ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH

INNOVARE ACADEMIC SCIENCES
Knowledge to Innovation

Vol 18, Issue 2, 2025

Online - 2455-3891
Print - 0974-2441

Research Article

CLINICAL AND MICROBIOLOGICAL PROFILE OF SECONDARY BLOODSTREAM INFECTIONS RESULTING FROM URINARY TRACT INFECTION CAUSED BY ENTEROBACTERALES

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Received: 07 December 2024, Revised and Accepted: 22 January 2025

ABSTRACT

Objectives: Bloodstream infection (BSI) is a common sequelae of urinary tract infections (UTIs) and it requires early detection and appropriate antibiotic therapy. This study analyzed the clinical and microbiological profile of secondary BSI resulting from UTI caused by Enterobacterales.

Methods: In this retrospective study, National Healthcare Safety Network criteria were used to define the cases of UTI and secondary BSI attributed to UTI. Data from medical records and laboratory reports of patients from January to May 2024 were compiled and analyzed.

Results: Among 932 urine samples with significant growth of Enterobacterales, 48 were blood cultures positive. Out of them, 26 patients (11 males and 15 females) met the criteria of BSI secondary to UTI as the same isolates also grew in blood specimens which was taken within the secondary BSI attribution period. Nine patients had catheter-associated symptomatic UTI (CA-SUTI) while 14 were non-CA-SUTI and 3 had asymptomatic bacteriuria. In urine culture, *Escherichia coli* (n=22, 68.1% multi-drug resistant and 31.8% non-multi-drug resistant [MDR]), *Klebsiella pneumoniae* (n=3, all MDR), and *Citrobacter koseri* (n=1, non-MDR) strains were isolated. Diabetes, renal calculi, fever, Foley's catheter, age >60 years, intensive care unit admission, and hospital stay >10 days were more among individuals with MDR infections. Cefoperazone-sulbactam, piperacillin/tazobactam, and nitrofurantoin had good outcomes.

Conclusion: Cefoperazone-sulbactam, piperacillin/tazobactam, and nitrofurantoin were effective for treating patients with BSI attributed to UTI in our hospital with good outcomes. Hence, these antibiotics might have a critical role as empirical therapy for such, particularly those with underlying health conditions and risk factors for MDR infections.

Keywords: Secondary bloodstream infections, Urinary tract infection, Enterobacterales, Multi-drug resistance.

 DOI: http://dx.doi.org/10.22159/ajpcr.2025v18i2.53668. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Urinary tract infections (UTIs) are among the most prevalent infections, occurring frequently both in the community and in healthcare setups [1]. It is also a leading cause of bacteremia and it contributes significantly to the rising antimicrobial resistance among uropathogens [2]. Bloodstream infection (BSI) is a serious infection which needs early diagnosis and appropriate antibiotic therapy. UTI may progress to BSI, septic shock, and multiple organ dysfunction syndrome (MODS) resulting in mortality. As per an estimate, up to 15% of cases with UTI also had bacteremia at presentation [3]. Secondary BSI in individuals with UTI is a significant concern due to its impact on patient outcomes and healthcare systems, in India and worldwide. The presence of bacteria in the bloodstream from a UTI not only significantly increases the risk of adverse clinical outcomes, including mortality but also increases the duration of hospital stay as well as healthcare costs. Patients with secondary BSI often require more aggressive and prolonged antibiotic therapy, which can lead to an increased risk of developing antibiotic resistance [4]. The majority of the UTI cases are attributed to Gram-negative bacilli, especially Enterobacterales [5]. The emergence of resistance to antimicrobials among Enterobacterales is a serious concern. The occurrence of multi-drug resistant (MDR) *Escherichia coli* strains is alarmingly high in India [6]. In this study, we have analyzed the clinical and microbiological profile of secondary BSI attributed to UTI caused by Enterobacterales.

METHODS

Study design

A retrospective cross-sectional single-center study was carried out in the department of microbiology at a tertiary care hospital in South India. An approval was received from the Institute Ethical Committee. Medical records and laboratory reports of patients admitted to the hospital from January to May 2024 were obtained and analyzed to identify cases of secondary BSI attributed to various types of UTI, namely, catheter-associated and non-catheter-associated - symptomatic UTI (SUTI), asymptomatic bacteremic UTI (ABUTI), and asymptomatic bacteriuria (ASB) as per the criteria set by CDC/National Healthcare Safety Network (NHSN) [7].

Case definitions

Catheter-associated symptomatic UTI (SUTI 1a) was considered if a patient, during the Infection Window Period (IWP), had indwelling urinary catheter (IUC) *in situ* for >2 successive days in hospital indoor ward on the date of the event (DOE) or it was removed the day before DOE in addition to significant growth ($\geq 10^5$ CFU/mL) of no more than two species of uropathogens recovered on urine culture and the patient had any one of the undermentioned symptoms consistent with UTI, such as fever >38.0°C, suprapubic tenderness, costovertebral angle pain/tenderness or urinary urgency, frequency, or dysuria in the absence of IUC.

Non-catheter-associated symptomatic UTI (SUTI 1b) was considered if a patient, during the IWP, had significant growth ($\geq 10^5$ CFU/mL) of no more than two species of uropathogens on urine culture and the patient had any one of the following symptoms - fever >38.0°C, suprapubic tenderness, costovertebral angle pain/tenderness OR urgency, frequency, or dysuria in the absence of IUC, provided the case did not meet the aforementioned criteria for IUC.

ABUTI was defined as a condition, in which a patient (with or without IUC), who had no signs/symptoms consistent with SUTI, showed significant growth (≥10^5 CFU/mL) of not more than two uropathogenic microbial species on urine culture and also had organism identified in blood culture with as a minimum of one matching bacterial agent to the uropathogenic bacterial species with >10^5 CFU/mL identified in the urine specimen. If there was no associated bacteremia, the condition was identified as ASB.

The diagnosis of secondary BSI attributed to UTI was made if a patient met the CDC/NHSN criteria for UTI and also had the same organism (or at least one matching organism if there are multiple organisms) identified in blood and urine, provided blood specimen was obtained during the secondary-BSI-attribution period (SBAP).

An isolate was classified as MDR if it exhibited resistance against at least one drug in three or more antibiotic categories [8].

Inclusion and exclusion criteria

Cases of secondary BSI attributed to UTI caused by Enterobacterales in adult patients ≥18 years of age, admitted from January to May 2024 were included in the study, whereas patients below 18 years of age, abacteremic cases, different/unmatched isolates from blood and urine specimens, non-Enterobacterales bacterial isolates, and blood specimens collected beyond the secondary BSI attribution period were excluded from the analysis.

Data collection and statistical analysis

The data from medical records and laboratory reports of patients were entered and compiled in Microsoft Excel (MS Excel 2011) database. The data includes clinical details such as diagnosis, date of admission and discharge or death, length of stay in the hospital, the presence of comorbidities such as diabetes, hypertension, existing renal disease, renal stones, stay in intensive care units (ICUs), symptoms of UTI, the presence of IUC, day of catheterization, DOE, IWP for UTI, secondary BSI attribution period, urine and blood culture reports along with antibiogram, therapeutic details such as antibiotics administered as empirical and targeted therapy, and clinical outcomes. Good clinical outcome was considered when a patient showed improvement of clinical condition and laboratory parameters at the time of discharge. If the patient had no response or worsening of clinical condition or death, it was considered poor clinical outcome. Data were analyzed using descriptive statistics.

RESULTS

From January to May 2024, a total of 1258 urine samples were positive for uropathogens with significant growth (≥10^5 CFU/mL), of which 932 had growth of Enterobacterales (Fig. 1). Positive blood cultures were observed in 48 of these patients. We found the same organism, i.e., matched Enterobacterales isolates from blood and urine specimens in 29 cases. Three of them failed to meet the criteria for secondary BSI attributed to UTI and were excluded from the study as the blood culture specimens were collected beyond the secondary BSI attribution period in these cases. Hence, 26 patients with BSI presumably attributed to urinary tract as primary site infection were incorporated in the study and their medical records were analyzed (Fig. 1).

Among the 26 cases, 11 (42.3%) were males and 15 (57.7%) females. Most patients were in 41–60 years age group (42.3%) (Table 1). Foley's catheter was present in 9 patients and they fulfilled the criteria for catheter-associated symptomatic UTI (SUTI 1a). Among the 17 patients who were not catheterized during their stay in the hospital, 14 had symptoms of SUTI and were categorized as non-catheter-associated symptomatic UTI (SUTI 1b), whereas 3 cases had no symptoms suggestive of ASB. The most common symptom was fever, reported by 76.9% (n=20) patients, followed by burning sensation when urinating occurring in 34.6% (n=9) and decreased urine output in 15.4% (n=4) patients. Tenderness/pain in the suprapubic or costovertebral region and urinary urgency or frequency were noted in 3.8% (n=1) of patients each.

Blood cultures from these patients revealed the same organism as in their urine specimens. These isolates were *E. coli* (n=22, 84.6%), *Klebsiella pneumoniae* (n=3, 11.5%), and *Citrobacter koseri* (n=1, 3.8%). ESBL production was found in 20 isolates. Multi-resistance was found in 18 isolates which includes 15 *E. coli* and 3 *K. pneumoniae*. Most of the isolates were resistant to ceftriaxone (n=20, 76.9%), cefotaxime (n=20, 76.9%), ciprofloxacin (n=17, 65.4%), norfloxacin (n=17, 65.4%), co-trimoxazole (n=13, 50.0%), and gentamicin (n=12, 46.2%). Resistance to amikacin, cefoperazone-sulbactam, piperacillin-tazobactam, meropenem, and imipenem were observed in fewer isolates (n=3, 11.5%). Table 2 gives the comparison of susceptibility results in matching blood and urine isolates.

The distribution of MDR and non-MDR bacterial isolates is detailed in Table 3.

Empirical antibiotic therapy was administered in 16 cases, of which cefoperazone-sulbactam was used most commonly (n=6), followed by meropenem (n=4), ceftriaxone (n=3), piperacillin/tazobactam (n=2), and norfloxacin (n=1). Table 4 shows the outcomes of various targeted therapies and provides comparison in terms of good and poor outcomes.

DISCUSSION

In our study, we analyzed clinical and microbiological profiles of secondary BSI related to UTI. During the study, out of 932 episodes of UTI caused by Enterobacterales, 48 (5.2%) had associated BSI. Among these cases, 26 (2.8%) were identified as secondary BSI attributed to UTI as they met the NHSN criteria for secondary BSI to be attributed to a primary site of infection [7]. In these cases, matching organisms were identified from both urine and blood, and the blood was collected within the SBAP, a timeframe of 14–17 days comprising IWP and repeat infection timeframe.

UTIs are generally uncomplicated in nature and not a medical emergency. However, if left untreated, a UTI may spread to the kidneys, leading to the invasion of renal tissues, and ultimately causing secondary BSI. When BSI of urinary origin triggers a widespread systemic

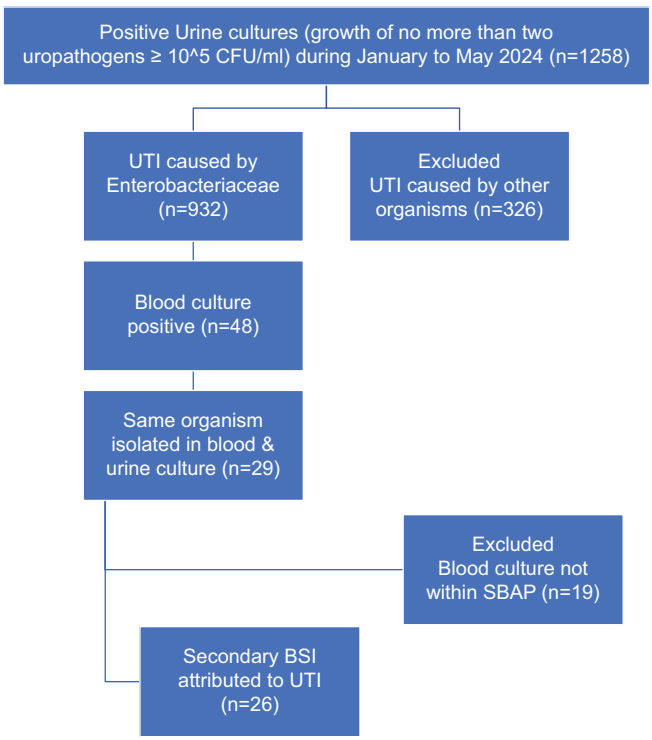

Fig. 1: Flow chart depicting selection of cases

Table 1: Age- and gender-wise distribution of patients

Age group	Male	Female	Total	%
20–40 years	1	5	6	23.1
41–60 years	3	8	11	42.3
61–80 years	5	1	6	23.1
Above 80 years	2	1	3	11.5
Total	11	15	26	100

Table 2: Comparison of susceptibility results in matching blood and urine isolates

Category	Number
Fully concordant	22
Differed by 2 antibiotics	2
Differed by 3 antibiotics	1
Differed by>3 antibiotics	1

Table 3: Comparison of predisposing factors, comorbidities, and uropathogens in bacteremic UTI by MDR and non-MDR isolates

Clinical and microbial factors	MDR (n=18) (%)	Non-MDR (n=8) (%)
Diabetes (n=16)	13 (81.3)	3 (18.8)
Hypertension (n=10)	8 (80)	2 (20)
Existing renal disease (n=14)	11 (78.6)	3 (21.4)
Renal stone (n=10)	6 (60)	4 (40)
Chronic kidney disease (n=4)	3 (75)	1 (25)
Age>60 years (n=9)	6 (66.7)	3 (33.3)
Intensive care unit admission (n=12)	9 (75)	3 (25)
Hospitalized for>10 days (n=6)	5 (83.3)	1 (16.7)
Foley's catheter (n=9)	7 (77.8)	2 (22.2)
Urinary tract instrumentation (n=4)	1 (25)	3 (75)
Fever (n=20)	15 (75)	5 (25)
Escherichia coli (n=22)	15 (68.2)	7 (31.8)
Klebsiella pneumoniae (n=3)	3 (100)	0 (0)
Citrobacter koseri (n=1)	0 (0)	1 (100)
Poor outcome (n=8)	6 (75)	2 (25)

Table 4: Clinical outcomes of patients for targeted antibiotic therapies

Targeted therapy	Good outcome	Poor outcome
Cefoperazone-sulbactam	7	0
Cefoperazone-sulbactam+Polymyxin B	0	1
Cefoperazone-sulbactam+Piperacillin/ tazobactam	0	1
Piperacillin/tazobactam	4	0
Piperacillin/tazobactam+Meropenem	0	2*
Meropenem	4	3
Nitrofurantoin	2	0
Ceftriaxone	1	0
Polymyxin B	0	1*
Total	18	8

*Poor clinical outcome with death

inflammatory response, multiorgan dysfunction, tissue damage, and life-threatening complications, it is referred to as urosepsis. Secondary BSI due to UTI occurs in 4% to 15% of cases of UTI [9]. In our study, BSI secondary to UTI caused by Enterobacterales was observed in 2.8% of cases. This low occurrence may indicate regional variation and good infection control measures in our hospital. Although at the admission time, there were cardiac ailments (*viz.* myocardial infarction, acute coronary syndrome, and cardiomyopathy) in 4 cases, respiratory disorders (*viz.* Acute respiratory distress syndrome, hospital-acquired and aspiration pneumonia) in 4 cases, neurological lesions (*viz.* cerebrovascular accident, encephalopathy) in 2 cases, and intestinal disorders (*viz.* small bowel ischemia, peritonitis, chronic liver disease) in 3 cases, most of our patients (n=20) with BSI secondary to UTI had cystitis, pyelonephritis, urosepsis, or acute kidney injury at the time of admission or developed during their stay in the hospital. This is in accordance with other studies which also observed an increased propensity of UTI in hospitalized patients which eventually progress to complications such as bacteremia, sepsis, and shock [9,10]. The most prevalent comorbidity among patients in our study was diabetes, affecting 61.5% (n=16) patients, followed by preexisting renal disease in 53.8% (n=14), hypertension in 38.5% (n=10), renal stones in 38.5% (n=10), and chronic kidney disease (CKD) in 15.4% (n=4). Predisposing factors observed were ICU admission in 46.2% (n=12), hospitalization for more than 10 days in 23.1% (n=6), and urinary tract instrumentation in 15.4% (n=4). A total of 8 patients had severe sepsis/septic shock, which lead to mortality in two patients and poor outcomes in three patients. Apart from them, mortality occurred in another patient as a result of peritonitis and hospital-acquired pneumonia. These predisposing factors and comorbid conditions are well-recognized in patients with urosepsis [11-13]. Varma *et al*. identified diabetes mellitus and pyelonephritis as prominent risk factors for bacteremia in UTI patients [14]. In addition, urinary tract obstruction, indwelling catheter, underlying critical diseases, solid tumors, neutrophilia, high CRP, and pyuria were also reported as risk factors for bacteremic UTI [15,16]. The development of microbial biofilms on indwelling catheters is a crucial factor in the pathogenesis of CA-UTI and strategies such as silver nanoparticle coating have been employed for prevention [17].

CDC/NHSN criteria were used to categorize the patients with UTI [7]. Among these patients with BSI secondary to UTI, 9 cases met the criteria for catheter-associated symptomatic UTI (SUTI 1a) and 14 met the criteria of non-catheter-associated symptomatic UTI (SUTI 1b). Whereas 3 cases without UTI symptoms were labeled as ASB. Blood and urine cultures of these patients recovered matching organisms, namely, *E. coli* (n=22, 84.6%), *K. pneumoniae* (n=3, 11.5%), and *C. koseri* (n=1, 3.8%). Most studies have documented preponderance of Enterobacterales, especially *E. coli* in bacteremic UTIs [10,18,19]. *E. coli* accounted for 61% of the bacterial spectrum of patients with BSI secondary in the German septicemia study, whereas other Enterobacterales accounted for 16%, *Staphylococcus aureus* 8%, and enterococci 6% [18]. In another study, Lee *et al*. reported that 95.1% of bacteremic UTIs were associated with Enterobacterales, of which 85% were attributed to *E. coli* [19].

We compared the antibiotic susceptibility results of each matching blood and urinary isolate. Completely concordant susceptibility results, i.e., no difference in susceptibility in matching blood and urine isolates were found in 22 cases, whereas discordant susceptibility was identified in 4 patients (Table 2). Our findings are similar to a study by Lam *et al*. [20]. They compared the antibiotic susceptibility of matching urine and blood isolates from 428 bacteremic UTI patients and found fully concordant susceptibility in 89% of cases, while only 7.7% isolate pairs had a difference in susceptibility for one antibiotic; 1.4% for two antibiotics, and 1.9% for three or more antibiotics. In view of the concordance of susceptibility pattern, they suggested that susceptibility urinary isolates may be used to predict that of blood isolates which may be critical in initiating an early targeted therapy [20].

The occurrence of ESBL-producing and MDR strains among Enterobacterales is alarmingly high in India [6]. As per an estimate, 39.66% and 82.6% of the *E. coli* isolates were ESBL producers and multidrug-resistant, respectively, whereas the resistance to imipenem, amikacin, and nitrofurantoin was <20% [6]. In our survey, out of 26 isolates, 20 (76.9%) were ESBL producers, and 18 (69.2%) were MDR displaying resistance to three or more antibiotic classes. Higher resistance was observed against ceftriaxone (n=20, 76.9%), cefotaxime (n=20, 76.9%), ciprofloxacin (n=17, 65.4%), norfloxacin (n=17, 65.4%), cotrimoxazole (n=13, 50.0%), and gentamicin (n=12, 46.2%). Amikacin, cefoperazone-sulbactam, piperacillin-tazobactam, imipenem, and meropenem were mostly

sensitive. There are studies that have identified factors predisposing to infection caused by MDR strains. In Spanish research, prior administration of antibiotics, *viz.*quinolones, cephalosporins, and carbapenem as well as longer hospital stay were associated to MDR, however, no association was found between poor clinical outcome and MDR [21]. The same group also reported community-onset healthcare-associated bacteremic UTI had worse clinical outcomes in comparison to hospital-acquired bacteremic UTI, although there was no association of MDR cases with these two categories of bacteremic UTI [2]. Another study reported a higher likelihood of MDR Enterobacterales infections among male patients, in the presence of recurrent UTI, prior hospitalization, hydronephrosis, renal stone, stone, IUC, new-onset renal dysfunction, severe sepsis, ICU admission, ineffective empirical antibiotics, and longer hospitalization [19]. We compared the predisposing factors, comorbidities, and uropathogens in patients with MDR and non-MDR isolates. Diabetes, hypertension, preexisting renal disease, CKD, ICU admission, more than 10 days of hospital stay, the presence of fever, and indwelling catheter were relatively more (>75%) in the patients with MDR strains. All *K. pneumoniae* and 68.2% *E. coli* isolates displayed multidrug resistance. Most cases (75%) of poor outcomes were found in the MDR group.

Sixteen of our patients received empirical antibiotics. Cefoperazone-sulbactam was the most commonly used drug for empirical therapy (n=6), followed by meropenem (n=4), ceftriaxone (n=3), piperacillin/tazobactam (n=2), and norfloxacin (n=1). Targeted therapy was chosen based on the antibiotic susceptibility and clinical condition of the patients. While 18 patients had good outcomes and were discharged in an improved condition, 8 patients had poor outcomes including three mortalities. Cefoperazone-sulbactam, piperacillin/tazobactam, nitrofurantoin, and ceftriaxone monotherapy had good outcomes in 7, 4, 2, and 1 patient, respectively, with no poor outcomes. Meropenem was associated with 4 good outcomes and 3 poor outcomes. Combination therapies such as cefoperazone-sulbactam + polymyxin B, cefoperazone-sulbactam + piperacillin/tazobactam, and piperacillin/tazobactam + meropenem were given in critically ill individuals with severe urosepsis due to MDR organisms and had poor outcomes and deaths. Among the three mortality cases, the first patient was a 56-year-old male diagnosed with encephalopathy and CKD, who developed CA-UTI and BSI caused by MDR *K. pneumoniae*. He died of septic shock and MODS after 5 days of hospitalization despite receiving meropenem empirically followed by polymyxin B targeted therapy. The second patient, a 30-year-old male with post-operative peritonitis following gastric perforation repair, developed CA-UTI and hospital-acquired pneumonia and succumbed to MDR *K. pneumoniae* sepsis after 37 days. The third patient, an 83-year-old lady with cerebrovascular accident and parkinsonism, died of *E. coli* urosepsis, MODS, and aspiration pneumonia after 3 days of hospitalization. The last two patients were treated with piperacillin/tazobactam + meropenem. Our findings display the complexity and potential challenges of managing severe infections by MDR organisms. Our findings highlight the complexity of treating secondary BSI-caused UTI. Although 69.2% (18 out of 26) of patients had good clinical outcomes, urosepsis resulted in mortality in 3 patients (11.5%) despite piperacillin/tazobactam + meropenem and polymyxin B therapy. This may indicate the critical role of other comorbid conditions in determining the final clinical outcome. In general, about 5–25% mortality has been documented in BSI of urinary sources, however, it varies widely as per the patients' factors and the nature of the causative pathogen [11]. Cefoperazone sulbactam, quinolones, piperacillin-tazobactum, and nitrofurantoin commonly retain their susceptibility against most uropathogens and are most commonly prescribed as empirical as well as targeted therapy for bacteremic UTI and urosepsis in Indian hospitals [22]. Fosfomycin also has superior antibacterial activity in urinary tract, however, it has higher adverse reactions and its use is limited to *E. coli* infections [23].

CONCLUSION

BSI is a frequent and critical complication of UTI, especially in the case of pyelonephritis and urolithiasis. Recognizing this association is crucial for early identification and prompt management to avoid complications. In our study, secondary BSIs developed in 2.8% of cases of UTI caused by Enterobacterales. Most of these were caused by *E. coli* (84.6%) and *K. pneumoniae* (11.5%). Among these isolates, 76.9% were ESBL producers and 69.2% were MDR. Comorbid conditions such as diabetes, renal calculi, the presence of fever, Foley's catheter, age >60 years, ICU admission, hospital stay of more than 10 days, and poor clinical outcomes were relatively more among patients with MDR Enterobacterales infections. Cefoperazone-sulbactam, piperacillin/tazobactam, and Nitrofurantoin had a greater number of good outcomes without any poor outcomes. Whereas poor outcomes and mortality were found in association with *K. pneumoniae* infection, MDR strains, and in the background of severe sepsis. Overall, these findings highlight the critical need for early detection, effective treatment strategies, and robust infection control measures to manage and prevent secondary BSIs in UTI patients, particularly those with underlying health conditions and risk factors for MDR infections.

CONTRIBUTION OF AUTHORS

All the authors contributed equally to concepts, design, data analysis, manuscript preparation, manuscript editing, and review of the article.

ACKNOWLEDGMENTS

Nil.

CONFLICT OF INTEREST

Nil.

FUNDING

Nil.

REFERENCES

1. Al-Hasan MN, Eckel-Passow JE, Baddour LM. Bacteremia complicating gram-negative urinary tract infections: A population-based study. J Infect. 2010;60(4):278-85. doi: 10.1016/j.jinf.2010.01.007, PMID 20114061
2. Gómez-Zorrilla S, Becerra-Aparicio F, López Montesinos I, Ruiz de Gopegui E, Grau I, Pintado V, *et al*. A large multicenter prospective study of community-onset healthcare associated bacteremic urinary tract infections in the era of multidrug resistance: Even worse than hospital acquired infections? Infect Dis Ther. 2021;10(4):2677-99. doi: 10.1007/s40121-021-00537-0, PMID 34626347
3. Bahagon Y, Raveh D, Schlesinger Y, Rudensky B, Yinnon AM. Prevalence and predictive features of bacteremic urinary tract infection in emergency department patients. Eur J Clin Microbiol Infect Dis. 2007;26(5):349-52. doi: 10.1007/s10096-007-0287-3, PMID 17431694
4. Khasawneh FA, Karim A, Mahmood T, Ahmed S, Jaffri SF, Tate ME, *et al*. Antibiotic de-escalation in bacteremic urinary tract infections: Potential opportunities and effect on outcome. Infection. 2014;42(5):829-34. doi: 10.1007/s15010-014-0639-8, PMID 24874607
5. Chin BS, Kim MS, Han SH, Shin SY, Choi HK, Chae YT, *et al*. Risk factors of all-cause in-hospital mortality among Korean elderly bacteremic urinary tract infection (UTI) patients. Arch Gerontol Geriatr. 2011;52(1):e50-5. doi: 10.1016/j.archger.2010.05.011, PMID 20579748
6. Ranjini CY, Kasukurthi LR, Madhumati B, Rajendran R. Prevalence of multidrug resistance and extended spectrum beta-lactamases among uropathogenic *Escherichia coli* isolates in a tertiary care hospital in South India: An alarming trend. Community Acquir Infect. 2015;2:19-24.
7. National Healthcare Safety Network (NHSN) Patient Safety Component Manual. Centers for Disease Control and Prevention; 2024. Available from: https://www.cdc.gov/nhsn/pdfs/pscmanual/pcsmanual_current.pdf [Last accessed on 2024 May 30].
8. Magiorakos AP, Srinivasan A, Carey RB, Carmeli Y, Falagas ME, Giske CG, *et al*. Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: An international expert proposal for interim standard definitions for acquired resistance. Clin Microbiol Infect. 2012;18(3):268-81. doi: 10.1111/j.1469-0691.2011.03570.x, PMID 21793988

9. Choi MH, Kim D, Park Y, Jeong SH. Impact of urinary tract infection-causative microorganisms on the progression to bloodstream infection: A propensity score-matched analysis. J Infect. 2022;85(5):513-8. doi: 10.1016/j.jinf.2022.08.039, PMID 36064046
10. Horcajada JP, Shaw E, Padilla B, Pintado V, Calbo E, Benito N, *et al*. Healthcare-associated, community-acquired and hospital-acquired bacteraemic urinary tract infections in hospitalized patients: A prospective multicentre cohort study in the era of antimicrobial resistance. Clin Microbiol Infect. 2013;19(10):962-8. doi: 10.1111/1469-0691.12089, PMID 23279375
11. Wagenlehner FM, Pilatz A, Weidner W, Naber KG. Urosepsis: Overview of the diagnostic and treatment challenges. Microbiol Spectr. 2015;3(5):1-18. doi: 10.1128/microbiolspec.UTI-0003-2012, PMID 26542042
12. Harikrishnan S, Vennila R, Monica R. Isolation and characterisation of anti-bacterial resistance patterns of bacterial isolates from urinary tract infection in diabetics. Int J Curr Pharm Res. 2021;13(1):57-59.
13. Sarkar S, Sadhu S, Roy R, Tarafdar S, Mukherjee N, Sil M, *et al*. Contemporary drifts in diabetes management. Int J App Pharm. 2023;15(2):1-9.
14. Varma M, Peravali SK, Vandana K, Kamath A, Singh RJ. A study of risk factors for bacteremia caused by urinary tract infections. Asian J Med Sci. 2018;9(5):25-30.
15. Shaw E, Benito N, Rodríguez-Baño J, Padilla B, Pintado V, Calbo E, *et al*. Risk factors for severe sepsis in community-onset bacteraemic urinary tract infection: Impact of antimicrobial resistance in a large hospitalised cohort. J Infect. 2015;70(3):247-54. doi: 10.1016/j.jinf.2014.09.011, PMID 25305497
16. Lalueza A, Sanz-Trepiana L, Bermejo N, Yaiza B, Morales-Cartagena A, Espinosa M, *et al*. Risk factors for bacteremia in urinary tract infections attended in the emergency department. Intern Emerg Med. 2018;13(1):41-50. doi: 10.1007/s11739-016-1576-6, PMID 27864665
17. Brindha SG, Hansiya V, Maheswari PU, Geetha N. A comparative *in vitro* anti-biofilm efficacy of phytosynthesized iron and silver nanoparticles. Int J App Pharm. 2020;12:72-6.
18. Rosenthal EJ. Epidemiology of septicaemia pathogens. Dtsch Med Wochenschr. 2002;127(46):2435-40. doi: 10.1055/s-2002-35463, PMID 12432483
19. Lee YC, Hsiao CY, Hung MC, Hung SC, Wang HP, Huang YJ, *et al*. Bacteremic urinary tract infection caused by multidrug-resistant *Enterobacteriaceae* Are associated with severe sepsis at admission: Implication for empirical therapy. Med (Baltim). 2016;95(20):e3694. doi: 10.1097/MD.0000000000003694, PMID 27196480
20. Lam PW, Wiggers JB, Lo J, MacFadden DR, Daneman N. Utility of urine cultures in predicting blood culture susceptibilities in patients with bacteremic urinary tract infection. Antimicrob Agents Chemother. 2019;63(1):e01606-18. doi: 10.1128/AAC.01606-18, PMID 30323048
21. Gómez-Zorrilla S, Becerra-Aparicio F, Sendra E, Zamorano L, Grau I, Pintado V, *et al*. Risk factors and clinical impact of multidrug resistance in healthcare-associated bacteremic urinary tract infections: A post-hoc analysis of a multicenter prospective cohort in Spain. J Hosp Infect. 2024;151:173-85. doi: 10.1016/j.jhin.2024.05.020
22. Shareef A, Vasavan A, Roy A, James AJ, Nair CC, Aiswarya S. Antibiotic de-escalation in bacteremic UTI and its impact on cost and length of stay-a prospective observational study in a tertiary care teaching hospital in south Kerala. Int J Pharm Sci Res. 2023;14(9):4572-79.
23. Sojo-Dorado J, López-Hernández I, Rosso-Fernandez C, Morales IM, Palacios-Baena ZR, Hernández-Torres A, *et al*. Effectiveness of fosfomycin for the treatment of multidrug-resistant *Escherichia coli* bacteremic urinary tract infections: A randomized clinical trial. JAMA Netw Open. 2022;5(1):e2137277. doi: 10.1001/jamanetworkopen.2021.37277, PMID 35024838