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Review Article

Gram-Positive Bacteria in Urinary Tract Infections: A Cause for Concern

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Abstract

Urinary tract infections (UTIs) represent one of the most prevalent bacterial infections worldwide, affecting millions of individuals annually. While Gram-negative bacteria, particularly *Escherichia coli*, have traditionally dominated the etiological landscape of UTIs, there is growing recognition of Gram-positive organisms as significant uropathogens. This comprehensive review examines the role of both Gram-positive cocci and bacilli in UTIs, including *Enterococcus* species, *Staphylococcus saprophyticus*, *Staphylococcus aureus*, *Streptococcus agalactiae*, *Lactobacillus* species, and *Corynebacterium urealyticum*. This review provides a comprehensive overview of their epidemiology, pathogenic mechanisms, clinical manifestations, diagnostic challenges, and the evolving patterns of antimicrobial resistance. The increasing prevalence of these organisms, particularly in healthcare-associated infections, complicated UTIs, and immunocompromised patients, necessitates enhanced clinical awareness and targeted therapeutic approaches. Understanding the unique characteristics and treatment considerations for Gram-positive uropathogens is crucial for optimizing patient outcomes and combating the rising threat of antimicrobial resistance.

Keywords: *Urinary Tract Infection; Gram-Positive Bacteria; Enterococcus; Staphylococcus saprophyticus; Streptococcus agalactiae; Lactobacillus Species; Corynebacterium urealyticum; Antimicrobial Resistance; Biofilm Formation; Catheter-Associated UTI*

Introduction

Urinary tract infections (UTIs) constitute a significant global health burden, with an estimated 150 million cases occurring annually worldwide [1]. The spectrum of UTIs ranges from uncomplicated cystitis to life-threatening urosepsis, with varying presentations depending on the causative organism, host factors, and anatomical involvement [2]. Traditionally, the microbiology of UTIs has been dominated by Gram-negative bacteria, with *Escherichia coli* accounting for 75 - 85% of uncomplicated cystitis cases in young, healthy women [3].

However, the epidemiological landscape of UTIs is evolving. Gram-positive bacteria are increasingly recognized as important uropathogens, particularly in specific patient populations and clinical scenarios [4]. This shift is attributed to several factors including the aging population, increased use of invasive urological procedures, rising prevalence of immunocompromised states, and the widespread use of broad-spectrum antibiotics [5,6].

The clinical significance of Gram-positive uropathogens extends beyond their increasing prevalence. Many of these organisms exhibit intrinsic or acquired antimicrobial resistance mechanisms, pose unique diagnostic challenges, and are associated with specific

complications that require tailored management approaches [7,8]. Furthermore, their ability to form biofilms on medical devices and their propensity to cause healthcare-associated infections make them particularly concerning in hospital settings [9].

This review provides a comprehensive analysis of Gram-positive bacteria causing UTIs, encompassing both cocci and bacilli, their pathogenic mechanisms, clinical implications, and therapeutic considerations. We aim to highlight the evolving role of these organisms in urinary tract pathology and emphasize the need for enhanced clinical recognition and appropriate management strategies.

Epidemiology and risk factors

The prevalence of Gram-positive bacteria in UTIs varies significantly based on patient demographics, clinical setting, and geographical location. In community-acquired UTIs, Gram-positive organisms account for approximately 10 - 15% of infections overall, but in healthcare-associated infections (HAIs), their prevalence rises to 25 - 30%, reflecting their increasing role in hospital-acquired pathogens [10,11].

Patient demographics

Certain patient populations demonstrate increased susceptibility to Gram-positive UTIs:

a. **Women of childbearing age:** Women of childbearing age are particularly susceptible to *Staphylococcus saprophyticus* infections, which show a distinct seasonal pattern with peak incidence during late summer and autumn months [12,13]. This seasonality is attributed to increased sexual activity during vacation periods and potential environmental factors affecting bacterial colonization [14].

b. **Elderly patients:** Elderly patients represent another high-risk group, with increased prevalence of enterococcal UTIs attributed to age-related changes in immune function, increased healthcare exposure, and higher rates of urological abnormalities [15,16].

c. **Pregnant women:** Pregnant women face higher risks for Group B *Streptococcus* (GBS) UTIs, with important implications for both maternal and neonatal health [17]. The prevalence of GBS bacteriuria in pregnancy ranges from 2 - 7%, with higher rates observed in women with diabetes mellitus [18]. However, we have seen asymptomatic bacteriuria due to *S. aureus* also in antenatal mothers. Pregnant women are at higher risk of developing sepsis due to UTI.

Healthcare-associated risk factors

Healthcare-associated UTIs show a disproportionately high prevalence of Gram-positive bacteria, particularly in patients with indwelling urinary catheters (catheter-associated UTIs - CAUTIs), recent urological instrumentation or surgery, and prolonged hospitalization with antibiotic exposure, immunocompromised states, including transplant recipients and patients receiving chemotherapy [19-22].

Association with comorbidities:

Specific medical conditions enlisted below predispose patients to develop Gram-positive UTIs:

a. Diabetes mellitus is associated with increased risk of enterococcal and GBS infections due to impaired immune function and glycosuria-related bacterial growth promotion [23,24].

b. Chronic kidney disease and patients on hemodialysis show higher rates of enterococcal UTIs, possibly related to frequent healthcare contact and immunosuppression [25].

c. Alcoholism has been specifically associated with *Staphylococcus aureus* UTIs, potentially due to alcohol-induced damage to bladder epithelium and compromised host defenses [26].

d. Developmental anomalies of the urinary tract and obstructions die to calculi are also responsible.

Figure 1 below shows pathogenesis of bacterial UTI.

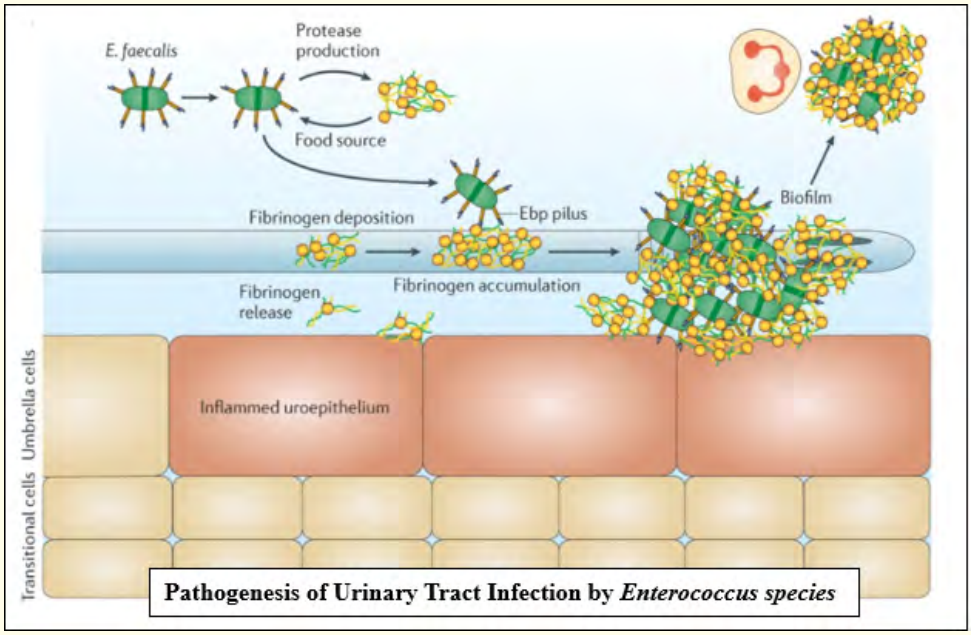

Figure 1: *Pathogenesis of UTI (Source: internet).*

Major gram-positive cocci incriminated in UTIs

Enterococcus species

Enterococci represent the most clinically significant gram-positive uropathogens, with *Enterococcus faecalis* and *E. faecium* being the predominant species isolated from urinary tract infections [27]. Other species occasionally implicated include *E. gallinarum*, *E. casseliflavus*, *E. avium*, and *E. durans*.

Microbiology and identification

Enterococci are facultatively anaerobic, catalase-negative, gram-positive cocci that typically occur in pairs or short chains [28]. They demonstrate remarkable environmental resilience, surviving in harsh conditions including high salt concentrations, extreme pH ranges, and elevated temperatures [29]. Key identifying characteristics include: Growth in 6.5% NaCl broth, hydrolysis of esculin in the presence of bile, growth at 45°C, and PYR (pyrrolidonyl arylamidase) positive reaction [30].

Modern identification relies heavily on automated systems such as VITEK 2, Phoenix, and MicroScan, as well as matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS) [31].

Pathogenic mechanisms

Enterococcal virulence in the urinary tract involves multiple mechanisms:

- **Adherence factors**: Enterococci express various surface proteins that facilitate adhesion to uroepithelial cells, including aggregation substance (AS), enterococcal surface protein (Esp), and collagen-binding protein [32,33]. The surface proteins also help in immune evasion.

- **Biofilm formation**: The ability to form biofilms on indwelling medical devices represents a crucial virulence mechanism, particularly in catheter-associated UTIs. The enterococcal biofilm is mediated by various factors including *esp* gene, gelatinase enzyme, and extracellular DNA [34,35].

Antimicrobial resistance: Intrinsic resistance mechanisms include low-level resistance to β-lactams, clindamycin, and trimethoprim-sulfamethoxazole. Acquired resistance, particularly to vancomycin and high-level aminoglycosides, poses significant therapeutic challenges [36].

Clinical presentations

Enterococcal UTIs can present across the spectrum of urinary tract disease:

- **Asymptomatic bacteriuria**: Common in elderly patients and those with indwelling catheters.
- **Cystitis**: Presents with typical lower urinary tract symptoms.
- **Pyelonephritis**: Can be severe, particularly in immunocompromised patients.
- **Complicated UTIs**: Associated with urological abnormalities or instrumentation [37,38].

Epidemiology and risk factors

Hospital-acquired enterococcal UTIs account for approximately 16% of nosocomial UTIs [39]. Risk factors include: Prolonged hospitalization, prior antibiotic therapy, particularly cephalosporins and fluoroquinolones, immunosuppression, genitourinary abnormalities, indwelling urinary catheters [40,41].

Staphylococcus saprophyticus

Staphylococcus saprophyticus represents the second most common cause of uncomplicated UTIs in young women, accounting for about 5 - 15% of cases [42].

Microbiology and identification

S. saprophyticus is a coagulase-negative *Staphylococcus* with distinctive characteristic features like: Novobiocin resistance with zone of inhibition generally less than 11 mm (key identifying feature), urease positive, hemagglutination of sheep erythrocytes, and strong adherence to uroepithelial cells [43,44].

Pathogenic mechanisms

The pathogenicity of *S. saprophyticus* in the urinary tract involves several factors:

a. **Adherence mechanisms**: The organism demonstrates strong adherence to uroepithelial cells through specific surface proteins, including a 160-kDa surface-associated protein and lipoteichoic acid [45,46].

b. **Urease production**: Urease activity contributes to pathogenesis by alkalinizing urine and potentially damaging uroepithelial cells [47].

c. **Surface proteins**: Various surface proteins contribute to bacterial adhesion and immune evasion [48].

Clinical features

S. saprophyticus UTIs typically present as:

- Acute uncomplicated cystitis in young, sexually active women.
- Seasonal clustering (late summer/early autumn).
- Symptoms indistinguishable from *E. coli* cystitis.
- Occasional progression to pyelonephritis.
- Association with sexual activity and honeymoon cystitis [49,50].

Epidemiological patterns

The unique epidemiology of *S. saprophyticus* includes: peak incidence in women aged 16 - 25 years, seasonal variation with summer/autumn predominance, association with sexual activity, lower recurrence rates compared to *E. coli* infections [51,52].

Staphylococcus aureus

While less common than other uropathogens, *S. aureus* UTIs are clinically significant due to their association with bacteremia and potential for severe complications [53].

Clinical significance

S. aureus bacteriuria often indicates:

- Hematogenous seeding of the urinary tract.
- Presence of a metastatic focus of infection.
- Need for comprehensive evaluation for endovascular infection.
- Higher risk of treatment failure if underlying bacteremia is not addressed [54,55].

Risk factors

Staphylococcus aureus urinary tract infections (UTIs), though less common than those caused by Gram-negative bacilli, are clinically significant and often associated with specific risk factors. These include hospitalization and invasive procedures, the presence of indwelling urinary catheters, intravenous drug use, diabetes mellitus, chronic alcoholism, and immunocompromised states. *S. aureus* UTIs are more frequently observed in males over the age of 50 and in individuals with a history of chronic alcohol use [56,57].

Pathogenic mechanisms

S. aureus UTIs often arise from hematogenous spread rather than ascending infection, reflecting its association with bacteremia and metastatic foci (e.g. endocarditis, abscesses). In the urinary tract, *S. aureus* adheres via surface proteins (like fibronectin-binding proteins) and invades host cells, evading immune clearance. Its virulence factors include toxins (like α-hemolysin) that damage renal tissue and biofilm formation on catheters or stents. Biofilm formation is also found *in vitro* in almost all *S. aureus* isolates causing UTI.

Clinical management and related considerations

S. aureus UTIs often present with frank hematuria, and require special management considerations listed as follows:

- Investigation for concurrent bacteremia.
- Evaluation for metastatic foci of infection.

- Longer treatment duration.
- Consideration of combination antimicrobial therapy.
- Assessment for underlying urological abnormalities [58].

Streptococcus agalactiae (Group B *Streptococcus*)

Group B *Streptococcus* (GBS) has emerged as an important uropathogen, particularly in specific patient populations [59].

Epidemiology

GBS UTIs are most commonly observed in: Pregnant women (2 - 7% prevalence), elderly patients, patients with diabetes mellitus, immunocompromised individuals [60,61].

Clinical implications

GBS UTIs carry specific clinical significance:

- **In pregnancy**: Associated with increased risk of preterm labor, chorioamnionitis, neonatal early-onset disease, need for intrapartum antibiotic prophylaxis [62,63].
- **In elderly patients**: May cause severe pyelonephritis, bacteremia, and high mortality rates if untreated [64].

Pathogenic mechanisms

GBS exploits capsular polysaccharides (e.g. serotype III) to resist phagocytosis and adhere to uroepithelial cells via surface adhesins (e.g. Srr-1). In pregnant women, GBS bacteriuria can lead to chorioamnionitis and neonatal sepsis due to vertical transmission. Its β-hemolysin/cytolysin and hyaluronidase degrade host tissues, facilitating invasion and systemic spread [65,66].

Gram-positive bacilli in UTIs

Lactobacillus species

While traditionally considered part of the normal urogenital flora, certain *Lactobacillus* species can act as uropathogens under specific circumstances [67].

Clinical significance

Lactobacillus UTIs are typically observed in: Patients with structural urinary tract abnormalities, immunocompromised individuals, following antibiotic therapy disrupting normal flora, elderly patients with indwelling catheters [68,69].

Pathogenic mechanism

Though typically commensal, pathogenic *Lactobacillus* strains cause UTIs in immunocompromised individuals or those with structural abnormalities. Virulence is strain-dependent, involving adhesion to damaged urothelium and biofilm formation on catheters. Overgrowth may follow antibiotic disruption of normal flora.

Diagnostic challenges

Distinguishing pathogenic from commensal *Lactobacillus* requires:

- Quantitative urine culture (> 10^5 CFU/mL).

- Clinical correlation with symptoms.
- Absence of other potential uropathogens.
- Consideration of patient risk factors [70].

Corynebacterium urealyticum

Corynebacterium urealyticum represents an important but underrecognized uropathogen, particularly in patients with alkaline urine [71].

Microbiology

Key characteristics include slow-growing, pleomorphic Gram-positive rods, strong urease activity, multiresistant to many antibiotics, preference for alkaline pH [72,73].

Clinical associations

C. urealyticum UTIs are associated with: Elderly, hospitalized patients, patients with indwelling catheters, immunocompromised states, alkaline urine pH, formation of struvite stones [74,75].

Pathogenic mechanisms

Virulence factors include urease production causing alkaline-encrusted cystitis and struvite stones via ammonia generation, damaging the urothelium. It forms biofilms on catheters and is intrinsically multidrug-resistant, complicating therapy [76]. Figure 2 and 3 below highlight various rare Gram positive uropathogens.

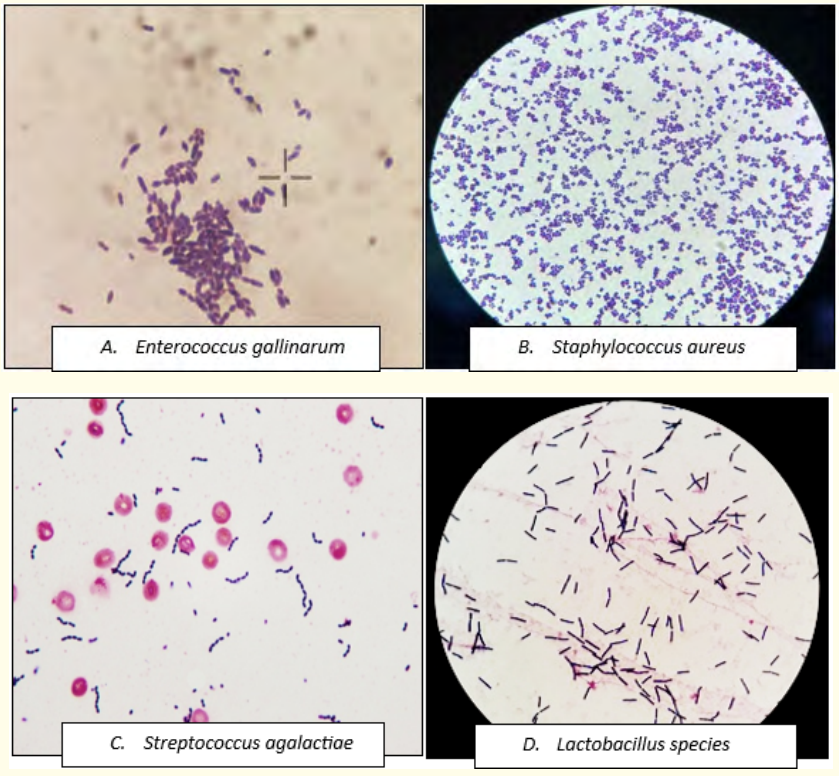

Figure 2: *Gram stain morphology of various gram positive uropathogens.*

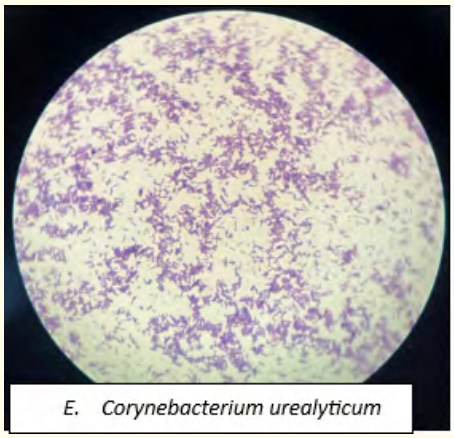

Figure 3: *Gram stain morphology of Corynebacterium urealyticum.*

Anaerobic gram positive bacteria causing UTI

Rarely, anaerobic bacteria are implicated in urinary tract infections (UTIs), particularly in cases that are chronic, recurrent, or associated with structural abnormalities or instrumentation. Anaerobic Gram-positive cocci contribute to approximately 1 - 3% of UTIs but are often overlooked due to standard aerobic culture techniques [77]. Key anaerobic cocci involved include *Peptostreptococcus spp.*, *Finegoldia magna*, *Anaerococcus spp.*, and *Parvimonas micra*. *Finegoldia magna* is notable for its biofilm production and expression of virulence factors like protein L, enhancing persistence in the urinary tract. Anaerobic Gram-positive bacilli also play a role in select cases. *Actinomyces israelii* can cause chronic, granulomatous infections characterized by sulfur granules, especially in patients with long-term intrauterine device (IUD) use. *Clostridium perfringens*, though rare, is associated with gas-forming infections such as emphysematous cystitis. *Cutibacterium acnes* has been isolated in polymicrobial urinary infections, particularly in patients with indwelling devices. Diagnosis requires a high index of suspicion and appropriate anaerobic culture methods or molecular diagnostics, with treatment guided by susceptibility and often involving agents like metronidazole or beta-lactam/beta-lactamase inhibitor combinations.

Diagnostic considerations

Laboratory detection challenges

The detection of gram-positive uropathogens presents several diagnostic challenges, owing to their variable growth characteristics, the potential for contamination, and limitations in traditional identification methods. These challenges necessitate a multifaceted approach combining classical microbiological techniques with modern diagnostic tools.

Culture interpretation

Interpreting culture results for Gram-positive uropathogens requires nuanced understanding, especially because many of these organisms-such as *Enterococcus spp.*, *Streptococcus agalactiae*, *Staphylococcus aureus*, *Lactobacillus spp.*, and *Corynebacterium urealyticum*-exhibit diverse growth behavior and clinical significance.

Traditional thresholds, such as $\geq 10^5$ CFU/mL, are often used to define significant bacteriuria. However, these criteria may not be universally applicable for Gram-positive bacteria. For example, *Enterococcus spp.* and *S. agalactiae* can be clinically significant even at lower colony counts, especially in symptomatic patients or certain risk groups like pregnant women or immunocompromised individuals [77,78].

Polymicrobial cultures frequently include Gram-positive organisms that are part of the normal urogenital flora. Distinguishing true pathogens from contaminants-such as *Lactobacillus spp.* or diphtheroids-poses a challenge. This is particularly critical in female patients, where vaginal flora can contribute to mixed growth.

Moreover, some Gram-positive organisms such as *Corynebacterium urealyticum* are slow-growing and may require extended incubation beyond the standard 24 - 48 hours. Failure to accommodate these needs can result in underreporting or missed diagnoses. Specialized media with prolonged incubation may be necessary to isolate such fastidious organisms [77,78].

Identification methods

Accurate identification of Gram-positive uropathogens is essential for guiding appropriate therapy and understanding their clinical relevance. This typically begins with:

a. **Gram staining**: Gram staining is the first-line, rapid screening tool in urine microscopy. It not only confirms the presence of Gram-positive cocci (e.g. *Enterococcus*, *Streptococcus*, *Staphylococcus*) or rods (e.g. *Lactobacillus*, *Corynebacterium*) but also offers preliminary insight into morphology and arrangement (e.g. chains, clusters, palisades). However, its utility is limited in samples with low bacterial loads or mixed flora.

b. **Biochemical tests**: Classical identification relies on a combination of biochemical reactions:

- Catalase test distinguishes *Staphylococcus* (positive) from *Streptococcus* and *Enterococcus* (negative).
- Coagulase test helps identify *S. aureus*.
- Bile esculin and PYR positivity support *Enterococcus* identification.
- CAMP test aids in the detection of *S. agalactiae*.
- Urease activity is a key feature of *Corynebacterium urealyticum*, and *Lactobacillus spp.* can be identified based on acid production from various carbohydrates.

While these methods are cost-effective and widely available, they are time-consuming and may yield inconclusive results, particularly for atypical or non-reactive strains.

c. **Culture characteristics**: The choice of culture media can enhance detection:

- Blood agar supports the growth of most Gram-positive uropathogens and allows hemolytic pattern evaluation (e.g., beta-hemolysis in *S. agalactiae*).
- Cystine-lactose-electrolyte-deficient (CLED) agar helps prevent swarming and supports the growth of both Gram-positive and Gram-negative uropathogens.
- Chromogenic media improve the differentiation and identification of specific uropathogens by color-coding colony morphology, aiding in the detection of organisms like *S. aureus* or *Enterococcus spp.*

d. **Modern diagnostic technologies:** Recent advancements have transformed pathogen identification:

- Automated identification systems (e.g. VITEK 2, Phoenix, MicroScan) provide rapid and standardized identification profiles with antimicrobial susceptibility data.
- MALDI-TOF MS has emerged as a powerful tool for species-level identification based on protein spectral fingerprints. It is particularly valuable for detecting *Corynebacterium*, *Lactobacillus*, and other fastidious or unusual isolates.

- Molecular techniques, like 16S rRNA gene sequencing, offer definitive identification of organisms with ambiguous phenotypic traits or in polymicrobial settings.
- PCR-based assays targeting resistance genes (e.g., vanA/vanB in *Enterococcus faecium*) and virulence factors can impart rapid diagnostic and epidemiological information.

Collectively, these methods enhance the reliability of gram-positive uropathogen detection, supporting timely clinical decision-making and antimicrobial stewardship [79,80].

Table 1 below shows various characteristic identifying features of gram positive bacteria causing UTI.

Bacterial strain	Identifying features	Other features or remarks
S. aureus	Gram positive cocci in clusters and positive catalase and coagulase reactions, golden yellow pigment on Nutrient agar	Almost always produces biofilms *in vitro*; can be seen more commonly in adult males and also in females
Group B *Streptococcus* spp.	Positive CAMP reaction, carotenoid pigment production	----
S. bovis (*S. gallolyticus*)	No growth in 6.5% NaCl, positive aesculin hydrolysis	Found almost always in males but very rare
Enterococcus spp.	Growth in 6.5% NaCl and positive aesculin hydrolysis	Usually due to *E. faecalis* and *E. faecium*, and rarely due to other species like *E. gallinarum*
Staphylococcus saprophyticus	Gram positive cocci in clusters, Coagulase negative, novobiocin resistant	Important uropathogens in females of childbearing age

Table 1: *Characteristic identifying features of gram positive bacteria causing UTI.*

Antimicrobial susceptibility testing

Accurate susceptibility testing is essential for guiding appropriate therapy against Gram-positive uropathogens.

Methodological considerations

Standardized guidelines issued by CLSI and EUCAST should be adhered to for antimicrobial susceptibility testing. Ensuring quality control with appropriate reference strains and interpreting results based on organism-specific breakpoints are vital to obtaining reliable results [81,82].

Resistance detection

Advanced molecular techniques aid in the detection of key resistance mechanisms. For example, vancomycin-resistant enterococci (VRE) are identified via molecular assays targeting van genes. Similarly, MRSA detection employs chromogenic media and PCR-based methods. β-lactamase production in staphylococci and enterococci should also be routinely assessed to guide therapeutic choices [83,84].

Antimicrobial resistance patterns

Enterococcal resistance

Enterococci exhibit both intrinsic and acquired resistance mechanisms.

Intrinsic resistance

These organisms inherently show low-level resistance to β-lactams, clindamycin, and trimethoprim-sulfamethoxazole, with variable susceptibility to fluoroquinolones. Notably, they are naturally resistant to cephalosporins [85,86].

Acquired resistance

Vancomycin resistance in enterococci is mediated by VanA, VanB, and VanC phenotypes, each with differing clinical implications [87,88]. High-level aminoglycoside resistance poses a challenge to combination therapy involving cell wall-active agents [89]. Furthermore, resistance to linezolid is an emerging issue due to its increased clinical use [90].

Staphylococcal resistance

S. aureus resistance patterns

Methicillin resistance, driven by the *mecA* gene, remains a significant concern. Though vancomycin-resistant *S. aureus* (VRSA) strains are still rare, they are clinically worrisome. Multidrug resistance is increasingly common, particularly in healthcare-associated isolates [91,92].

S. saprophyticus resistance

This species is generally susceptible to most antibiotics but exhibits intrinsic resistance to novobiocin. Reports of emerging fluoroquinolone resistance in certain regions underscore the need for ongoing surveillance [93].

Resistance trends and surveillance

Global surveillance data reveal rising VRE prevalence and regional differences in MRSA rates. Resistance to newer agents is also emerging, reinforcing the necessity for continued monitoring and robust antimicrobial stewardship initiatives [94].

Treatment considerations

Empirical therapy

Empirical treatment of gram-positive UTIs should be guided by the patient's risk factors, local resistance data, the severity of infection, and previous culture results [95,96].

Targeted therapy

Enterococcal UTIs

For uncomplicated infections caused by susceptible strains, ampicillin or amoxicillin remains effective, while nitrofurantoin is suitable for cystitis. Fosfomycin may serve as an alternative. In complicated infections, especially those involving VRE, vancomycin, linezolid, or daptomycin may be necessary, and combination therapy should be considered for severe presentations [97].

Staphylococcal UTIs

S. saprophyticus infections are typically treated with trimethoprim-sulfamethoxazole or nitrofurantoin, with fluoroquinolones and β-lactams as alternatives [98]. For *S. aureus*, nafcillin, oxacillin, or first-generation cephalosporins are recommended for MSSA, while MRSA infections warrant treatment with vancomycin, linezolid, or daptomycin. Severe infections may require combination therapy [99].

Streptococcal UTIs

Group B streptococci (GBS) are generally treated with penicillin. Macrolides serve as alternatives for penicillin-allergic individuals, with clindamycin as another option [100].

Duration of therapy

The duration of antimicrobial therapy should be tailored to the clinical scenario. Uncomplicated cystitis usually requires 3-7 days of treatment, while complicated UTIs may need 7-14 days. Pyelonephritis typically demands a minimum of 10-14 days, and bacteremia warrants extended therapy guided by source control and response [101,102].

Prevention and control measures

Infection prevention

Healthcare-associated prevention

Effective catheter management, including proper insertion and timely removal, is vital. Adherence to hand hygiene protocols and environmental cleaning-especially of high-touch surfaces-are key to preventing nosocomial infections [103].

Community-based prevention

Patient education on hygiene and management of comorbidities can help reduce community-acquired infections. Vaccination, particularly against *Streptococcus pneumoniae*, should be considered in high-risk populations [104].

Antimicrobial stewardship

Antimicrobial stewardship programs should emphasize appropriate, evidence-based prescribing, optimize treatment durations, and incorporate regular resistance monitoring. Continuous education for healthcare providers is essential to sustain these efforts [105].

Future directions and research needs

Diagnostic innovations

Advances in rapid molecular diagnostics promise faster detection of resistance genes at the point of care. The development of host-response biomarkers and investigations into the urinary microbiome may further refine diagnostic strategies [106].

Therapeutic developments

Research is ongoing into novel antimicrobial agents targeting resistant organisms, synergistic combination therapies, and immunotherapeutic options such as monoclonal antibodies and vaccines. Antimicrobial peptides, both natural and synthetic, are also being explored for their potential [107].

Resistance prevention strategies

Future strategies to curb resistance may include bacteriophage therapy, quorum sensing inhibitors, and agents designed to disrupt biofilms. Probiotic interventions aimed at restoring protective flora are also under investigation [108].

Conclusion

Gram-positive bacteria represent an increasingly important but less recognized cause of urinary tract infections, particularly in healthcare settings and specific patient populations. The clinical significance of these organisms extends beyond their growing prevalence to include challenging antimicrobial resistance patterns, unique pathogenic mechanisms, and specific treatment considerations.

Enterococcus species, *Staphylococcus saprophyticus*, *S. aureus*, and *Streptococcus agalactiae* represent the most clinically relevant Gram-positive cocci, while organisms such as *Lactobacillus* species and *Corynebacterium urealyticum* exemplify important but underrecognized Gram-positive bacilli causing UTIs. The management of Gram-positive UTIs requires a nuanced understanding of each organism's epidemiology, resistance patterns, and clinical implications. Healthcare providers must maintain heightened awareness of these pathogens, particularly in high-risk patients, and ensure appropriate diagnostic and therapeutic approaches.

Looking forward, continued surveillance of resistance trends, development of novel diagnostic tools, and investigation of innovative therapeutic strategies will be essential to address the evolving challenge posed by Gram-positive uropathogens. The integration of antimicrobial stewardship principles, infection prevention measures, and evidence-based treatment protocols will be crucial for optimizing patient outcomes while preserving antimicrobial effectiveness.

As our understanding of the urinary microbiome and host-pathogen interactions continues to evolve, new opportunities for prevention and treatment of Gram-positive UTIs will undoubtedly emerge. The clinical community must remain vigilant and adaptive to successfully address this important and growing healthcare challenge.

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