

Bloodstream Infections in Non-ICU Hospitalized Patients: Impact of Pathogen Group on Clinical Outcomes—A Retrospective Cohort Study From Türkiye

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Background: Bloodstream infections (BSIs) in non-intensive care unit (ICU) wards are common yet less well characterized than ICU BSIs. Differences in monitoring intensity, diagnostic timelines, empirical therapy, and local resistance may shape outcomes, but pathogen-specific data in non-ICU settings remain limited. To address this gap, we provide regional data from Türkiye.

Methods: We conducted a retrospective cohort study at a tertiary-care center in Türkiye, including 537 adult non-ICU inpatients with first monomicrobial BSI episodes between January 2020 and November 2023. Pathogens were grouped as Gram-negative, Gram-positive, or fungal. Demographic, clinical, microbiological, and outcome data were analyzed. Independent predictors of mortality were evaluated using multivariable logistic regression.

Results: Among 537 patients (mean age 66.4 ± 16.4 years), Gram-negative pathogens predominated (65.0%), followed by Gram-positive (25.0%) and fungal pathogens (10.1%). The most frequent microorganisms were *Escherichia coli* (27.7%), *Klebsiella* spp. (20.7%; including clinically significant resistance), and *Staphylococcus aureus* (16.9%). Overall, 12.5% required ICU transfer, and in-hospital mortality was 23.3%, higher in fungal infections (46.3%) than bacterial infections ($p < 0.001$). Fungal BSIs were associated with delayed initiation of appropriate therapy. In adjusted analyses, higher Charlson Comorbidity Index (OR 1.20; $p < 0.001$), fungal pathogens (OR 2.41; $p = 0.026$), ICU transfer (OR 24.66; $p < 0.001$), and longer time from admission to infection onset (OR 1.03; $p = 0.003$) were independently associated with mortality.

Conclusion: In non-ICU settings, early recognition, rapid organism identification, and tailored antimicrobial/antifungal stewardship are essential—particularly given local resistance pressures (eg, carbapenem-resistant *Klebsiella*) and the elevated risk with candidemia. Implementing pathways that expedite diagnosis and timely appropriate therapy may improve patient outcomes.

Keywords: bloodstream infection, non-ICU patients, pathogen distribution, clinical outcomes

Introduction

BSIs are common and serious, yet much of the contemporary evidence derives from ICU cohorts.¹ A substantial proportion also occurs in non-ICU settings (eg, internal medicine and surgical wards), and large-scale surveillance indicates that up to half of hospital-acquired BSIs arise on general wards rather than in ICUs.²

Non-ICU wards differ from ICUs in ways directly relevant to BSI epidemiology and management: less continuous monitoring and different staffing ratios, longer diagnostic and therapeutic lead times, distinct pre-test probabilities of infection sources (eg, urinary or intra-abdominal vs ventilator-associated), different device-exposure profiles, and local resistance ecologies that diverge from ICU case-mix. These setting-level differences can shift pathogen distribution, the

appropriateness of initial therapy, and patient outcomes; therefore, non-ICU BSIs warrant investigation as a distinct care context rather than inference from ICU data.^{3,4}

Several risk factors contribute to the development of BSIs in non-ICU hospital wards, including advanced age, chronic comorbidities, and immunosuppressive therapies.^{1,4} The widespread use of invasive devices is associated with increased BSI risk, particularly in patients with prolonged hospital stays or repeated hospitalizations.^{3,5} Notably, the source of infection in non-ICU settings is often genitourinary or intra-abdominal, reflecting the underlying vulnerability of these patient populations.⁴ In addition, recent surgery, parenteral nutrition, and previous exposure to broad-spectrum antibiotics have been identified as independent risk factors for both bacterial and fungal BSIs.^{5,6}

The microbiologic spectrum of non-ICU BSIs encompasses Gram-negative and Gram-positive bacteria as well as fungi. Ward-based series report a shift toward Gram-negative pathogens—especially Enterobacterales such as *Escherichia coli* and *Klebsiella* spp.—with candidemia contributing a meaningful share of episodes.^{1,7} In a recent non-ICU cohort, Enterobacterales predominated and multidrug resistance was common, underscoring stewardship needs beyond critical care.⁵ Fungal pathogens, particularly *Candida* spp., are also important—especially among immunocompromised or high-risk patients.⁶

This study characterizes non-ICU BSIs by pathogen group (Gram-negative, Gram-positive, and fungal) and identifies independent predictors of in-hospital mortality in a large single-center cohort from Türkiye (2020–2023), informing empiric therapy and infection-prevention strategies.

Materials and Methods

Study Design and Setting

This retrospective cohort study was conducted at Eskişehir Osmangazi University Faculty of Medicine, a 1,010-bed tertiary-care hospital in Türkiye, between January 2020 and November 2023. The study included all adult (≥ 18 years) patients with positive blood cultures for Gram-positive, Gram-negative, or fungal pathogens in non-ICU wards. Clinical and demographic data of 537 eligible patients were retrospectively reviewed from medical records. No formal sample size calculation was performed due to the retrospective design.

Inclusion of Patients

We included adult (≥ 18 years) non-ICU inpatients with their first monomicrobial BSI episode during January 2020 and November 2023, where the index date was the date of the first positive blood culture drawn on a non-ICU ward.

Exclusion of Patients

Patients were excluded if (i) blood cultures were obtained during their stay in an ICU; (ii) medical records were incomplete or missing; (iii) blood culture positivity was attributed to contamination (ie, a single positive blood culture for common skin commensals without clinical or laboratory evidence of infection); or (iv) the episode was polymicrobial. To avoid intra-patient correlation, if a patient experienced more than one BSI episode during the study period, only the first episode was analyzed and subsequent episodes were excluded.

Definitions

BSI was defined as at least one positive blood culture for a pathogenic organism with compatible clinical or laboratory evidence. Contamination was defined as isolation of common skin commensals (eg, coagulase-negative staphylococci, *Corynebacterium* spp., *Bacillus* spp.) in a single blood culture bottle without clinical or laboratory evidence of infection, according to established guidelines.⁸ Infections were classified as primary (unknown-source) when no infectious focus at another body site (eg, urinary tract, respiratory, intra-abdominal, skin/soft tissue, catheter-related) was identifiable after review of clinical examination, laboratory results, available imaging, and microbiologic data; secondary BSI was assigned when a specific site was recognized as the likely origin.^{9,10} Immunosuppression was defined as the presence of hematological malignancy, solid tumor under active chemotherapy, chronic corticosteroid or other immunosuppressive therapy, or history of organ transplantation.

Comorbidities were evaluated both individually (eg, diabetes mellitus, solid tumor, chronic kidney disease, cardiovascular disease, hematological malignancy, immunosuppression) and cumulatively using the Charlson Comorbidity Index (CCI), as previously described.¹¹ Mortality was evaluated as both 30-day and total in-hospital mortality. Thirty-day mortality was assessed only while patients remained hospitalized; deaths occurring after discharge were not captured. We also generated a descriptive year-stratified summary of pathogen distributions (Gram-negative, Gram-positive, fungal) as counts and row-wise percentages; these data are presented in [Supplementary Table S1](#).

Identification of Microorganism

Blood samples were aseptically collected into BACTEC™ Lytic/10 Anaerobic/F and BACTEC™ Plus Aerobic/F bottles (Becton Dickinson, Sparks, MD, USA) and incubated for up to 7 days in the BACTEC™ FX instrument. Positive vials were Gram-stained and subcultured onto Sheep Blood Agar (SBA), Chocolate Agar, Eosin-Methylene Blue (EMB) Agar, and Inhibitory Mold Agar. To minimize the risk of false negatives, all culture-negative bottles were subcultured onto Chocolate Agar at the end of the incubation period.

Identification of bacterial and fungal pathogens was performed using the MALDI-TOF mass spectrometry system (MALDI Biotyper; Bruker Daltonics). Bacterial susceptibility testing was conducted with the BD Phoenix M50 automated microbiology system, while antifungal susceptibility was assessed using Micronaut-AM (Bruker Daltonics) according to the manufacturer's instructions and interpreted using EUCAST guidelines.

Ethics Approval and Consent to Participate

This retrospective cohort study was approved by the Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee, with reference number 2023–34. The requirement for informed consent was waived because the study involved secondary analysis of existing medical records with no direct patient contact. Patient confidentiality was protected throughout: all datasets were de-identified/anonymized prior to analysis, only aggregated results are reported, and no identifiable information was retained. The study was conducted in accordance with the principles of the Declaration of Helsinki and national data-protection regulations.

Statistical Analysis

Continuous variables were presented as mean $\pm$ standard deviation (SD) or as median with interquartile range (IQR) and minimum–maximum values, depending on the distribution (normality by Shapiro–Wilk). Two-group comparisons used the independent-samples *t*-test or Mann–Whitney U; comparisons across ≥ 3 groups used one-way ANOVA or Kruskal–Wallis with Bonferroni-adjusted post hoc tests. Categorical variables were compared with Pearson's chi-square test (Fisher's exact test when appropriate). To identify independent predictors of in-hospital mortality, we fitted a multivariable logistic regression model (enter method) including variables with $p < 0.10$ in univariable analyses or deemed clinically relevant. Results are reported as odds ratios (ORs) with 95% confidence intervals (CIs). Analyses were performed in R (R Core Team, 2024). A two-sided *p*-value of < 0.05 was considered statistically significant.

Results

Study Population

Throughout the study period, a total of 1562 positive blood culture episodes from 1105 individual patients were identified. After excluding 410 patients due to contaminated blood cultures, 27 patients due to missing clinical data, and 131 patients with polymicrobial infections, 537 patients with monomicrobial BSIs were included in the final analysis. Among these, 349 had Gram-negative, 134 had Gram-positive, and 54 had fungal infections ([Figure 1](#)).

The study included 537 patients with a mean age of 66.4 ± 16.4 years, of whom 55.7% were male. The majority of patients had at least one chronic comorbidity, most commonly cardiovascular disease (45.2%), diabetes mellitus (28.8%), or solid tumors (33.1%). More than half of the patients (52.1%) were immunosuppressed. Over half of the cohort (53.9%) had at least one invasive device, with indwelling urinary catheter (31.6%) and central venous catheters (23.7%) being the most frequent. The median CCI was 5 (IQR 3–7; range 0–15), and the median time from hospital admission to

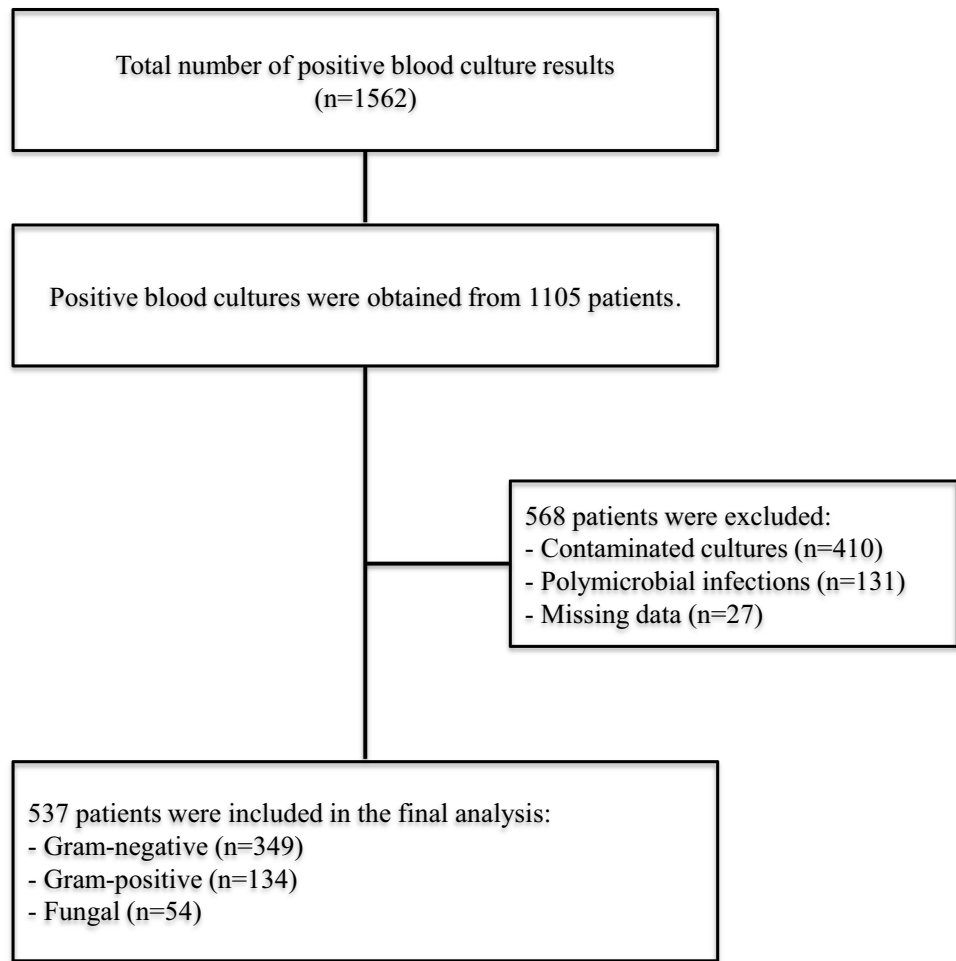


Figure 1 Flowchart of patient selection and inclusion.

bacteremia onset was 3 days (IQR 0–9; range –5 to 107). The most common sources of BSI were primary BSI (38.9%), urinary tract (18.6%), and intra-abdominal infections (18.1%); less frequent sources were grouped as other: skin/soft tissue (3.9%), cardiovascular (2.8%), bone/joint (0.6%), and central nervous system (0.4%). During hospitalization, 12.5% of patients required transfer to the ICU, while the overall in-hospital mortality rate was 23.3%. Detailed demographic and clinical characteristics are summarized in [Table 1](#).

Table 1 Demographic and Clinical Characteristics of Patients

	All Patients (n: 537)
Age, mean ± SD (min–max)	66.4 ± 16.4 (18–97)
Sex	
Male, n (%)	299 (55.7)
Female, n (%)	238 (44.3)
Charlson Comorbidity Index median (IQR) [min–max]	5 (3–7) [0–15]
Presence of comorbidity, n (%) [†]	507 (94.4)
Cardiovascular disease	243 (45.2)
Solid tumor	178 (33.1)

(Continued)

Table 1 (Continued).

	All Patients (n: 537)
Diabetes mellitus	155 (28.8)
Chronic kidney disease	87 (16.2)
Hematological malignancy	81 (15.1)
Immunosuppressed, n (%)	280 (52.1)
Presence of Invasive device, n (%) [†]	290 (53.9)
Indwelling urinary catheter	170 (31.6)
Central venous catheter	127 (23.7)
Nephrostomy / Urostomy	26 (4.8)
Percutaneous transhepatic catheter	24 (4.5)
Tracheostomy	13 (2.4)
Other	25 (4.6)
Source of BSI, n (%)	
Primary	209 (38.9)
Urinary tract infection	100 (18.6)
Intra-abdominal infection	97 (18.1)
Catheter-related infection	63 (11.7)
Pneumonia	27 (5.0)
Other	41 (7.7)
ICU transfer required, n (%)	67 (12.5)
Duration from admission to BSI (days) mean $\pm$ SD, Median (IQR) [min–max]	7.19 $\pm$ 12.27 3 (0–9) [–5–107]
Length of stay in ward (days) median (IQR) [min–max]	16 (9–26) [0–149]
Length of stay in hospital (days) median (IQR) [min–max]	17 (10–28) [0–149]
Status on day 30, n (%)	
Discharged	364 (67.8)
Follow-up ongoing	75 (14.0)
In intensive care unit	10 (1.9)
Deceased	88 (16.4)
Duration between culture collection and 30-day mortality, median (IQR) [min–max] (n=88)	13 (7–18) [1–28]
Overall in-hospital mortality, n (%)	125 (23.3)
Duration between culture collection and mortality (overall in-hospital mortality), median (IQR) [min–max] (n=125)	16 (7–25) [1–73]

Notes: [†]Some patients had more than one chronic disease and/or more than one invasive device.

Abbreviations: ICU, intensive care unit; BSI, bloodstream infection; IQR, interquartile range; SD, standard deviation.

Microbiological Findings

The most frequently isolated causative microorganisms were *E. coli* (27.7%), *Klebsiella* spp. (20.7%), and *S. aureus* (16.9%). Among the 54 *Candida* BSIs, *C. parapsilosis* (22, 40.7%) was the most common species, followed by *C. albicans* (17, 31.5%), *C. glabrata* (9, 16.7%), *C. tropicalis* (5, 9.3%), and *C. krusei* (1, 1.9%). The detailed distribution of all causative microorganisms is presented in Table 2. Antimicrobial susceptibility patterns of the most common pathogens are summarized in Table 3. Notably, resistance rates were high for both *E. coli* and *Klebsiella* spp., particularly for ceftriaxone and ciprofloxacin. In *Klebsiella* spp., carbapenem resistance was also substantial, observed in

Table 2 Distribution of Causative Microorganisms

Microorganism	n	%
<i>Escherichia coli</i>	149	27.7
<i>Klebsiella</i> spp.	111	20.7
<i>Staphylococcus aureus</i>	91	16.9
<i>Candida</i> spp.	54	10.1
<i>Enterococcus faecium/faecalis</i>	29	5.4
<i>Pseudomonas aeruginosa</i>	20	3.7
<i>Acinetobacter</i> spp.	19	3.5
<i>Stenotrophomonas maltophilia</i>	17	3.2
<i>Enterobacter</i> spp.	13	2.4
Coagulase-negative staphylococci	9	1.7
<i>Serratia</i> spp.	7	1.3
<i>Proteus</i> spp.	6	1.1
Other*	12	2.2
Total	537	100.0

Notes: Other includes rare identified pathogens (such as *Morganella* spp. and *Streptococcus pneumoniae*) not listed individually due to their low frequency.

Table 3 Antimicrobial Susceptibility Patterns of the Most Common Pathogens

Pathogen	Antibiotic	Number of Isolates Tested (n)	Resistant n (%)
<i>Escherichia coli</i>	Ciprofloxacin	149	65 (43.6)
	Ceftriaxone (ESBL)	149	75 (50.3)
	Meropenem (CR)	149	18 (12.1)
<i>Klebsiella</i> spp.	Ciprofloxacin	111	76 (68.5)
	Ceftriaxone (ESBL)	111	82 (73.9)
	Meropenem (CR)	111	63 (56.8)
<i>Staphylococcus aureus</i>	Oxacillin (MRSA)	91	24 (26.4)
<i>Candida</i> spp.	Fluconazole	54	7 (13.0)
	Echinocandins	54	5 (9.3)
<i>Enterococcus faecium/faecalis</i>	Ampicillin	29	12 (41.4)
	Vancomycin (VRE)	29	1 (3.4)

Notes: Ceftriaxone resistance was used as a surrogate marker for ESBL production. Echinocandins (anidulafungin, caspofungin, micafungin). Echinocandin resistance was defined according to EUCAST clinical breakpoints for any of anidulafungin, caspofungin, or micafungin.

Abbreviations: ESBL, Extended-spectrum beta-lactamase; CR, Carbapenem-resistant; MRSA, Methicillin-resistant *S. aureus*; VRE, Vancomycin-resistant *Enterococcus* spp.

56.8% of isolates. Methicillin resistance was identified in 26.4% of *S. aureus* isolates. Among *Candida* spp., resistance to fluconazole and echinocandins was 13.0% and 9.3%, respectively.

Clinical Characteristics and Outcomes by Pathogen Group

Pathogen distribution was Gram-negative 65.0% (n=349), Gram-positive 25.0% (n=134), and fungal 10.1% (n=54). Year-by-year distributions were consistently Gram-negative–predominant with smaller Gram-positive and fungal proportions; annual culture volume peaked in 2022 (199 vs 104–120 in 2020–2021 and 114 in 2023). Comparison of clinical characteristics and outcomes by pathogen group is presented in Table 4. Chronic kidney disease was significantly more common in the Gram-positive group (29.1%, $p < 0.001$). Immunosuppression was more common among patients with Gram-negative (57.3%) and fungal (51.9%) infections than in those with Gram-positive infections (38.8%, $p = 0.001$).

Table 4 Comparison of Demographic, Clinical, and Outcome Variables Between Gram-Negative, Gram-Positive, and Fungal Bloodstream Infections

Variable	Gram-Negative (n=349)	Gram-Positive (n=134)	Fungal (n=54)	p-value
Age, mean $\pm$ SD	64.6 $\pm$ 15.9	62.9 $\pm$ 16.3	65.7 $\pm$ 16.5	0.466*
Male sex, n (%)	195 (55.8)	78 (58.2)	26 (48.1)	0.451**
CCI, median (IQR) [min–max]	5 (4–7) [0–14]	4 (3–7) [0–12]	5 (3–7) [0–15]	0.199*
Presence of comorbidity, n (%) [†]	327 (93.7)	128 (95.5)	51 (94.4)	0.741**
— Cardiovascular disease, n (%)	152 (43.6)	71 (53.0)	20 (45.4)	0.078**
— Solid tumor, n (%)	127 (36.4)	31 (23.1)	20 (37.0)	0.076**
— Diabetes mellitus, n (%)	108 (30.9)	33 (24.6)	14 (25.9)	0.344**
— Chronic kidney disease, n (%)	44 (12.6)	39 (29.1)	4 (7.4)	< 0.001**
— Hematological malignancy, n (%)	58 (16.6)	16 (11.9)	7 (13.0)	0.393**
Immunosuppressed, n (%)	200 (57.3)	52 (38.8)	28 (51.9)	0.001**
Presence of invasive device, n (%) [‡]	177 (50.7)	76 (56.7)	37 (68.5)	0.039**
— Indwelling urinary catheter	100 (28.7)	41 (30.6)	29 (53.7)	0.001**
— Central venous catheter	62 (17.8)	48 (35.8)	17 (31.5)	< 0.001**
BSI Type, n (%):				
— Primary	139 (39.8)	42 (31.3)	28 (51.9)	0.028**
— Secondary	210 (60.2)	92 (68.7)	26 (48.1)	
ICU transfer required, n (%)	39 (11.2)	14 (10.4)	14 (25.9)	0.007**
Duration from admission to BSI (days) mean $\pm$ SD, median (IQR) [min–max]	6 $\pm$ 11 2 (0–70) [0–92]	5 $\pm$ 8 2 (0–8) [–5–57]	16 $\pm$ 20 11 (5–19) [0–107]	< 0.001*
Day of appropriate therapy initiation (days), median (IQR) [min–max]	0 (0–3) [–24–24]	0 (0–2) [–19–41]	4 (1–5) [0–23]	< 0.001*
Length of ward stay, (days) mean $\pm$ SD, median (IQR) [min–max]	20 $\pm$ 18 14 (8–25) [0–149]	21 $\pm$ 15 17 (10–26) [0–79]	30 $\pm$ 24 22 (17–32) [3–115]	< 0.001*
Total hospital stay, (days) mean $\pm$ SD, median (IQR) [min–max]	21 $\pm$ 19 15 (9–27) [3–149]	22 $\pm$ 15 19 (11–27) [0–79]	33 $\pm$ 24 27 (19–34) [7–124]	< 0.001*

(Continued)

Table 4 (Continued).

Variable	Gram-Negative (n=349)	Gram-Positive (n=134)	Fungal (n=54)	p-value
30-day mortality, n (%)	55 (15.9)	18 (13.5)	15 (27.8)	0.051**
In-hospital mortality, n (%)	74 (21.2)	26 (19.4)	25 (46.3)	< 0.001**

Notes: Bold highlights significant difference, $p < 0.05$. *Kruskal–Wallis Test, **Pearson Chi-Square Test. †Some patients had more than one chronic disease and/or more than one invasive device. Negative values indicate that appropriate therapy was initiated prior to blood culture collection, or that blood cultures were obtained before hospital admission.

Abbreviations: ICU, intensive care unit; CCI, Charlson Comorbidity Index; BSI, bloodstream infection; IQR, interquartile range; SD, standard deviation.

Primary BSIs were most frequently observed in patients with fungal infections (51.9%) and least frequent in those with Gram-positive infections (31.3%), with a statistically significant difference among pathogen groups ($p = 0.028$).

The presence of an invasive device was most frequent in the fungal group (68.5%, $p = 0.039$), particularly for indwelling urinary catheters (53.7%, $p = 0.001$). Central venous catheter use was also significantly higher in the Gram-positive (35.8%) and fungal (31.5%) groups compared to the Gram-negative group (17.8%, $p < 0.001$).

The interval from admission to BSI onset was longest in fungal infections (11 days, IQR 5.2–19.0) versus Gram-negative and Gram-positive (both 2 days, $p < 0.001$). Time to appropriate therapy was also longest in the fungal group (median 4.0 days, IQR 1.3–5.0) versus bacterial groups (both median 0.0 days, $p < 0.001$).

Both the median length of stay in the ward and total hospital stay were longest in the fungal group ($p < 0.001$). The requirement for ICU transfer was significantly higher in patients with fungal infections (25.9%) than in the other groups ($p = 0.007$).

Comparison Between Survivor and Mortality Cohorts

A comparison of demographic, clinical, and microbiological characteristics between the mortality and survivor cohorts is presented. Patients who died during hospitalization had significantly higher CCI scores, a greater prevalence of solid tumors and immunosuppression, and were more likely to require ICU transfer. The mortality group also exhibited higher rates of indwelling urinary catheter use and fungal infections. Furthermore, the duration from admission to BSI onset, length of ward stay, and total hospital stay were significantly longer in the mortality cohort. Post hoc comparisons confirmed that fungal infections were significantly more common in the mortality group, while no significant differences were observed between Gram-negative and Gram-positive infections. There were no significant differences between groups regarding age, sex, or the day of appropriate therapy initiation (Table 5).

Table 5 Comparison of Various Variables for Mortality

	Mortality Cohort (n:125)	Survivor Cohort (n:412)	p-value
Age, mean $\pm$ SD	65.1 $\pm$ 14.1	64.3 $\pm$ 16.3	0.857*
Gender			
Female, n (%)	52 (41.6)	186 (45.1)	0.551**
Male, n (%)	73 (58.4)	226 (54.9)	
CCI, median (IQR) [min–max]	6 (4–8) [0–13]	5 (3–6) [0–15]	< 0.001*
Presence of comorbidity, n (%) [†]	123 (98.4)	384 (93.2)	0.046**
— Cardiovascular disease, n (%)	54 (43.2)	189 (45.9)	0.672**
— Solid tumor, n (%)	64 (49.6)	113 (27.5)	< 0.001**

(Continued)

Table 5 (Continued).

	Mortality Cohort (n:125)	Survivor Cohort (n:412)	p-value
— Diabetes mellitus, n (%)	23 (17.8)	132 (32.4)	0.003**
— Chronic kidney disease, n (%)	13 (10.1)	74 (18.0)	0.046**
— Hematological malignancy, n (%)	24 (18.6)	55 (13.4)	0.186**
Immunosuppressed, n (%)	93 (72.1)	187 (45.5)	< 0.001**
Presence of invasive device, n (%) [†]	77 (59.7)	213 (51.8)	0.144**
— Indwelling urinary catheter	51 (40.8)	119 (28.9)	0.016**
— Central venous catheter	38 (30.4)	89 (21.6)	0.056**
ICU transfer required, n (%)	56 (44.8)	11 (2.7)	< 0.001**
Pathogen group			< 0.001**
— Gram negative, n (%)	74 (59.2)	275 (66.7)	
— Gram positive, n (%)	26 (20.8)	108 (26.2)	
— Fungal, n (%)	25 (20.0)	29 (7.0)	
BSI Type, n (%):			0.220**
— Primary	55 (44.0)	154 (37.4)	
— Secondary	70 (56.0)	258 (62.6)	
Duration from admission to BSI (days), median (IQR) [min–max]	7 (2–17) [0–107]	2 (0–7) [–5–92]	< 0.001*
Day of appropriate therapy initiation (days), median (IQR) [min–max]	1 (0–5) [–24–24]	0 (0–3) [–19–41]	0.014*
Length of ward stay (days), median (IQR) [min–max]	19 (11–33) [0–108]	15 (9–25) [0–149]	0.007*
Length of hospital stay (days), median (IQR) [min–max]	26 (16–41) [4–124]	15 (9–25) [0–149]	< 0.001*

Notes: Bold highlights significant difference, $p < 0.05$. *Mann–Whitney U-Test, **Pearson Chi-Square Test. [†]Some patients had more than one chronic disease and/or more than one invasive device. Negative values indicate that appropriate therapy was initiated prior to blood culture collection, or that blood cultures were obtained before hospital admission.

Abbreviations: ICU, intensive care unit; BSI, bloodstream infection; CCI, Charlson Comorbidity Index; IQR, interquartile range; SD, standard deviation.

Multivariable Analysis of Mortality Predictors

Based on the univariable analyses, variables with $p < 0.10$ or clinical relevance were included in the multivariable model. Multivariable logistic regression revealed that higher CCI (OR: 1.20, 95% CI: 1.10–1.32; $p < 0.001$), ICU transfer requirement (OR: 24.66, 95% CI: 11.98–50.74; $p < 0.001$), presence of a fungal pathogen (OR: 2.41, 95% CI: 1.11–5.20; $p = 0.026$), and longer time from hospital admission to BSI onset (OR: 1.03 per day, 95% CI: 1.01–1.06; $p = 0.003$) were independent predictors of in-hospital mortality (Table 6). Other variables, including sex, presence of an invasive device,

Table 6 Multivariable Logistic Regression Analysis for Predictors of In-Hospital Mortality

Variable	Odds Ratio (OR)	95% CI	p-value
Sex (male)	0.92	0.56–1.48	0.719
Charlson Comorbidity Index (per point)	1.20	1.10–1.32	< 0.001

(Continued)

Table 6 (Continued).

Variable	Odds Ratio (OR)	95% CI	p-value
ICU transfer required	24.66	11.98–50.74	< 0.001
Presence of invasive device	1.02	0.61–1.70	0.932
Gram positive pathogen	1.01	0.55–1.84	0.975
Fungal pathogen	2.41	1.11–5.20	0.026
Duration from admission to BSI (per day)	1.03	1.01–1.06	0.003
Day of appropriate therapy initiation	1.00	0.94–1.06	0.999

Note: Bold indicates statistical significance at $p < 0.05$.

Abbreviations: OR, odds ratio; CI, confidence interval; ICU, intensive care unit; BSI, bloodstream infection.

Gram-positive pathogen, and day of appropriate therapy initiation, were not significantly associated with mortality in the multivariable model.

Discussion

This study provides a comprehensive evaluation of BSIs in non-ICU hospitalized patients, a group often underrepresented in the literature. We found that Gram-negative bacteria were most common, followed by Gram-positive bacteria and fungi. For context, published non-ICU cohorts report mortality of 14.0% for Gram-negative bacteremia, 13.9% for catheter-related BSIs encompassing Gram-negative, Gram-positive, and fungal pathogens, and 27.9% for candidemia; our overall rate is 23.3%.^{6,12,13} These findings underscore the need for increased vigilance and pathogen-specific management strategies in non-ICU settings.

Annual BSI counts peaked in 2022; the timing may overlap with pandemic-phase fluctuations. By contrast, no marked shift in pathogen distributions was observed between pre- and post-pandemic periods—the profile remained predominantly Gram-negative. Given that the extent of COVID-19's influence on BSI occurrence remains unclear, co-infections (especially hospital-acquired superinfections) are typically reported as uncommon yet clinically consequential.¹⁴

Although ICU settings are often emphasized in BSI studies, recent research has shown that non-ICU patients also represent a clinically important population with significant morbidity and mortality.^{1,15} In many cohorts, Gram-negative bacteria such as *E. coli* and *Klebsiella* spp. are often reported as predominant pathogens, followed by Gram-positive organisms related to device use or healthcare exposure.¹² Our findings are consistent with this distribution, with Gram-negative pathogens accounting for 65.0% of all BSIs in our cohort. Notably, *E. coli* (27.7%) and *Klebsiella* spp. (20.7%) were the most frequently isolated microorganisms, while *S. aureus* (16.9%) represented the leading Gram-positive pathogen. *Candida* spp. ranked fourth overall (10.1%), highlighting the emerging role of fungal pathogens in non-ICU settings. Despite their lower frequency, fungal BSIs were disproportionately associated with in-hospital mortality, reinforcing previous evidence that candidemia is a serious complication with poor prognosis outside the ICU environment.⁶

The combination of extensive comorbidity and the high prevalence of multidrug-resistant organisms in non-ICU settings highlights a significant clinical challenge. Our results demonstrate that highly resistant pathogens are not limited to critical care units but are also frequent among vulnerable patients in general hospital wards, emphasizing the urgent need for rigorous infection control and antimicrobial stewardship beyond the ICU environment.⁵ This situation also complicates the selection of appropriate empirical antibiotic therapy.

A considerable proportion of BSIs were classified as primary (38.9%). This may reflect diagnostic limitations in non-ICU wards, especially in patients with advanced age, multiple comorbidities, and immunosuppression, where clinical manifestations can be subtle. The absence of a clearly identified source can complicate antimicrobial decision-making and delay appropriate therapy, potentially worsening patient outcomes.^{10,16} When analyzed by pathogen group, primary BSIs were most frequently observed in patients with fungal infections and least common among those with Gram-

positive pathogens. Post hoc analysis confirmed that this difference was statistically significant only between the fungal and Gram-positive groups. Nevertheless, primary BSI was not significantly associated with in-hospital mortality in our cohort.

In the univariable analyses, solid tumors and immunosuppression were identified as significant risk factors for in-hospital mortality, consistent with prior evidence in cancer cohorts where malignancy and immune defects increase vulnerability to BSIs and their complications.^{17,18} In the multivariable analysis, overall comorbidity burden, as measured by the CCI, remained an independent predictor of in-hospital mortality, aligning with findings from several studies showing CCI's robust performance in mortality risk stratification for patients with BSIs.^{5,17} Additionally, the need for ICU transfer was strongly associated with mortality, underscoring the clinical significance of acute deterioration as a critical event in non-ICU BSI patients.¹⁹

Another noteworthy finding of our study was that both the onset of BSI and the initiation of appropriate antimicrobial therapy were significantly delayed in patients with fungal BSIs compared to those with Gram-negative or Gram-positive infections. This delay is consistent with previous reports indicating that nosocomial candidemia often occurs as a late complication during hospitalization, particularly in patients with prolonged use of invasive devices or broad-spectrum antibiotics.^{1,2,19} Multiple studies have demonstrated that even modest delays in antifungal treatment can significantly increase mortality risk, underscoring the urgent need for rapid diagnostic strategies and heightened clinical suspicion in at-risk populations.^{6,20}

Although delayed initiation of appropriate therapy in fungal BSIs correlated with higher mortality in univariable analyses, the association lost significance in the multivariable model including all pathogen groups. This likely reflects limited power due to the small fungal denominator and the dominant contribution of comorbidity burden and acute deterioration (eg, ICU transfer) to mortality risk. In non-ICU wards, under-recognition of fungal BSIs likely stems from the lack of specific clinical signs, limited availability or use of rapid diagnostics, their tendency to emerge as late complications of prolonged hospitalization, and the absence of standardized approaches in heterogeneous (non-ICU) patient populations. These realities argue for rapid diagnostic strategies and heightened clinical suspicion in at-risk patients.

Building on the adjusted analyses, we propose a ward-level mortality cascade for fungal BSI, linking recognition and treatment delays to disproportionate in-hospital mortality. Although fungal BSIs constitute a small subgroup, they remained independently associated with death. In wards where non-fungal etiologies dominate, empiric treatment pathways are primarily geared toward bacterial coverage. In this context, fungal episodes are more often classified as primary BSI, occur later during hospitalization, and have a longer time to appropriate therapy—a pattern suggestive of culture-triggered rather than early empiric antifungal treatment. In multivariable models, the increasing admission-to-onset interval tracked with higher mortality risk, with fungal etiology retaining an independent association. Collectively, these ward-specific delays provide a plausible pathway by which a numerically small subgroup exerts a disproportionate impact on mortality.

Strengths and Limitations

The main strength of this study is the relatively large, well-characterized cohort of non-ICU hospitalized patients, including both bacterial and fungal BSIs, and the use of multivariable analysis to identify independent mortality predictors. However, as a single-center retrospective study, the findings may not be generalizable to all settings. Diagnostic work-ups were clinician-directed rather than standardized, and imaging/culture timing varied; early empiric therapy could have sterilized a primary focus. These constraints may have inflated the proportion classified as primary BSI; therefore, source-based comparisons warrant cautious interpretation. Due to space constraints, antimicrobial resistance analyses were limited to the most common pathogens, and resistance profiles of rare organisms were not detailed. Despite these limitations, our results provide valuable information for clinicians managing BSIs outside the ICU.

Conclusions

In summary, this study highlights the distinct epidemiological and clinical features of BSIs among non-ICU hospitalized patients. Gram-negative bacteria were the most common pathogens, but fungal infections were associated with the highest mortality rates. The high prevalence of multidrug-resistant organisms—particularly among *Klebsiella* spp.—and the frequent occurrence of BSIs in patients with multiple comorbidities pose major challenges for clinical management. Our findings underscore the importance of early recognition, greater diagnostic vigilance in non-ICU wards, as these patients receive less frequent monitoring than those in ICUs, appropriate antimicrobial therapy, and robust infection control measures in this vulnerable population. Tailoring empirical treatment strategies based on local resistance data and implementing antifungal stewardship programs to ensure timely and appropriate therapy for candidemia is essential. Future work should include prospective multicenter studies and the evaluation of rapid diagnostic approaches to shorten time-to-effective treatment and reduce mortality in non-ICU settings.

Data Sharing Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

This retrospective cohort study was approved by the Eskişehir Osmangazi University Non-Interventional Clinical Research Ethics Committee (reference no. 2023-34). The requirement for informed consent was waived due to the secondary analysis of existing medical records without direct patient contact. All datasets were de-identified prior to analysis, and only aggregated results are reported. The study was conducted in accordance with the principles of the Declaration of Helsinki and national data-protection regulations.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that they have no competing interests.

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