Review paper

Urinary tract infections: epidemiological and clinical aspects

Zakażenia układu moczowego: aspekt epidemiologiczno-kliniczny

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Słowa kluczowe: zakażenia układu moczowego, uropatogeny.

Abstract

Urinary tract infections are one of the most common infections affecting outpatients and hospital patients. They are believed to affect 150 million people annually and can present as an asymptomatic infection or infections of varying course and location. Patients most often present with symptoms of dysuria or increased frequency of urination. Urinary tract infections can be divided into lower and upper urinary tract infections, and the most common aetiological agents are Enterobacterales bacilli such as: *Escherichia coli*, *Proteus* spp., *Klebsiella* spp., *Enterobacter* spp., and Gram-positive cocci *Enterococcus* spp., *Streptococcus agalactiae*, and *Staphylococcus saphrophyticus*. Urinary tract diseases are a major public health burden, and significantly affect the quality of life of affected individuals. The choice of antibiotic and dosage should take into account the patient's health status, the effectiveness of the drug, along with its side effects.

Streszczenie

Zakażenia układu moczowego są jednym z najczęstszych zakażeń dotyczących pacjentów ambulatoryjnych oraz szpitalnych. Uważa się, że dotyczy 150 milionów ludzi rocznie i może ono przebiegać w postaci bezobjawowej infekcji lub zakażeń o różnym przebiegu i umiejscowieniu. Chorzy zwykle zgłaszają się z objawami dyzurii lub zwiększoną częstością oddawania moczu. Zakażenia układu moczowego można podzielić na zakażenia dolnego i górnego odcinka dróg moczowych, a najczęstszymi czynnikami etiologicznymi są pałeczki z rzędu *Enterobacterales*, takie jak *Escherichia coli*, *Proteus* spp., *Klebsiella* spp., *Enterobacter* spp. bądź ziarenkowce Gram-dodatnie *Enterococcus* spp., *Streptococcus agalactiae*, *Staphylococcus saphrophyticus*. Choroby układu moczowego stanowią duże obciążenie dla zdrowia publicznego, a także znacznie wpływają na jakość życia osób, u których one wystąpiły. Przy wyborze antybiotyku i dawkowania powinno uwzględnić się stan zdrowia pacjenta, skuteczność leku wraz z jego działaniami niepożądanymi.

Introduction

Urinary tract infections (UTIs) in children and adults are one of the most common nosocomial (40%) and post-hospital (10–20%) infections. Approximately 15% of all antibiotics are prescribed for UTIs [1, 2]. Urinary tract infections can present as acute, symptomatic infections of varying severity or can occur as asymptomatic bacteriuria. Very often, UTIs are caused by bacteria constituting the physiological flora of the gastrointestinal tract or microorganisms colonising the skin [3]. Urinary tract infections are favoured by anatomical abnormalities, functional bladder disorders, bladder-ureter reflux, bladder catheterisation, diagnostic and surgical procedures in the urinary tract area, prostatic hypertrophy, diabetes mellitus, kidney stones, immunosuppression, pregnancy, and sexual activity [4, 5]. The predominant aetiological agent of UTI is uropathogenic *Escherichia coli*, accounting for 80–90% of out-of-hospital infections and 40% of hospital cases of UTIs [5, 6]. The development of urinary tract infection is usually by the ascending route [7]. The main symptoms are dysuria, haematuria, pyuria, nycturia, frequent urination, difficulty urinating, pain or discomfort in the suprapubic area, bladder tenderness, fever, and foul-smelling urine [8]. Urinary tract infections can be accompanied by complications such as kidney stones, prostatitis and epididymitis, pyelonephritis, sepsis, or septicaemia [9].

Pathogenesis

Urinary tract infections are a very heterogeneous group of clinical conditions, ranging from asymp-

tomatic bacteriuria that is not a medical condition and does not require treatment with few exceptions, to life-threatening conditions in the form of urosepsis [3, 10]. Definitions of UTI can be presented as an inflammatory reaction occurring on the transitional epithelium lining the urinary tract caused by bacteria, viruses, or fungi, with subjective or physical symptoms in the patient [10, 11]. Bacteria exhibit characteristics that allow them to invade the urinary tract. One of these features is the ability of microorganisms to adhere to the transitional epithelium. This is done by means of adhesins found in the bacterial wall, which bind to receptors present in the walls of urothelial cells. This process leads to the penetration of bacteria into the epithelial cells of the urinary tract and the development of infection. Uropathogens, such as *Escherichia coli*, survive by attacking the bladder epithelium. They produce toxins and proteases to release nutrients from host cells and synthesise siderophores to obtain iron. Another characteristic of *E. coli* is its ability to escape immune mechanisms by leaving the urothelial cells before they exfoliate. This allows the microorganisms to spread infection in the urinary tract. Uropathogens can enter the kidney and, attaching via adhesins or pili, colonise the renal epithelium and then produce tissue-damaging toxins. Consequently, microorganisms can cross the epithelial barrier of the renal tubules, gain access to the bloodstream, and initiate bacteraemia [12]. The ability of bacteria to adhere to the transitional epithelium of the urinary tract leads to their build-up and formation of a structure called a biofilm (Figure 1). A biofilm is an organised multicellular form surrounded by an extracellular polymeric substances (EPS) matrix [13]. A biofilm can be formed by bacteria of one or many genera or even species. They can be autotrophic microorganisms, heterotrophic microorganisms, and saprophytes [14]. Up to 95% of bacteria have the ability to form this three-dimensional structure on the surface of living cells and biomaterials [13, 15].

It used to be thought that urine should be sterile. However, recent studies of the flora colonising the human body have concluded that the urinary tract is not sterile and has its own microbiota [16, 17]. The microorganisms residing in the urinary tract are of low biomass and cannot be cultured by standard methods used in microbiological diagnosis. It is likely that they exert a protective effect by protecting against colonisation by uropathogens. It is known that the composition of the microbiota is altered in all pathological conditions [17]. The development of urinary tract infection can occur via the ascending, bloodstream, and lymphatic routes [11]. The most common route for the development of UTI is through the ascending urethra into the bladder [7, 10]. Infections spread by the haematogenous route do not exceed 2% of all UTIs. They occur infrequently in severely immunocompromised patients. The source of infection is often the intestinal flora, and the primary focus of infection is the renal parenchyma. Infection via the lymphatic vascular route is extremely rare. Increased pressure in the urinary bladder causes lymph to flow toward the renal parenchyma, and this can lead to the development of a UTI [10].

Urinary tract infections can be divided into the following:

- lower urinary tract infections (urethritis, cystitis, prostatitis),
- infections of the upper urinary tract (pyelonephritis, according to the new nomenclature, acute bacterial tubulointerstitial nephritis) (Figure 2).

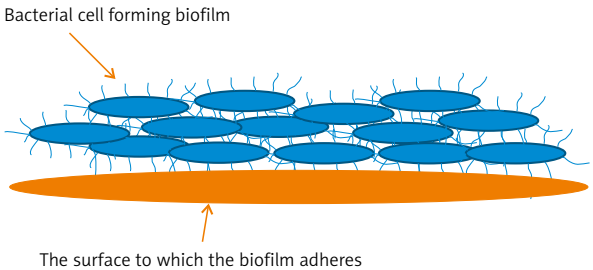

Figure 1. Diagram of the bacterial biofilm. Source: own study

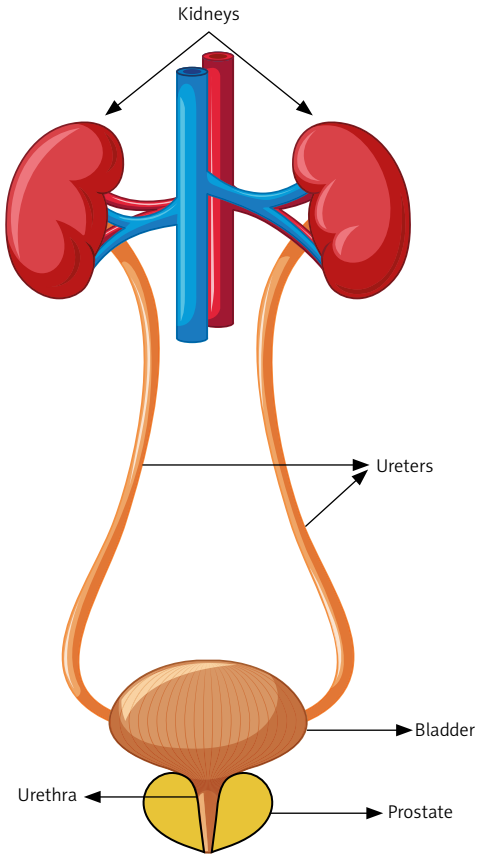

Figure 2. Schematic of the urinary tract (+ prostate gland present in men). Source: own study

UTI can be acute, chronic, or recurrent. However, the most clinically useful division is between uncomplicated (primary) and complicated (secondary) infections [3, 11]. The differentiation of complicated and uncomplicated infections is important, especially for the choice of therapy, because the risk of therapeutic failure and the occurrence of multiple complications is higher in complicated UTIs [18]. These infections usually affect patients with anatomical and/or functional abnormalities of the urinary tract, kidney stones, a urinary catheter, or diabetes mellitus, as well as disorders of both local and systemic defence mechanisms [3, 11]. Uncomplicated UTIs are defined as acute, sporadic, or recurrent, and can occur in patients with no anatomical or functional defects in the urinary tract or other associated diseases. They can affect both the lower and upper urinary tract [12].

Under physiological conditions, the urinary system has several defence mechanisms to prevent uropathogens from colonising the urinary tract and to eliminate them from the system. These include the following:

- length of the urethra;
- peristalsis of the ureters;
- physiological flora of the urethral outlet and vagina in women;
- the density and acidity of the urine;
- operation of the vesicoureteral valves;
- secretion of the prostate gland with antimicrobial activity;
- mechanisms that prevent the proliferation of bacteria in the bladder;
- mechanisms that prevent colonisation of the urinary tract:
- mechanical flushing of microorganisms during micturition,
  - uromodulin,
  - protective mucopolysaccharide layer present on the bladder mucosa,
  - presence of immunoglobulins IgG, IgA,
  - oligosaccharides,
  - physiological bacterial flora [10, 11, 19].

The length of the urethra is of great importance in protecting against the development of urinary tract infections. Women are much more likely to develop UTIs than men because of the shorter urethra and its close proximity to the vagina and rectum. The longer urethra in men provides much better protection against microbial entry into the bladder than in women [10, 11, 19]. The peristalsis of the ureters and the efficient operation of the vesicoureteral valves are responsible for the correct direction of flow of urine from the renal pelvis to the bladder and prevent retrograde outflow of urine. Antimicrobial activity is also demonstrated by the process of urine thickening and acidification. High concentrations of urea and organic acids are important in inhibiting the growth of microorganisms, but also high or low molality concerning highly concentrated or diluted urine [10]. The physiological flora of the urethral outlet and vagina in women prevents uropathogens from colonising the urinary tract by blocking access to receptors on the surface of the bladder mucosa. It consists mainly of lactic acid bacilli, coagulase-negative staphylococci, mycobacteria, and streptococci. In men, the antimicrobial effect is demonstrated by prostatic secretions containing prostatic antimicrobial factor (PAF). Both the presence of PAF and a longer urethra in men are major indicators of less frequent urinary tract infections. Under physiological conditions, microorganisms that have entered the bladder do not have the opportunity to multiply efficiently and are eliminated externally through micturition. Efficient flushing of bacteria, mechanisms that block the adhesion of pathogens to the bladder walls, as well as the antimicrobial properties of urine and mucous membranes prevent the development of urinary tract infections. The volume of urine retained in the bladder after micturition is also important, the larger it is, the more likely the development of a UTI [10]. Uromodulin, a glycoprotein detected in urine by Tamm and Horsfall in 1950, is an extremely important protein that prevents bacteria from adhering to the walls of the urinary tract. Under normal conditions, it is produced in the loop of Henle in the thick section of the ascending part constituting the main component of physiological proteinuria. It is excreted in the amount of 20–50 mg/day. The appearance of uromodulin in the interstitial tissue of the kidneys may indicate the development of pyelonephritis, because under physiological conditions it is found only in the urine. Mucopolysaccharides covering the mucosa of the bladder walls also prevent colonisation by uropathogens, although their mechanism of action is not fully understood. Inhibition of bacterial adhesion also occurs in the presence of immunoglobulins in the urine. Antibodies are directed against the somatic antigen O or against the ciliary antigen P of *Escherichia coli*. Immunoglobulins IgG and IgA, as well as secretory IgA, are found in the urine of patients with pyelonephritis. In addition, various oligosaccharides are present in the material studied, which bind to microbial adhesins, thus blocking their adhesion to the urinary tract mucosa [10]. Despite the many defence mechanisms that prevent the development of UTIs, a number of factors can be listed that promote urinary tract infections [20]. These are divided into physiological and pathological factors, and include the following:

- Physiological factors: advanced age, pregnancy, and puerperium;
- Pathological factors: urinary stasis, retrograde urinary outflow, kidney stones, urinary tract catheterisation, immunosuppressive drugs, abuse of nonsteroidal anti-inflammatory drugs (NSAID), and metabolic disorders (diabetes mellitus, gout, hypokalaemia, hypercalcaemia) [10, 11, 21].

Table 1. Data sheets on the number of cases of sepsis caused by Gram-negative bacteria in 2022 and in the period 01/01/2023 to 30/09/2023. Source: Own study by a co-author from the Military Institute of Medicine – National Research Institute in Warsaw

Date	Average length of hospitalisation [days]	Men	Women	Children	Others	Total
1.01–31.12.2022	13,45	64	53	1	0	118
1.01–30.09.2023	11,96	37	32	1	0	70

Urinary tract catheterisation is a factor that significantly promotes the development of urinary tract infections, so this procedure should be used only in strictly defined situations, when, for example, a patient requiring long-term immobilisation, with perineal wounds to promote their healing, or a patient with urinary incontinence and urinary retention caused by a sub-bladder obstruction. It is important to keep the catheter in the bladder as short as possible (for as little time as possible). The procedure for placing it in the urinary tract should be carried out with aseptic principles using disposable equipment. In addition, care should be taken to ensure the tightness of the catheter-drain-tank system and to prepare a plan of care for the patient (including adequate fluid supply) [22]. Working with a catheterised patient requires medical personnel to follow a sanitary regime. Care procedures among patients should be carried out with disposable materials, under aseptic conditions, to prevent the transmission of pathogens to other patients. Factors that increase the risk of developing UTIs in patients with a urinary catheter are prolonged catheterisation time, colonisation of the bag, chronic kidney disease, reduced immunity, and diabetes [23, 24]. Bacterial virulence mechanisms also contribute to the development of urinary tract infections. Among these are the production of urease, the ability to colonise the large intestine and urethral area, and the ability to multiply in the urine [25].

Epidemiology

Urinary tract infections are considered one of the most common infectious diseases. They affect more than 150 million people annually. Complicated UTIs place the greatest burden on the health care system as the most common cause of hospitalisation [26]. The incidence of UTIs results in 8 million visits to hospital emergency departments and 100,000 hospital admissions [27]. Among patients presenting to the ED with septicaemia, the isolate is derived from urine in 27% of cases, a condition referred to as urosepsis [28]. For hospitalised patients, the number of urosepsis cases increases to 42% [29]. According to the ICD10, there is no diagnosis that uniquely identifies urosepsis and septicaemia with a point of origin in the urinary tract. Based on data from the Military Medical Institute – National Research Institute, a hospital with 1000 beds, the number of cases of septicaemia caused by Gram-negative bacteria (the most common aetiological agent of urosepsis) is shown to be close to 100 (Table 1). In smaller health care units containing close to 500 beds, the number of cases of septicaemia originating in the urinary tract is around 50–60 per year, with a predominance among men. In the case of children, the number may be underestimated because they are most often treated in highly specialised centres dedicated to children, such as the Children's Health Centre in Międzylesie or the Mother and Child Institute. In women, UTIs usually occur between the ages of 16 and 35 years, with 10% of patients getting the disease every year and between 40% and 60% of women getting it at least once in their lifetime [18, 27, 30, 31]. Among women, recurrences are common, with nearly half having a second infection within a year [30]. It is estimated that between 30% and 44% of women will have a second UTI within 6 months of their first infection [27]. In men, urinary tract infections are much less common, with fewer than 10 cases for every 10,000 men under the age of 65 per year [27]. Catheter-related urinary tract infections account for about 9% of all hospital-acquired infections, and it is believed that about 65–70% of these infections are preventable [32]. Urinary tract infections are the second most common bacterial infection in children. They affect 8% of girls and up to 2% of boys during the first 7 years of life. There is a peak incidence in infancy, another in childhood, and increased incidence occurs again during adolescence. Children with the highest incidence of UTIs are newborns, infants, young girls, and uncircumcised boys [33].

Symptoms of UTIs

Patients with urinary tract infections present with symptoms of dysuria or increased frequency of urination [34]. The clinical picture of a UTI can vary widely from asymptomatic bacteriuria to severe, life-threatening urosepsis [25]. Symptoms of infections involving the lower urinary tract most commonly include dysuria, nycturia, frequent urination, and involuntary urination. In older women, there may additionally be an unpleasant urine odour, a feeling of incomplete bladder emptying, uterine prolapse, and malaise [5, 25, 35, 36]. On the other hand, patients with bacterial tubulointerstitial nephritis (formerly acute pyelonephritis) have fever, chills, nausea, vomiting, low back pain and abdominal pain, and headache. Gold-

flam's sign, or low back pain, can also be observed [25, 36].

Aetiology of UTIs

Urinary tract infections are common infections among both inpatients and outpatients [37]. They pose a serious public health problem due to the increasing drug resistance of uropathogens. They are most commonly caused by Enterobacterales as well as Gram-positive bacteria and fungi [12, 33]. Uncomplicated UTIs are caused by uropathogenic *Escherichia coli* (UPEC) in about 85% of cases; in complicated infections, the proportion of other Gram-negative Enterobacterales such as *Proteus* spp., *Klebsiella* spp., *Enterobacter* spp., and *Providencia* spp. and non-fermenting bacilli *Pseudomonas aeruginosa* and *Acientobacter* spp. increases [5, 25, 38, 39]. For Gram-positive bacteria in uncomplicated infections, the main aetiological agents are *Enterococcus* spp. and *Streptococcus agalactiae*, and in women of childbearing age, *Staphylococcus saprophyticus* is the agent in about 10% of cases. In contrast, *Enterococcus* spp., *Staphylococcus* spp., and species other than *S. saprophyticus*, *Streptococcus* spp., and *Corynebacterium urealyticum* are most commonly isolated in complicated infections [12, 25, 38]. In extramural urinary tract infections, *E. coli* is also the most common uropathogen because of its inclusion in the intestinal microbiota, which allows it to easily colonise the urinary tract [38]. Anaerobic bacteria can also be responsible for urinary tract infections. Because of the widespread colonisation of the urogenital tract by these microorganisms, they can contaminate urine samples collected from the midstream or cause infection [40]. The most commonly isolated are anaerobic Gram-negative bacilli, such as *Bacteroides fragilis*, *Porphyromonas* spp., and *Prevotella* spp. but also Gram-positive *Clostridium* spp. and anaerobic Gram-positive cocci and *Acitnomyces* spp. They cause urethral abscesses, cystitis, acute and chronic prostatitis, prostatic abscesses, renal abscesses, perinephric abscesses, scrotal abscesses, and pyelonephritis, among others [25]. In developing countries, mycobacteria are also a cause of UTIs [41]. Urinary tract infections can also be caused by fungi. This is known as candiduria. It is often observed in hospitalised patients and is mostly asymptomatic, with *Candida albicans* being the most commonly isolated species [25, 42, 43]. This is followed by *C. glabrata* and *C. tropicalis*. In recent years, the proportion of *C. glabrata* in candiduria has increased, and among neonates, *C. parapsilosis* is the predominant species causing candidiasis [43]. The presence of yeast-like fungi in the urine can be caused by pyelonephritis, cystitis, prostatitis, epididymitis, and testicular or disseminated candidiasis. The main risk factors for candiduria are diabetes mellitus, disease, malignancy, urinary catheters, taking broad-spectrum antibiotics, immunosuppressive treatment, urinary tract obstruction, and hospitalisation in an intensive care unit [42, 43]. In asymptomatic patients, the presence of *Candida* in the urine is not a basis for starting antifungal therapy. Exceptions are neutropaenic patients, very low birth weight infants, and patients undergoing urological procedures [42]. If fungi are cultured in a single urine sample, it is important to remember that cultures must be repeated to confirm the fungal aetiology of the UTI [25]. Among the viruses causing UTIs, adenoviruses (especially type 11) commonly cause haemorrhagic cystitis in children (more often in boys) and kidney and bone marrow transplant patients, in addition to BK virus and cytomegalovirus (CMV). In places such as Africa, where *Schistosoma haematobium* is endemic, UTIs can be caused by this parasite and are often associated with kidney stones and ureteral stricture [25, 41].

Treatment of UTIs

Urinary tract diseases are a major public health burden and significantly affect the quality of life of affected individuals [12]. The choice of antibiotic and dosage should take into account the patient's health status, the effectiveness of the drug, and its side effects [35]. Amoxicillin was, until a certain point, the first-line antibiotic for the treatment of urinary tract infections, but unfortunately, with the rise of *E. coli* resistance, it has become a less therapeutically acceptable choice [38, 44]. Nitrofurantoin, trimethoprim, sulfamethoxazole, ciprofloxacin, fosfomycin, and ampicillin are the drugs most commonly prescribed for the treatment of UTIs [12, 35, 38, 44]. Trimethoprim/sulfamethoxazole, on the other hand, should only be used in cases where resistance among the population to this chemotherapeutic is known to be less than 20% or information is placed on the result about the susceptibility of the microorganism to this drug [35]. Urinary tract infections are becoming increasingly difficult to treat due to the increasing resistance of uropathogens [45]. Gram-negative Enterobacterales producing class C β-lactamases (AmpC cephalosporinases) show resistance to third-generation cephalosporins, as well as to β-lactamase inhibitors (clavulanic acid, sulbactam, tazobactam). Extended substrate spectrum β-lactamases (ESBLs) are also of concern, because microorganisms producing these enzymes, in addition to resistance to penicillins, cephalosporins, monobactams (except aztreonam), often show resistance to other groups of antimicrobial drugs. ESBL-type enzymes, unlike AmpC, show sensitivity to β-lactamase inhibitors [4, 12]. Among uropathogens, carbapenemase-producing microorganisms (Gram-negative bacilli of the Enterobacteriaceae family, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*) falling into 3 classes according to Ambler's classification are increasingly present. Carbapenemase class A – KPC, class B – metallo-β-lactamases, and class D – OXA

[4, 12]. Due to the increasing resistance of microorganisms, new antimicrobial drugs have been introduced, among others, new inhibitors of β-lactamases with non-β-lactam structure, i.e. avibactam, relebactam, and vaborbactam [4, 12]. Avibactam combined with ceftazidime has application in the treatment of urinary tract infections, especially for strains that produce β-lactamases with an extended substrate spectrum and class A and D carbapenemases. Avibactam has also been combined with aztreonam, and this has resulted in an antimicrobial product that is resistant to metallo-β-lactamases [4, 46]. Another new combination that can be used to treat urinary tract infections, including pyelonephritis, is meropenem/aborbactam (vaborbactam). It is active against microorganisms that are producers of class A (ESBL, KPC) and class C β-lactamases AmpC. Uropathogens that produce KPC carbapenemase or AmpC cephalosporinases can also be effectively treated with imipenem/cilastatin/relebactam [4, 46].

Multidrug resistance is also common among Gram-positive cocci. *Enterococci* are naturally resistant to cephalosporins, clindamycin, low concentrations of aminoglycosides, trimethoprim/sulfamethoxazole. Unfortunately, enterococci have the ability to acquire resistance to high concentrations of aminoglycosides (HLAR) and glycopeptides [12, 46]. Resistance to glycopeptides, including vancomycin (VanA, VanB phenotype), which is considered one of the last lines of defence against multidrug-resistant pathogens, is among the most clinically and epidemiologically significant [12, 46].

Treatment of candiduria is recommended only for symptomatic infections. Asymptomatic candiduria in uninfected patients is not an indication for treatment [42, 45]. The drug of choice is fluconazole, which reaches therapeutic concentrations in urine. Other antifungal drugs of the azole and echinocandin group do not reach sufficient urinary concentrations. Amphotericin B deoxycholate is an alternative antifungal agent if fluconazole cannot be used due to resistance, allergy, or failure [42].

In addition, intravesical infusions containing hyaluronic acid and chondroitin sulphate can be used in the treatment of interstitial cystitis, overactive bladder, and in the prevention of recurrent UTIs, affecting the restoration of the glycosaminoglycan layer [45]. Treatment of ZUM with antibiotics is an effective method and is commonly used, but in uncomplicated infections the body often recovers on its own. In mild forms of UTI, patients can try other methods as an alternative to antibacterial drugs to speed up the recovery process, such as hydration, which means taking plenty of water and avoiding drinks that irritate the bladder (alcohol and caffeinated drinks). Water promotes the removal of unnecessary metabolites from the body while retaining essential nutrients and electrolytes needed by the body. Drinking an adequate amount of water dilutes urine and accelerates its removal from the body, thus making it more difficult for bacteria to access the urinary organs and cause infection (Figure 3) [38, 39, 47].

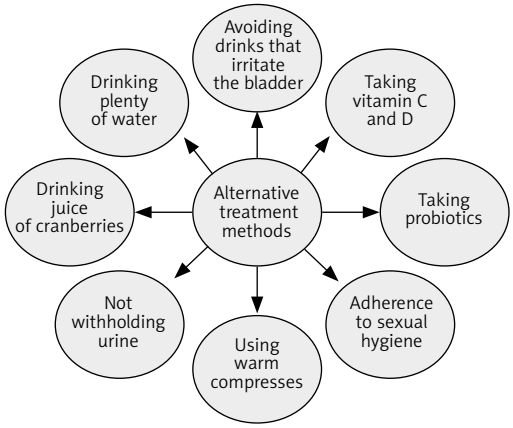

Figure 3. Alternative treatments for UTIs [38, 39, 47, 48]

The introduction of antibiotics into the clinic has reduced morbidity and mortality from bacterial infections. However, in recent years we have witnessed an increase in antibiotic resistance among bacteria, including uropathogenic ones [38]. Antibiotic prophylaxis remains the most effective method of management in the treatment of UTIs, so to develop effective antimicrobial drugs it is necessary to understand their mechanism of action [38]. The alarmingly high trend in the incidence of drug-resistant uropathogens has spurred researchers to seek alternative control measures and new therapeutic options [12]. However, non-antibiotic prophylactic strategies, such as cranberry, vitamin C, and methenamine salts, lack strong evidence-based science for their introduction as routine management options and alternatives to antibiotics [47, 48].

Conclusions

Urinary tract infections are among the most common infections in both hospital and non-hospital settings. The main aetiological agent is uropathogenic *Escherichia coli* (UPEC). Urinary tract colonisation is favoured by the biofilm-forming ability of uropathogens. Identifying the microorganism and determining its drug susceptibility is extremely important and significantly reduces the cost and toxicity of antibiotic therapy. The drugs most commonly prescribed for the treatment of UTIs are nitrofurantoin, trimethoprim, sulfamethoxazole, ciprofloxacin, fosfomycin, and ampicillin. In mild forms of UTIs, alternative treatments may be used. In most cases, however, an antibiotic is prescribed, and this can contribute to the increase in antimicrobial resistance of microorganisms. The increasing rates of drug resistance and the high frequency of recurrent infections pose

a heavy burden on society. Therefore, in combating this problem, it is important for doctors to know about the epidemiology and resistance of bacteria not only in the urinary tract. Ideally, alternative therapies should be developed that are effective against the development of resistance in the microbial world.

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Conflict of interest

The authors declare no conflict of interest.

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