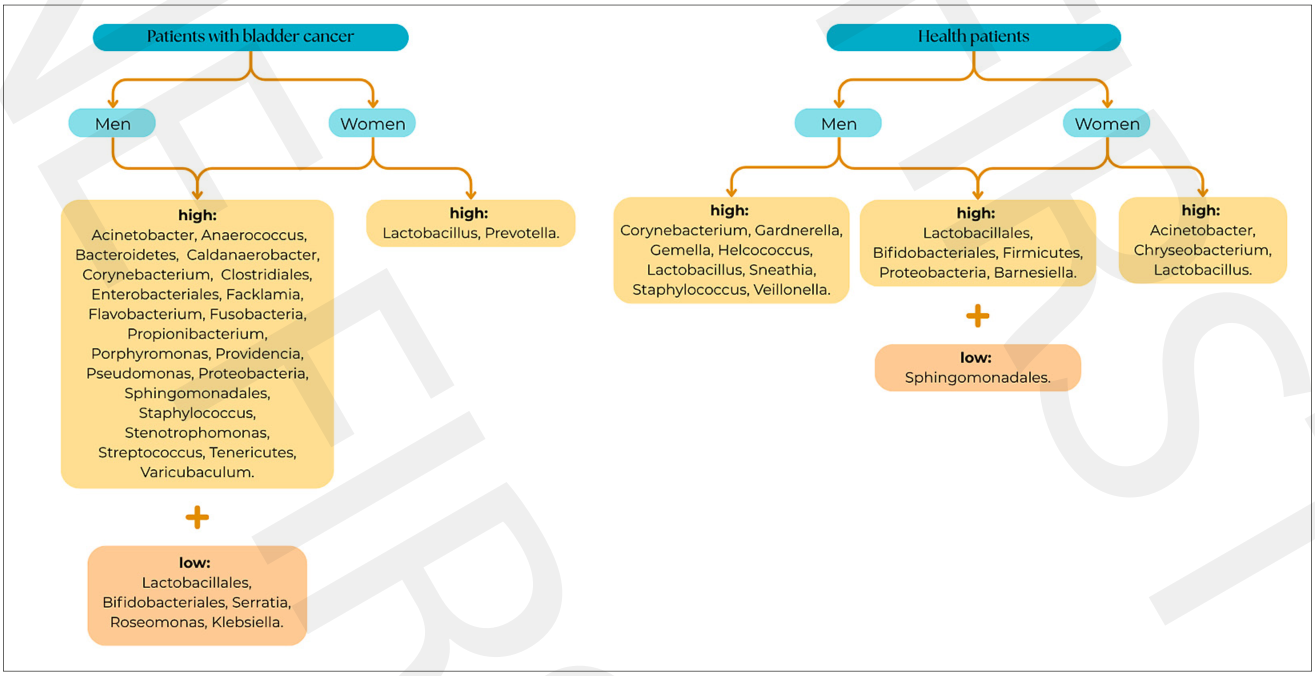

Figure 2. Summary of research results

Conflict of Interest. None.

Funding Source. The study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical Approval. None.

Patient Consent. None.

Declaration of generative AI and AI-assisted technologies in the manuscript preparation process. During the preparation of this review the authors used Rayyan.ai in order to facilitate the selection of studies. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the published article.

REFERENCES

1. van Elsland D, Neefjes J. Bacterial infections and cancer. EMBO Rep. 2018;19(11):e46632. doi:10.15252/embr.201846632
2. Zitvogel L, Daillère R, Roberti MP, et al. Anticancer effects of the microbiome and its products. Nat Rev Microbiol. 2017;15(8):465–478. doi:10.1038/nrmicro.2017.44
3. Roy S, Trinchieri G. Microbiota: a key orchestrator of cancer therapy. Nat Rev Cancer. 2017;17(5):271–285. doi:10.1038/nrc.2017.13
4. Ferlay J, Ervik M, Lam F, et al. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer. Published 2024. https://gco.iarc.who.int/today (accessed: 2025.12.12)
5. Aragón IM, Herrera-Imbroda B, Queipo-Ortuño MI, et al. The Urinary Tract Microbiome in Health and Disease. Eur Urol Focus. 2018;4(1):128–138. doi:10.1016/j.euf.2016.11.001
6. Heidar NA, Bhat TA, Shabir U, et al. The Urinary Microbiome and Bladder Cancer. Life (Basel). 2023;13(3):812. doi:10.3390/life13030812
7. Ginwala R, Bukavina L, Sindhani M, et al. Bladder cancer microbiome and its association with chemoresponse. Front Oncol. 2025;15:1506319. doi:10.3389/fonc.2025.1506319
8. Abernethy MG, Tsuei A. The bladder microbiome and interstitial cystitis: is there a connection? Curr Opin Obstet Gynecol. 2021;33(6):469–473. doi:10.1097/GCO.0000000000000747
9. Surber J, Semmler M, Enderlin D, et al. Microbiome landscapes of the bladder, intestine, and vagina in bladder cancer: a systematic review. Discov Oncol. 2025;16(1):525. doi:10.1007/s12672-025-02165-3
10. Papavasileiou G, Tsilingiris D, Spyrou N, et al. Obesity and main urologic cancers: Current systematic evidence, novel biological mechanisms, perspectives and challenges. Semin Cancer Biol. 2023;91:70–98. doi:10.1016/j.semcancer.2023.03.002
11. Sheng Z, Liu J, Wang M, et al. Exploring bladder cancer through urinary microbiota: innovative "urinetypes" classification and establishment of a diagnostic model. J Transl Med. 2025;23(1):809. doi:10.1186/s12967-025-06518-y
12. Parra-Grande M, Oré-Arce M, Martínez-Priego L, et al. Profiling the Bladder Microbiota in Patients With Bladder Cancer. Front Microbiol. 2022;12:718776. doi:10.3389/fmicb.2021.718776
13. Sheng Z, Xu J, Wang M, et al. The role of urinary microbiota in primary and recurrent bladder cancer: insights from a propensity score matching study. BMC Cancer. 2025;25(1):468. doi:10.1186/s12885-025-13817-6
14. Moynihan M, Sullivan T, Provenzano K, et al. Urinary Microbiome Evaluation in Patients Presenting with Hematuria with a Focus on Exposure to Tobacco Smoke. Res Rep Urol. 2019;11:359–367. doi:10.2147/RRU.S233386
15. Kang C, Lee J, Baek MG, et al. Urinary microbiome in non-muscle invasive bladder cancer: impact of sample types and sex differences. BMC Microbiol. 2025;25(1):623. doi:10.1186/s12866-025-04367-9
16. Li N, Wang L, Yang Q, et al. Identification and Evaluation of the Urinary Microbiota Associated With Bladder Cancer. Cancer Innov. 2025;4(4):e70012. doi:10.1002/cai2.70012
17. Nardelli C, Aveta A, Pandolfo SD, et al. Microbiome Profiling in Bladder Cancer Patients Using the First-morning Urine Sample. Eur Urol Open Sci. 2023;59:18–26. doi:10.1016/j.euros.2023.11.003
18. Wu P, Zhang G, Zhao J, et al. Profiling the Urinary Microbiota in Male Patients With Bladder Cancer in China. Front Cell Infect Microbiol. 2018;8:167. doi:10.3389/fcimb.2018.00167
19. Wu C, Wei X, Huang Z, et al. Urinary microbiome dysbiosis is associated with an inflammatory environment and perturbed fatty acids metabolism in the pathogenesis of bladder cancer. J Transl Med. 2024;22(1):628. doi:10.1186/s12967-024-05446-7
20. Li JKM, Wang L, Tse RTH, et al. A cross-sectional study on the effects of intravesical BCG on urinary microbiota in bladder cancer patients. Int Urol Nephrol. 2026;58(1):67–76. doi:10.1007/s11255-025-04607-x
21. Liu Y, Zhang J, Chen H, et al. Urinary microbiota signatures associated with different types of urinary diversion: a comparative study. Front Cell Infect Microbiol. 2024;13:1302870. doi:10.3389/fcimb.2023.1302870
22. Mingdong W, Xiang G, Yongjun Q, et al. Causal associations between gut microbiota and urological tumors: a two-sample mendelian randomization study. BMC Cancer. 2023;23(1):854. doi:10.1186/s12885-023-11383-3
23. Uzelac M, Xin R, Chen T, et al. Urinary Microbiome Dysbiosis and Immune Dysregulations as Potential Diagnostic Indicators of Bladder Cancer. Cancers (Basel). 2024;16(2):394. doi:10.3390/cancers16020394
24. Russo F, Esposito S, Tripodi L, et al. Insights into Porphyromonas somerae in Bladder Cancer Patients: Urinary Detection by ddPCR. Microorganisms. 2024;12(10):2049. Published 2024 Oct 10. doi:10.3390/microorganisms12102049
25. Zeng J, Zhang G, Chen C, et al. Alterations in Urobiome in Patients With Bladder Cancer and Implications for Clinical Outcome: A Single-Institution Study. Front Cell Infect Microbiol. 2020;10:555508. Published 2020 Dec 15. doi:10.3389/fcimb.2020.555508
26. Yacouba A, Tidjani Alou M, Lagier JC, et al. Urinary microbiota and bladder cancer: A systematic review and a focus on uropathogens. Semin Cancer Biol. 2022;86(Pt 3):875–884. doi:10.1016/j.semcancer.2021.12.010
27. Surber J, Semmler M, Enderlin D, et al. Microbiome landscapes of the bladder, intestine, and vagina in bladder cancer: a systematic review. Discov Oncol. 2025;16(1):525. doi:10.1007/s12672-025-02165-3
28. Ghabousian A, Shafigh A, Tayebi S, et al. The Potential Role of Urinary Microbiota in Bladder Carcinogenesis: A Systematic Review. Urol J. 2024;21(4):208–220. doi:10.22037/uj.v20i.8036