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## DIAGNOSTIC AND TREATMENT METHODS FOR URINARY TRACT INFECTIONS IN HEMATOLOGICAL PATIENTS

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## ABSTRACT

**Research Objectives:** To evaluate diagnostic and therapeutic methods for urinary tract infections (UTIs) in hematological patients, focusing on both conventional antimicrobial therapy and alternative treatment strategies in this immunocompromised population.

**Methods:** Comprehensive literature review of diagnostic approaches including urine culture techniques, pathogen identification, and antimicrobial resistance patterns. Analysis of therapeutic strategies encompassing empirical and targeted antimicrobial therapy, alongside alternative modalities including cranberry supplementation, probiotics, urinary alkalinization, NSAIDs, and immunotherapy.

**Results:** Hematological patients face elevated UTI risk (34.39% prevalence) with predominant pathogens including *E. coli* (19.99%) and *Klebsiella* spp. (5.12%), frequently exhibiting multidrug resistance. Rapid microbiological diagnosis with susceptibility testing is critical for preventing progression to urosepsis. Alternative therapies demonstrate prophylactic potential but cannot replace antimicrobial treatment in established infections.

**Conclusions:** Effective UTI management in hematological patients requires rapid diagnostics, aggressive empirical therapy guided by local resistance patterns, and prompt de-escalation following susceptibility results. Alternative approaches serve valuable adjunctive roles but must not delay definitive antimicrobial therapy. Multidisciplinary collaboration and continuous protocol adaptation based on evolving resistance patterns optimize outcomes in this vulnerable population.

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## KEYWORDS

Urinary Tract Infection, Hematological Patients, Antimicrobial Resistance, Multidrug-Resistant Pathogens, Empirical Therapy, Immunosuppression

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## 1. Introduction

Infections represent one of the most frequent complications in hematological patients. Infectious symptoms occur in up to 92.3% of patients receiving high-dose therapy (HDT) and autologous hematopoietic stem cell transplantation (HSCT).[1] Based on retrospective data from the Canadian Myelodysplastic Syndromes (MDS) Registry spanning 2006-2022, the frequency and severity of infectious complications were determined. Approximately 31% of patients experienced fever or infection, of which 19% required hospitalization, and 9% died as a consequence.[2] Among oncological patients, including the hematological subgroup, the global risk of urinary tract infection was estimated at 34.39%, developing due to immunosuppression resulting from the underlying disease or as an adverse effect of its treatment.[3]

Urinary tract infection (UTI) is defined as the presence of microorganisms in the urinary tract above the bladder sphincter, characterized by significant bacteriuria in a urine sample collected for laboratory analysis and symptoms of active urinary tract infection. Patients in hematological departments are particularly susceptible to such infections due to immunosuppression, presence of catheters, and comorbidities. These patients frequently develop infections with multidrug-resistant strains.[4] Based on article analysis, the frequency of UTI occurrence was estimated according to etiology: the most common was *Escherichia coli* at approximately 19.99%, followed by *Klebsiella* spp. at 5.12%.[3]

Due to hematopoietic system dysfunction, hematological patients are particularly vulnerable to urinary tract infection complications, a consequence of significant immunosuppression in the course of leukemias and lymphoproliferative disorders. Risk of infection is further increased by comorbidities, instrumentation of the urinary tract, and prolonged indwelling bladder catheterization. Additionally, extended hospitalization of hematological patients increases the risk of infection with hospital-acquired multidrug-resistant strains.

The objective of this work is to summarize currently utilized diagnostic and treatment methods for UTI applicable to hematological patients, with the aim of enhancing diagnostic and therapeutic efficacy, as this problem affects all departments and constitutes a genuine threat to patient health and life.

## 2. Methods

A comprehensive narrative review of the literature was conducted, encompassing both primary research studies and secondary sources including systematic reviews, meta-analyses, and clinical guidelines. The search strategy was designed to capture all relevant literature examining diagnostic methods and therapeutic approaches for urinary tract infections in hematological patients across various healthcare settings.

The databases MEDLINE (PubMed), EMBASE, Cochrane Central Register of Controlled Trials, and Web of Science were systematically searched according to the Medical Subject Headings (MeSH) strategy. The search terms employed were: ("urinary tract infection" OR "UTI" OR "cystitis" OR "bacteriuria") AND ("hematological patients" OR "hematologic malignancy" OR "leukemia" OR "lymphoma" OR "immunosuppression" OR "neutropenia") AND ("diagnosis" OR "treatment" OR "antimicrobial therapy" OR "antibiotic resistance"). No language restrictions were applied initially, though only articles available in English and Polish were ultimately included in the final analysis.

Publications were included for analysis where hematological patients with urinary tract infections of any severity were described, diagnostic methods or therapeutic interventions were evaluated, and data on antimicrobial resistance patterns, treatment efficacy, safety profiles, or clinical outcomes were available. Studies were excluded if they involved only pediatric populations exclusively, if they examined UTIs in non-hematological immunocompromised patients without relevant comparison, or if they lacked sufficient methodological detail to assess quality.

Two independent reviewers performed the initial selection of titles and abstracts, followed by full-text evaluation of studies meeting preliminary inclusion criteria. Any discrepancies between reviewers were resolved through consensus discussion, with the possibility of expert consultation when necessary.

Data extracted from included studies comprised: type of publication (original research, systematic review, meta-analysis, clinical guidelines, case series), study design (randomized controlled trial, cohort study, case-control study, observational study), country and setting (hospital ward, intensive care unit, outpatient clinic), population characteristics (age, sex, type of hematological malignancy, degree of immunosuppression), diagnostic methods employed (urine culture thresholds, pathogen identification), therapeutic interventions (antimicrobial agents, dosing regimens, duration of therapy, alternative treatments), antimicrobial resistance patterns, primary and secondary endpoints analyzed, and the main conclusions of the study authors.

Given the heterogeneity of study designs, patient populations, diagnostic criteria, and outcome measures across the included literature, a quantitative meta-analysis was not feasible. Therefore, the synthesis was narrative, critical, and qualitative in nature, focusing on identifying consistent patterns and best practices in diagnosis and treatment while acknowledging methodological limitations, regional variations in resistance patterns, and potential sources of bias.

## 3. Results of Literature Review

### 3.1 Diagnosis of Bladder Infections

In hematological patients, the criteria for diagnosing urinary tract infections do not differ from those applied in other oncological patients or those without malignancy history. The primary approach is differential diagnosis based on typical clinical symptoms suggestive of UTI, such as fever, dysuria, urinary urgency, changes in urine color, or turbidity.[5] To confirm the presence of bacteria in urine, a culture must be performed. The standard approach is midstream urine collection, the simplest method allowing bacterial detection, quantification, and culture for antibiotic resistance testing. Many laboratories define  $10^5$  CFU/mL (colony-forming units) in urine as the threshold. However, this threshold overlooks many significant infections. Alternative recommendations exist that advocate UTI diagnosis at  $10^3$  CFU/mL, depending on the bacterial species detected or collection method.[6]

When midstream urine collection is problematic, instrumental sampling using catheterization or suprapubic aspiration is possible. These urine collection methods are characterized by higher sterility, resulting in a lower colony count threshold for UTI diagnosis. For samples obtained via suprapubic aspiration, the colony count necessary for infection diagnosis is  $10^3$  CFU/mL.[6]

Another indicator requiring attention is the bacterial species detected in the urine sample. Detailed examination of colonies growing on laboratory media allows differentiation between sample contamination

with bacterial flora naturally present on urinary tract mucous membranes and near the urethral meatus from bacterial groups classified as pathogenic. Pathogens causing urinary tract infections include: *Escherichia coli*, *Staphylococcus saprophyticus*, *Klebsiella* species (spp.), *Enterobacter* spp., *Proteus* spp., *Morganella morganii*, *Staphylococcus aureus*, and *Enterococcus* spp.[7] However, in hematological and immunosuppressed patients, the most common infection source is antibiotic-resistant hospital flora,[4] which poses a particular threat to patient health and life and creates numerous challenges in eradicating these microorganisms from the patient's urinary tract.

**Table 1.** Major Multidrug-Resistant Pathogens in Hematological Patients with UTI

| Pathogen                       | Resistance Pattern                   | Prevalence in Oncological Patients | Clinical Significance                        |
|--------------------------------|--------------------------------------|------------------------------------|--|
| <i>Klebsiella pneumoniae</i>   | Carbapenem-resistant (KPC, NDM, OXA) | High                               | Severe infections, limited treatment options |
| <i>Staphylococcus aureus</i>   | Methicillin-resistant (MRSA)         | Moderate                           | Hospital-acquired, biofilm formation         |
| <i>Acinetobacter baumannii</i> | Carbapenem-resistant                 | 21%                                | High mortality, pan-resistant strains        |
| <i>Escherichia coli</i>        | ESBL-producing                       | Most common (19.99%)               | First-line therapy failure                   |
| <i>Pseudomonas aeruginosa</i>  | Extended resistance                  | Moderate                           | Catheter-associated infections               |
| <i>Enterococcus</i> spp.       | Vancomycin-resistant (VRE)           | Increasing                         | Difficult eradication                        |

Note: Data compiled from references [4, 8, 18, 19]. ESBL = Extended-Spectrum Beta-Lactamase; KPC = *Klebsiella pneumoniae* Carbapenemase; NDM = New Delhi Metallo-beta-lactamase; OXA = Oxacillinase.

According to studies in oncological patients, UTIs caused by multidrug-resistant (MDR) pathogens were documented, including carbapenem-resistant *Klebsiella pneumoniae*, methicillin-resistant *Staphylococcus aureus* (MRSA), and 21% carbapenem-resistant *Acinetobacter baumannii*. [8] The increased risk of antibiotic-resistant hospital flora infection in hematological patients results from the necessity of prolonged hospitalizations, frequent invasive procedures, and cumulative prior antibacterial therapies. Infection risk increases proportionally with hospital length of stay, which is particularly significant in hematological departments where hospitalizations often last days or weeks. [9]

In the context of microbiological examination of samples from patients with urinary tract infections, monitoring antibiotic resistance of detected microorganisms is particularly important. [10] Hematological patients constitute a group with significantly reduced immunity; therefore, treatment of confirmed infection should be implemented as rapidly as possible. [11] For therapy to be effective, antibiotic treatment must be adjusted based on culture results and antibiogram. [12] This approach enables rapid implementation of targeted therapy and minimizes the risk of urosepsis development, which in immunosuppressed patients may progress rapidly and constitute a direct life threat, especially when inappropriate initial therapy is employed. [13]

### 3.2 Treatment Methods

#### 3.2.1 Antibiotic Therapy

Treatment of urinary tract infections in hematological patients requires particularly careful antibiotic selection. Due to neutropenia, immunosuppression, and frequent hospitalizations, these patients constitute a high-risk group for developing infections caused by microorganisms with significant antibiotic resistance. Treatment duration should be adjusted to the patient's clinical condition, detected bacteria, and antibiotic resistance. In treating hematological patients, basic treatment regimens for urinary tract infections developed for the general population may be employed. These should constitute empirical treatment, applied when UTI symptoms occur and implemented immediately after specimen collection for culture, before microbiological urine test results become available. [14] Following antibiogram results, treatment should be appropriately modified to targeted therapy incorporating the obtained results.

Empirical antibiotic selection in hematological patients depends on several key factors, including local epidemiological data on microbial resistance, severity of the patient's clinical condition, history of previous infections caused by multidrug-resistant (MDR) strains, and information regarding antibiotic therapy administered in recent weeks. The presence of catheters that may serve as colonization sites or other hospital-acquired infection risk factors is also significant. [15]

In empirical therapy of urinary tract infections in hematological patients, fluoroquinolones are most commonly employed due to their broad spectrum of activity against Gram-negative bacteria.[16] Trimethoprim-sulfamethoxazole is particularly recommended when *Stenotrophomonas maltophilia* infection risk exists or when the patient is already receiving this drug prophylactically. Nitrofurantoin is primarily applicable in uncomplicated lower urinary tract infections, provided the patient does not have severe immunosuppression and renal involvement is not suspected. Other broad-spectrum antibiotics, such as  $\beta$ -lactams with  $\beta$ -lactamase inhibitors, are utilized when ESBL-producing strain infection risk exists.[17]

In severely ill, febrile patients or those with suspected hospital-acquired infection, consideration of broader-spectrum agents selected according to local microbial resistance profiles is necessary. Following urine culture and antibiogram results, therapy should be narrowed as rapidly as possible, employing the most effective antibiotic with the narrowest spectrum of activity (de-escalation). This approach reduces MDR bacterial selection risk and limits subsequent complications, including urosepsis.

In hematological patients, urinary tract infections are frequently caused by ESBL-producing Enterobacterales, carbapenemase-positive strains (KPC, NDM, OXA), *Pseudomonas aeruginosa* with extended resistance, and *Enterococcus* spp., including VRE. Therefore, rapid verification of microbial resistance and therapy personalization are crucial for avoiding severe complications such as sepsis and worsening prognosis in hematological patients.[18,19]

### 3.2.2 Symptomatic and Supportive Treatment

In clinical practice treating the general population with urinary tract infections, non-antibiotic methods are also employed. These may limit antibiotic use in mild UTI cases or serve as supportive and symptomatic treatment. Alternative therapies include urine alkalinization, probiotics, cranberry, NSAIDs, and immunotherapy. Although many of these methods may support antibiotic therapy, direct evidence that they can completely replace it is lacking. Therefore, in immunosuppressed patients, these methods may be utilized as prophylaxis or supportive treatment; however, they should be applied cautiously and must not delay primary antibiotic treatment implementation.[20,21,22]

Table 2 summarizes the key characteristics, efficacy, and clinical applications of alternative therapeutic approaches.

**Table 2.** Alternative and Supportive Therapeutic Approaches for UTI in Hematological Patients

| Intervention                                  | Mechanism of Action  | Efficacy   | Safety Profile  | Clinical Application in Hematological Patients                              |
|---|--|--|---|---|
| <b>Cranberry</b>                              | PAC inhibit <i>E. coli</i> adhesion to bladder epithelium                    | 30% UTI risk reduction; juice > capsules (35% vs 26%)                        | Generally safe; warfarin interaction  | Prophylaxis in low-risk patients; adjunctive therapy only                   |
| <b>Probiotics (<i>Lactobacillus</i> spp.)</b> | Competitive exclusion, antimicrobial metabolite production, immunomodulation | 50% reduction in recurrent UTI episodes                                      | Excellent (>90% adherence); rare translocation risk in severe immunosuppression | Prophylaxis during remission; avoid during severe neutropenia               |
| <b>Urinary Alkalinization</b>                 | pH modification reduces dysuria symptoms                                     | Symptomatic relief; no proven antimicrobial effect                           | Drug interactions (warfarin, diuretics); crystalluria risk                      | Symptomatic treatment only; monitor pH and concurrent medications           |
| <b>NSAIDs</b>                                 | Anti-inflammatory; pain reduction  | Effective symptom relief but lower cure rates; increased pyelonephritis risk | Increased complication risk vs. antibiotics                                     | Symptomatic treatment only; must be combined with antibiotics               |
| <b>Immunotherapy (MV140 vaccine)</b>          | Immune stimulation against uropathogens                                      | 50-90% recurrence prevention at 12 months                                    | Excellent; mild fatigue, nausea   | Limited efficacy during active immunosuppression; consider during remission |
| <b>Increased Hydration</b>                    | Mechanical flushing; reduced bacterial contact time                          | 50% reduction in recurrent UTI episodes                                      | Excellent; no adverse effects   | Universal application; does not interfere with diagnostics or treatment     |

Note: PAC = Proanthocyanidins; Data compiled from references [20-34]. All alternative approaches should complement, not replace, antimicrobial therapy in established infections.

### 3.2.3 Cranberry

Cranberry (*Vaccinium macrocarpon*) is employed as an alternative supportive method in urinary tract infection (UTI) prophylaxis and treatment. The principal active substances are proanthocyanidins (PAC), anthocyanins, benzoic acid, and ursolic acid, which inhibit *Escherichia coli* bacterial adhesion to bladder epithelium. Based on a 2021 meta-analysis, cranberry supplementation was shown to reduce UTI risk by 30% in susceptible populations.

Cranberry juice was demonstrated to be more effective than capsules (35% vs. 26% reduction), potentially due to superior bioavailability of active compounds, although optimal PAC dosage has not been established but typically ranges from 36–72 mg/day. Cranberry use as adjuvant therapy is emphasized, potentially reducing antibiotic necessity in mild cases or as supportive treatment.

Results appear promising despite limitations including study heterogeneity, short observation periods, and potential drug interactions, e.g., with warfarin, necessitating further randomized clinical trials. In clinical practice, cranberry may be recommended to patients with low complication risk as an element of non-antibiotic strategy or as prophylaxis for UTI in at-risk groups and oncological patients with concurrent urinary tract infections.[20,23]

### 3.2.4 Urine Alkalinization

Urine alkalinization using sodium or potassium citrate preparations is widely employed in alleviating uncomplicated UTI symptoms, including dysuria and frequency, by rapidly increasing urine pH within one hour, as confirmed in pharmacokinetic studies. These products are classified as over-the-counter (OTC). Through citrate metabolism to bicarbonates in the Krebs cycle or direct action in renal tubules, they modify the chemical environment in the urinary tract, potentially reducing pain symptoms. Despite their popularity, systematic evidence of urine alkalinization therapy efficacy in UTI treatment is lacking.[24]

Urine alkalinization can significantly affect antibiotic solubility in UTI treatment, increasing crystalluria risk for sulfamethoxazole, amoxicillin, and ciprofloxacin, particularly at pH >7, correlating with clinical reports and the EUADR database (87 cases for cotrimoxazole, 52 for ciprofloxacin, 25 for amoxicillin). Simultaneously, pH-dependent relationships have been demonstrated in vivo: alkalinization improves trimethoprim and cotrimoxazole activity against *E. coli* at pH 7, increases nitrofurantoin excretion but reduces its activity above pH 6.5, while not affecting amoxicillin. Nevertheless, results are uncertain as randomized clinical trials confirming these effects are lacking.[22]

In clinical practice, alkalinization is recommended as supportive, symptomatic, or adjuvant therapy in low-risk populations. However, particular caution regarding interactions with warfarin and potassium-sparing diuretics is warranted. Urine pH monitoring is also important, especially in catheterized patients, elderly patients, or those with crystalluria history. Combining alkalinizing therapy with antibiotics should be conducted under medical supervision to minimize adverse effect and interaction risks while maximizing combined treatment benefits. In hematological patients, this therapy may be applied, though it should be introduced cautiously. Urine alkalinization must not weaken or delay proper treatment implementation and should be used as supportive therapy.

### 3.2.4 Probiotics

Probiotics, primarily preparations containing *Lactobacillus* strains (*L. crispatus*, *L. rhamnosus* GR-1, *L. reuteri* RC-14) and bifidobacteria, represent a promising non-antibiotic strategy in recurrent urinary tract infection prophylaxis in premenopausal women with history of  $\geq 3$  UTI episodes annually. In randomized double-blind trials, vaginal *Lactobacillus* spp. supplementation in an 8-day/month regimen for 4 months reduced symptomatic UTI frequency at 4 months from 70.4% to 40.9%, while combination with oral lactic acid bacteria and bifidobacteria probiotics reduced it to 31.8%. Effects persisted at 12 months (54.5% vs. 95.4%), with mean recurrence number declining from 3.83 to 2.04 and time to first recurrence extending from 69 to 142 days.[25]

Mechanisms include spatial competition with uropathogens *E. coli*, *K. pneumoniae*, *P. mirabilis*; production of antibacterial metabolites including hydrogen peroxide, lactic acid, and bacteriocins; biofilm inhibition; and immunomodulation through increased vaginal microbiota *Lactobacillus*, affecting *E. coli* reduction. Oral preparations supported effects through intestinal microbiota, though vaginal administration

was more effective independently compared to oral. No difference was demonstrated between vaginal and combined supplementation, suggesting significant local colonization impact.[26]

Probiotics are considered safe due to absence of serious adverse events and inducing subjective improvement in 70–79% of patients vs. 20% with placebo; adherence >90%. In the context of antibiotic resistance and recurrent UTI, vaginal probiotics in a 1 tablet/8-day regimen or combined in a 2 capsules orally/day regimen for 4–12 months represent an alternative to chronic prophylaxis, though meta-analyses indicate the necessity of large-scale multicenter studies on this topic. However, they may constitute an alternative prophylaxis or supportive treatment pathway for hematological patients, especially in chronic diseases with prolonged immunosuppression states, planned hematological treatment that may result in immunity reduction or involves extended hospitalization. Such therapy may be applied prophylactically; however, in treatment, this method should be used as supportive to proper antibiotic therapy and should not delay it, as this may lead to severe infection course and septic states.

### 3.2.5. NSAIDs

Non-steroidal anti-inflammatory drugs (NSAIDs), such as ibuprofen, have been studied as non-antibiotic therapy in uncomplicated urinary tract infections (UTI) in women. A randomized trial demonstrated that initial symptomatic treatment with ibuprofen reduced antibiotic prescriptions but resulted in slower symptom resolution and increased the proportion of patients requiring rescue antibiotic therapy due to NSAID treatment failure. Higher risk of infection progression to pyelonephritis was also observed, suggesting limited safety of NSAID monotherapy as first-line treatment.[27]

Recent developments in uncomplicated UTI treatment with NSAIDs have shown that compared to antibiotics, anti-inflammatory treatment is associated with reduced efficacy and cure rates in the first 3–7 days of therapy, with more frequent subsequent antibiotic initiation. Meta-analyses comparing NSAIDs and antibiotics demonstrated increased risk of complications such as pyelonephritis, despite reduced antibiotic consumption. These results suggest NSAIDs effectively alleviate pain, urgency, and frequency but do not provide adequate infection control in some patients.[28]

Another study involving women with mild, uncomplicated UTI showed that some patients treated with NSAIDs alone achieved spontaneous symptom reduction and resolution without antibiotic therapy, but symptom severity was greater than in the group receiving basic antibiotic therapy. This translates to longer symptom duration and poorer patient comfort, which is significant in multimorbid and professionally active patients. Authors emphasize the necessity of patient selection and enabling rapid antibiotic re-treatment in the absence of improvement.[29]

Based on available data, NSAIDs may be considered as short-term or supportive therapy in selected patients with mild, uncomplicated UTI, at low complication risk, and provided rapid antibiotic initiation is possible in case of symptom persistence or intensification. Antibiotic therapy should not be replaced by NSAIDs as standard first-line treatment, especially in patients with severe symptoms, fever, flank pain, comorbidities, or history of complicated UTI, due to greater infection progression risk and lower early cure rates.[30] In hematological patients, such therapy should be employed solely as symptomatic treatment for reducing burdensome symptoms such as pain or fever but should be combined with appropriate etiological treatment, namely antibiotic therapy dependent on the causative uropathogen.

### 3.2.6 Immunotherapy – Novel Experimental Treatment Method

Immunotherapy represents a novel experimental non-antibiotic strategy for recurrent urinary tract infection (rUTI) prophylaxis, particularly in patients with  $\geq 2$  episodes in 6 months or  $\geq 3$  in 12 months. Studies indicate that UTI pathogenesis is closely associated with bacterial adhesion to urinary tract epithelium, biofilm formation capacity, and evasion of host immune response. The therapeutic mechanism derives from stimulation of urinary tract mucosa immune response and systemic response. Preclinical and early clinical studies on vaccines based on surface antigens such as type 1 fimbriae, P-fimbriae, or iron transport proteins demonstrate potential in inducing humoral and cellular responses, which may limit urinary tract colonization by pathogens and reduce UTI recurrence frequency. Authors emphasize, however, that despite promising experimental study results, UTI immunization remains challenging due to pathogen heterogeneity and immune response complexity within the urinary tract.[31]

Similar effects were obtained for polyvalent MV140 vaccine based on whole, inactivated cells of *E. coli*, *K. pneumoniae*, *E. faecalis*, and *P. vulgaris*. Dosing regimen was established as 2 doses/day for 3 months. A prospective study demonstrated recurrent urinary tract infection (UTI) rate decreased from 4.79 to 1.58/year,

with significantly higher efficacy in postmenopausal women. No differences were demonstrated regarding sex, BMI, regular sexual activity, hypertension, diabetes, depression, paraplegia, or in catheterized patients. Approximately 73% of immunotherapy patients reported milder symptoms, with satisfaction rating of 7.52/10. Rare adverse events such as fatigue and nausea were noted, which did not significantly impact the experience. MV140 demonstrates 50–90% absence of UTI recurrence at 12 months in European studies, in women and men with recurrent UTI, including complicated cases. Despite favorable treatment outcomes, multicenter randomized trials are needed to confirm long-term efficacy and optimize regimens to achieve optimal prophylaxis and recurrent urinary tract infection treatment effects.[32] However, applying this method in hematological patients requires consideration of significant immunosuppression states in these patients, which may simultaneously translate to reduced method efficacy in recurrent UTI prophylaxis.

### 3.3 Risk Factor Modification – Hydration

Increased hydration represents a simple, non-invasive strategy for recurrent urinary tract infection (rUTI) prophylaxis, particularly in women with uncomplicated UTI. The mechanism is based on increasing urine flow through the bladder, increasing diuresis volume, mechanical flushing of uropathogens from the urinary tract, and urine dilution, reducing bacterial (*E. coli*) contact time with bladder mucosa and decreasing colonization. In a multicenter randomized trial, drinking an additional 1–1.5 L of water daily with total hydration of 2.5–3 L for 12 months reduced rUTI episodes by 50% compared to the control group without intervention, with similar adherence and absence of significant adverse events.[33,34] This method should be employed in all patients regardless of health status and comorbidities. It limits infection probability and enhances bladder self-cleansing of residual bacterial colonies while not affecting the diagnostic process or proper antibiotic treatment implementation.

## 4. Discussion

This comprehensive review demonstrates the complex challenges associated with diagnosis and treatment of urinary tract infections in hematological patients. The global prevalence of UTIs in oncological patients, estimated at 34.39% [3], underscores the magnitude of this clinical problem, with hematological patients at exceptionally high risk due to prolonged hospitalizations, frequent invasive procedures, and severe immunocompromise [4].

The diagnostic approach requires heightened vigilance, as the traditional threshold of  $10^5$  CFU/ml may be inadequate when clinically significant infections occur at lower colony counts [6]. While *E. coli* (19.99%) and *Klebsiella* spp. (5.12%) predominate [3], the critical distinction lies in the substantially higher prevalence of multidrug-resistant organisms, including carbapenem-resistant pathogens and ESBL-producing Enterobacteriaceae [4, 8, 18, 19]. This phenomenon correlates with hospitalization duration [9] and creates a vicious cycle where high-risk patients harbor resistant organisms.

Rapid microbiological diagnosis with antimicrobial susceptibility testing is critical [10, 11, 12], as hematological patients face substantially elevated risk of rapid progression to urosepsis [13]. This mandates aggressive empirical therapy followed by prompt de-escalation based on susceptibility patterns. Empirical therapy must be guided by local resistance epidemiology and patient-specific risk factors [15], with fluoroquinolones [16] facing increasing resistance and broader-spectrum agents [17] reserved for critically ill patients.

Non-antibiotic approaches require careful consideration in hematological patients. Cranberry supplementation demonstrates 30% UTI risk reduction [20, 23] but cannot replace antimicrobial treatment in established infections. Urinary alkalization offers symptomatic relief [24] but presents concerns regarding drug interactions [22]. Probiotic therapy shows efficacy in preventing recurrent UTIs [25, 26], though concerns about systemic translocation exist in profoundly immunosuppressed patients. NSAIDs provide symptomatic relief [27, 28, 29] but demonstrate lower cure rates and increased pyelonephritis risk [30], warranting use only as adjunctive therapy. Immunotherapy with MV140 vaccine shows promise [31, 32] but requires intact immune function, limiting applicability during active disease or intensive chemotherapy.

Increased hydration (1-1.5 liters additional daily) represents a universally applicable strategy, reducing recurrent UTI episodes by 50% [33, 34] without adverse effects or interference with standard therapy.

Clinical practice considerations include: first, historical approaches from immunocompetent populations cannot be extrapolated to hematological patients, demanding more aggressive empirical therapy; second, local antibiogram data must guide therapy choices; third, multidisciplinary collaboration optimizes outcomes through expert antimicrobial stewardship.

Future research should focus on prospective studies evaluating optimal empirical regimens stratified by immunosuppression degree, rapid molecular diagnostics, novel antimicrobials for MDR organisms, and immunotherapy efficacy across varying immunocompromise levels. Cost-effectiveness analyses and quality improvement initiatives would inform resource allocation and practice optimization.

## 5. Conclusions

This comprehensive review demonstrates that urinary tract infections in hematological patients represent a significant clinical challenge requiring specialized diagnostic and therapeutic approaches distinct from those applied to immunocompetent populations. The high prevalence of UTIs in this population, combined with substantially elevated rates of multidrug-resistant pathogens, necessitates fundamental modifications to standard management protocols.

Rapid microbiological diagnosis with antimicrobial susceptibility testing remains the cornerstone of effective UTI management in hematological patients. The traditional diagnostic thresholds and empirical treatment algorithms developed for general populations must be adapted to account for the unique vulnerabilities of immunosuppressed patients, including their propensity for rapid progression to life-threatening complications such as urosepsis.

Antimicrobial therapy must be guided by local resistance epidemiology and patient-specific risk factors, with aggressive empirical coverage followed by prompt de-escalation based on culture results. The emergence of ESBL-producing organisms and carbapenem-resistant pathogens represents an evolving threat that demands continuous surveillance and adaptation of treatment protocols. Multidisciplinary collaboration between hematology, infectious diseases, and clinical microbiology services is essential for optimizing antimicrobial stewardship and patient outcomes.

Alternative and adjunctive therapeutic approaches, including cranberry supplementation, probiotics, urinary alkalinization, and increased hydration, may serve valuable prophylactic or supportive roles in carefully selected patients. However, these interventions must never delay or replace definitive antimicrobial therapy in established infections, particularly in profoundly immunosuppressed individuals. Immunotherapy with vaccines such as MV140 shows promise for recurrent UTI prevention but requires intact immune function, limiting applicability during active disease or intensive chemotherapy.

Healthcare systems should implement evidence-based protocols specifically designed for hematological patients, incorporating local resistance patterns, risk stratification criteria, and clear guidance for empirical therapy selection. Regular monitoring and quality improvement initiatives are essential to track outcomes and adapt practices as resistance patterns evolve.

Future research must address critical knowledge gaps including optimal empirical regimens stratified by immunosuppression severity, rapid molecular diagnostic platforms, novel antimicrobial agents for resistant organisms, and the role of immunotherapy across varying degrees of immune compromise. Cost-effectiveness analyses will inform resource allocation in settings with limited budgets where expensive antimicrobials must be judiciously employed.

In conclusion, effective management of UTIs in hematological patients requires a paradigm shift from standard approaches, embracing specialized protocols that acknowledge the unique pathophysiology, microbiology, and clinical trajectory of infections in this vulnerable population. Continuous re-evaluation of practices in light of emerging evidence and evolving resistance patterns remains essential for optimizing outcomes and preserving antimicrobial effectiveness for future generations.

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