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Community acquired bacteremia in older adults: International and prospective infectious diseases-international research initiative (ID-IRI) study

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ABSTRACT

Objectives: Community-acquired bloodstream infections (CA-BSIs) are a major cause of mortality in older adults, yet prospective international data are limited. This study evaluated clinical features, microbiology, and mortality predictors in older patients with CA-BSI.

Methods: This prospective, observational study was conducted in 72 referral centers across 16 countries between June 1 and September 1, 2024. Patients aged ≥65 years with confirmed CA-BSI were included. Demographic, clinical, laboratory, and treatment data were collected. The primary outcome was 30-day all-cause mortality. Univariate and multivariate logistic regression was used to identify predictors.

Results: 574 patients were enrolled (median age 74 years; 48.1% female), and 30-day mortality was 26.3%. Urinary tract infection was the most common source (33.7%), and 30.5% had no identifiable origin. Gram-negative organisms predominated (58.6%). Independent mortality predictors included SOFA score ≥5, thrombocytopenia (<50,000/μL), *Staphylococcus aureus* bacteremia, pneumonia, bacteremia of unknown origin, and higher Charlson Comorbidity Index. Higher Katz Activities of Daily Living scores were protective.

Conclusion: CA-BSI in older adults is associated with high mortality. Outcomes are driven by comorbidity burden, functional status, infection severity, and causative pathogen, highlighting the need for early risk stratification and tailored management.

Introduction

Community-acquired infections are those occurring in individuals without recent healthcare exposure and constitute a substantial, often under-recognized component of the global infectious disease burden [1]. In addition, compared to younger populations, the incidence of infectious diseases is higher in older adults, with bloodstream infection (BSI) representing a serious concern [2]. This increase is attributed to age-related immunosenescence, a high prevalence of comorbid conditions, and the functional decline [3].

Although multiple studies have shown that the incidence of BSIs rises with age, reaching its peak in individuals over 65 years [4], available data on community-acquired BSIs in this population remain limited, are predominantly retrospective, and often fail to distinguish between community and hospital-acquired infections, analyzing them as a single cohort. In this international study, we aimed to prospectively perform a comprehensive analysis of patients with community-acquired (CA)-BSIs and to produce evidence-based insights to improve patient management for older adults.

Methods

Study Design: This study was conducted using a prospective, observational design. Older adult patients hospitalized with CA-BSIs were eligible for inclusion if they had confirmed bacteremia and clinical manifestations consistent with a bloodstream infection. Patient enrollment occurred between June 1, 2024, and September 1, 2024. The study was carried out under the coordination of the Infectious Diseases-International Research Initiative (ID-IRI) (https://infectdisiri.com). ID-IRI is a global collaborative network of clinical researchers who voluntarily participate in multicenter infectious disease research projects. Participating centers contributed data on eligible inpatients during the study period.

a) Inclusion Criteria
   1. Patients ≥65 years of age
   2. BSI categorized as community-onset (present or incubating at admission)
   3. Clinical findings compatible with BSIs
b) Exclusion Criteria
   1. Patients under the age of 65 years
   2. Patients with polymicrobial growth in the blood cultures
   3. Patients with BSIs caused by non-bacterial pathogens
   4. Patients with hospital-acquired infections

Setting: This study was conducted across 72 referral centers located in 16 countries (Türkiye, Saudi Arabia, Romania, Pakistan, North Macedonia, Kazakhstan, Italy, Iran, India, Egypt, Croatia, Bulgaria, Brazil, Bosnia and Herzegovina, Albania, and Afghanistan).

Data Collection: All participating researchers followed the patients, recorded data and submitted through a web-based case report system designed for standardized entry across all participating centers. For each patient demographic data, clinical and laboratory findings, underlying medical conditions, and 30-day all-cause mortality were recorded.

Definitions

a) **Older adult:** Patients aged 65 years and older were classified as older adults [5].
b) **BSI:** BSI was defined as the presence of at least one positive blood culture in a patient exhibiting systemic signs of infection and receiving systemic antibiotic therapy, consistent with widely accepted clinical and research criteria [6–8]. Common skin contaminants were considered clinically significant only when isolated from two or more separate blood cultures obtained within 48 hours [7,8].
c) **Community-acquired BSI** was defined by a positive blood culture obtained at the time of hospital admission or within the 48 hours after hospital admission for patients who did not fit the criteria for a health care- associated infection [9]. Devices such as nephrostomies were not considered exclusion criteria when they were inserted during the index hospitalization in response to the presenting CA-BSI and were not pre-existing at infection onset. The same applies to central venous catheters placed after admission.
d) **Appropriate empirical treatment:** Antimicrobial treatment regimens were selected to include at least one agent demonstrating confirmed *in vitro* activity against the isolated pathogen, as determined by AST results. All participants ensured that antimicrobial agents were administered with appropriate dosing, timing, and route, in alignment with current clinical guidelines.
e) **Guided antibiotic treatment** refers to the selection and administration of antimicrobial therapy based on microbiological or diagnostic evidence, such as *in vitro* susceptibility results.

f) **Empirical treatment strategies** refer to "none" when antimicrobial treatment was on hold until the microbiological evidence was available; "monotherapy" when single antibiotic regimen was provided, or "combination therapy" when more than one antibiotics were provided.
g) **Modified antibiotic treatment** refers to the adjustment of an ongoing antimicrobial regimen based on new clinical information, microbiological test results, pathogen identification, or antimicrobial susceptibility data.

Bacterial identification: Microbial identification was conducted utilizing commercially available systems (e.g., Vitek II; Biomerieux, Paris, France) alongside conventional biochemical and/or enzymatic assays.

Antimicrobial Susceptibility: All microbiology laboratories of the participating hospitals followed either CLSI [10] or EUCAST [11] guidelines for AST. AST was performed using automated systems and disc diffusion methods in accordance with standard, officially published guidelines. Colistin and vancomycin testing results were included in the analysis if microdilution method was used. For antibiotics not tested against a given isolate, those isolates were excluded from the denominator in susceptibility rate calculations. During data analysis: (i) cefoxitin-resistant Staphylococci were considered resistant to all beta-lactams; (ii) Enterococci were classified as resistant to all cephalosporins; and (iii) all Gram-positive bacteria were designated as resistant to colistin.

Comorbidity: Charlson Comorbidity Index score was used to assess comorbidity burden in our patients [12].

Outcome: The primary outcome was defined as 30-day all-cause mortality. All patients were followed for 30 days after bacteremia onset. For those discharged before day 30, follow-up was completed using outpatient records or telephone contact.

Statistical Analysis: Normality of numerical variables was assessed with the Shapiro-Wilk test, which showed non-normal distributions. Survivors and non-survivors were compared using the Mann-Whitney U test, and associations between categorical variables and mortality were evaluated with the Pearson chi-square test. Variables with $P < 0.10$ in univariate analyses were entered into a multiple binary logistic regression model using backward selection to identify independent predictors of mortality. Adjusted effects were estimated, with significance set at $P < 0.05$ for univariate tests and $P < 0.10$ for the multivariable model [13], and all computations were performed using the SPSS software (version 23).

Results

In this study, 574 older adult patients with CA-BSIs were included. The median age of the patients was 74 years (range: 65-99), and 286 (48.1%) were female. A total of 151 patients (26.3%) died within 30 days of bacteremia onset. The median time to death was 8 days (IQR, 3-16.5).

The sources of the BSIs: In 175 (30.5%) cases, the source of bacteremia remained unidentified The identified sources of BSIs included urinary tract infection (n = 200, 34.8%), pneumonia (n = 68, 11.8%), intra-abdominal infection (n = 52, 9.1%), skin-soft tissue infection (n = 37, 6.5%), cardiovascular system infection (n = 14, 1.9%), bone-joint infection (n = 14, 2.3%), central nervous system infection (n = 12, 2.1%) and others (1 febrile neutropenia, 1 pelvic inflammatory disease) (Table 1). Source control through abscess drainage was performed in 9 of 574 cases, including liver abscess (n = 2), cerebral abscess (n = 1), psoas abscess (n = 1), scrotal abscess (n = 1), soft tissue abscess (n = 1), and septic arthritis (n = 3) (Table 2).

Microbial Etiology: Gram-negative bacteria were identified in 348 patients (58.6%), whereas Gram-positive bacteria were detected in 246 patients (41.4%) with BSIs. *Escherichia coli* was the most common pathogen detected in 196 (33%) cases followed by *Staphylococcus aureus* (n = 86, 14.5%) and *Klebsiella pneumoniae* (n = 79, 13.3%). Coagulase-negative staphylococci were detected in 50 cases (8.4%), and *Enterococcus faecalis* in 37 cases (6.2%). *Pseudomonas aeruginosa* accounted for 20 cases (3.4%), while both *Enterococcus faecium* and *Proteus mirabilis* were found in 15 cases each (2.5%). *Streptococcus pneumoniae* was identified in 12 cases (2.0%). *Streptococcus mitis* was detected in 7 cases (1.2%). Other pathogens were each detected in less than 1% of cases and are presented in detail in Table 3.

Common comorbid conditions: Hypertension was the most prevalent comorbidity (n = 364, 63.4%), followed by diabetes mellitus (n = 234, 40.8%), congestive heart failure (n = 135, 23.5%), chronic obstructive pulmonary disease (n = 77, 13.4%), and dementia/Alzheimer's disease (n = 75, 13.1%). Cerebrovascular disease was less common (n = 18, 3.1%). Solid tumors were identified in 46 patients (8%), most frequently bladder cancer (n = 9), followed by prostate, colon, and breast cancers (n = 5 each). Endometrial, gastric, and pancreatic cancers were observed in 4 patients each, while hepatocellular carcinoma was present in 3 patients. Nasopharyngeal and lung cancers were each reported in 2 patients, and ovarian, choledochal, and testicular cancers were the least frequent (n = 1 each). Finally, nine patients had hematologic disorders [acute myeloid leukemia (n = 4), non-Hodgkin lymphoma (n = 3), Hodgkin lymphoma (n = 1), and thrombocytopenia (n = 1)].

Results of the Univariate Analysis: In our cohort of older adults with community-onset bloodstream infections, several factors were independently associated with mortality. Clinical characteristics linked to higher risk included the presence of pneumonia ($P < 0.001$), urinary tract infection ($P < 0.001$), bacteremia of unknown origin ($P = 0.004$), use of central venous catheters ($P < 0.001$), urinary catheters ($P < 0.001$), and tracheostomy ($P = 0.006$). Additional risk factors included a subsequent bloodstream infection within 30 days ($P < 0.001$), elevated body temperature ≥38.3°C ($P = 0.004$), pulse rate≥100 beats/min ($P = 0.030$), higher SOFA scores (≥5, $P < 0.001$), and MAP ≤65 mmHg ($P < 0.001$). Laboratory and microbiological parameters associated with mortality included thrombocytopenia (platelet count <50,000/μL, $P < 0.001$) and infections caused by *S. aureus* ($P = 0.001$) or *E. coli* ($P = 0.007$). Furthermore, patients with higher CCI scores ($P < 0.001$) and lower Katz Index scores, indicative of poorer functional status ($P < 0.001$), indicated significantly higher mortality (Tables 1-3).

Multivariate analysis of independent mortality predictors: Multivariate logistic regression was used, and the sensitivity of the model in correctly classifying non-survivors was 55.1%, while its ability to correctly classify survivors was 91.1%. Several factors were associated with increased risk. Among infections, pneumonia (OR = 2.13, $P = 0.031$), bacteremia of unknown origin (OR = 2.15, $P = 0.005$), and *S. aureus* bacteremia (OR = 2.53, $P = 0.007$) were significant predictors, each approximately doubling the odds. Markers of disease severity were the strongest predictors: SOFA score ≥5 (OR = 4.25, $P = 0.001$) and platelet count <50,000/μL (OR = 3.41, $P = 0.005$) were highly significant. CCI score also increased risk (OR = 1.16, $P = 0.002$), while higher Katz Index was protective (OR = 0.70, $P = 0.001$).

Other variables, including female gender, urinary catheter use, absence of *E. coli* BSI, and MAP ≤65 mmHg, showed increased odds but did not reach statistical significance (Table 4).

Antibiotic susceptibility: Antibiotic susceptibility patterns of the common antibiotics used in patients were shown in Table 5.

Table 1
Univariate analyses for the community-onset BSIs in older adults.

		Survived		Died		*P*
		n	%	n	%	
Gender	Female	195	70.7	81	29.3	0.111
	Male	228	76.5	70	23.5	
MDR	No	401	74.0	141	26.0	0.513
	Yes	22	68.8	10	31.3	
Empirical Treatment	No	44	71.0	18	29.0	0.073
	Mono	260	77.2	77	22.8	
	Combined	119	68.0	56	32.0	
Modified Treatment	No	157	68.9	71	31.1	**0.049**
	Yes, necessary	173	74.9	58	25.1	
	Yes, unnecessary	93	80.9	22	19.1	
Pneumonia	No	385	76.1	121	23.9	**<0.001**
	Yes	38	55.9	30	44.1	
Skin and soft tissue infection	No	394	73.4	143	26.6	0.503
	Yes	29	78.4	8	21.6	
Urinary tract infection	No	256	68.4	118	31.6	**<0.001**
	Yes	167	83.5	33	16.5	
Intra-abdominal infection	No	387	74.1	135	25.9	0.548
	Yes	36	69.2	16	31.8	
Bone and joint infection	No	411	73.3	150	26.7	0.123
	Yes	12	92.3	1	7.7	
Central nervous system infection	No	413	73.6	149	26.4	0.38
	Yes	10	77.8	2	22.2	
Cardiovascular system infection	No	411	71.6	149	28.4	0.30
	Yes	12	85.7	2	14.3	
Bacteremia of unknown origin	No	308	77.2	91	22.8	**0.004**
	Yes	115	65.7	60	34.3	
Central venous catheter	No	348	78.0	98	22.0	**<0.001**
	Yes	75	58.6	53	41.4	
Urinary catheter	No	212	81.9	47	18.1	**<0.001**
	Yes	211	67.0	104	33.0	
Nephrostomy catheter	No	422	73.6	151	26.4	0.550
	Yes	1	100.0	0	0.0	
Tracheostomy	No	421	74.3	146	25.7	**0.006**
	Yes	2	28.6	5	71.4	
Colostomy-gastrostomy	No	422	73.8	150	26.2	0.446
	Yes	1	50.0	1	50.0	
Intracardiac device	No	421	73.6	151	26.4	0.397
	Yes	2	100.0	0	0.0	
Subsequent BSI within 30 days	No	423	76.5	130	23.5	**<0.001**
	Yes	0	0.0	21	100.0	
Patient age	65-75	241	77.2	71	22.8	0.104
	76-85	126	70.0	54	30.0	
	>85	56	68.3	26	31.7	
Highest body temperature[a]	<38.3	281	70.3	119	29.8	**0.004**
	≥38.3	142	81.6	32	18.4	
Pulse rate (per minute)[a]	<100	264	77.0	79	23.0	**0.030**
	≥100	159	68.8	72	31.2	
SOFA score[a]	<5	301	89.1	37	10.9	**<0.001**
	≥5	122	51.7	114	48.3	
MAP[a]	≤65	18	40.0	27	60.0	**<0.001**
	>65	405	76.6	124	23.4	

[a] On the day when the blood cultures are taken.

Table 2
Comparison results of continuous variables in community-onset BSI data using univariate testing.

	Status	N	Mean	SD	Percentiles			*P*
					25th	Median	75th	
CCI	Survived	423	5.40	2.271	4.00	5.00	7.00	**<0.001**
	Died	151	7.13	2.963	5.00	6.00	9.00	
Katz Index	Survived	423	3.57	2.124	2.00	4.00	6.00	**<0.001**
	Died	151	1.49	1.876	.00	.00	3.00	

CCI: Charlson comorbidity index; **Katz Index:** Independence in activities of daily living score.

Discussion

BSIs in older adults are usually associated with high mortality, particularly if not diagnosed and treated promptly [14,15]. Although CA-BSI is a relatively benign form of bacteremia compared to hospital-acquired BSIs among older adults [14], our multicenter study found that mortality with CA-BSIs remained substantial at 26.6%, highlighting the significant clinical impact of these infections. In addition, we have shown that several patient and infection-related factors were associated with increased mortality. Pneumonia, bacteremia of unknown origin, and *S. aureus* BSI were all linked to a higher risk of death. Among the clinical parame-

Table 3
Univariate analyses for laboratory data and the most common infecting pathogens.

Laboratory Data	Survived			Died		*P*
		n	%	n	%	
Platelet count (/μL)[a]	<50,000	16	43.2	21	56.8	**<0.001**
	≥50,000	420	75.4	137	24.6	
Hemoglobin (g/dL)[a]	<12	306	72.3	117	27.7	0.358
	≥12	130	76.0	41	24.0	
WBC (/μL)[a]	<10,000	176	72.7	66	27.3	0.758
	≥10,000	260	73.9	92	26.1	
CRP level (mg/dL)[a]	<10	65	74.7	22	25.3	0.764
	≥10	371	73.2	136	26.8	
Procalcitonin (ng/mL)[a]	<0.1	8	80.0	2	20.0	0.613
	≥0.1	300	72.8	112	27.2	
Common Bacteria						
Coagulase-negative Staphylococci	No	398	73.2	146	26.8	0.660
	Yes	37	78.7	10	21.3	
Staphylococcus aureus	No	385	75.8	123	24.2	**0.001**
	Yes	44	57.1	33	42.9	
Escherichia coli	No	279	70.1	119	29.9	**0.007**
	Yes	157	80.5	38	19.5	
Enterococcus faecalis	No	407	73.1	150	26.9	0.417
	Yes	27	79.4	7	20.6	
Enterococcus faecium	No	426	73.6	153	26.4	0.550
	Yes	10	66.7	5	33.3	
Klebsiella pneumoniae	No	383	74.4	132	25.6	0.200
	Yes	52	67.5	25	32.5	
Proteus mirabilis	No	426	73.6	153	26.4	0.550
	Yes	10	66.7	5	33.3	
Pseudomonas aeruginosa	No	421	73.3	153	26.7	0.869
	Yes	15	75.0	5	25.0	
Streptococcus pneumoniae	No	427	73.4	155	26.6	0.899
	Yes	9	75.0	3	25.0	
Rare pathogens						
Streptococcus mitis	Yes	6	85.7	1	14.3	
Enterococcus spp.	Yes	4	80.0	1	20.0	
Acinetobacter baumannii	Yes	3	42.9	4	57.1	
Streptococcus agalactiae	Yes	4	80.0	1	20.0	
Salmonella spp	Yes	3	75.0	1	25.0	
Streptococcus spp.	Yes	1	25.0	3	75.0	
Bacteroides fragilis	Yes	2	66.7	1	33.3	
Listeria monocytogenes	Yes	1	33.3	2	66.7	
Klebsiella oxytoca	Yes	1	50.0	1	50.0	
Pseudomonas putida	Yes	3	100.0	0	0	
Stenotrophomonas maltophilia	Yes	2	66.7	1	33.3	
Streptococcus gallolyticus	Yes	3	100.0	0	0	
Streptococcus gordonii	Yes	3	100.0	0	0	
Streptococcus viridans	Yes	2	66.7	1	33.3	
Brucella melitensis	Yes	1	100.0	0	0	
Streptococcus dysgalactiae	Yes	2	100.0	0	0	
Streptococcus pyogenes	Yes	2	100.0	0	0	
Enterobacter cloacae	Yes	2	100.0	0	0	
Achromobacter spp.	Yes	1	100.0	0	0	
Acinetobacter lwoffii	Yes	1	100.0	0	0	
Acinetobacter towneri	Yes	1	100.0	0	0	
Campylobacter fetus	Yes	1	100.0	0	0	
Campylobacter jejuni	Yes	1	100.0	0	0	
Clostridium perfringens	Yes	0	0	1	100.0	
Corynebacterium striatum	Yes	1	100.0	0	0	
Enterobacter spp.	Yes	1	100.0	0	0	
Enterococcus avium	Yes	0		1	100.0	
Helicobacter cinaedi	Yes	1	100.0	0	0	
Nocardia farcinica	Yes	1	100.0	0	0	
Oligella urethralis	Yes	1	100.0	0	0	
Pantoea agglomerans	Yes	1	100.0	0	0	
Proteus vulgaris	Yes	1	100.0	0	0	
Sphingomonas paucimobilis	Yes	1	100.0	0	0	
Streptococcus constellatus	Yes	1	100.0	0	0	
Streptococcus gallinarum	Yes	1	100.0	0	0	
Streptococcus sanguinis	Yes	1	100.0	0	0	
Turicella otitidis	Yes	1	100.0	0	0	
Veillonella parvula	Yes	0	0	1	100.0	

Table 4
Multiple Binary logistic regression model findings on community-onset bacteremia in predicting mortality.

Risk factors	Risk	Reference	*P*	OR	90% CI for OR	
					Lower	Upper
Gender	Female	Male	0.082	1.524	0.948	2.448
Pneumonia	Yes	No	0.031	2.133	1.073	4.243
Bacteremia of unknown origin	Yes	No	0.005	2.146	1.264	3.642
Urinary catheter	Yes	No	0.060	1.641	0.978	2.754
Staphylococcus aureus	Yes	No	0.007	2.526	1.286	4.960
Escherichia coli	No	Yes	0.050	1.727	0.986	3.024
SOFA score[a]	≥5	<5	0.001	4.245	2.573	7.005
Platelet count (/μL)[a]	<50,000	≥50,000	0.005	3.414	1.459	7.989
MAP[a]	≤65	>65	0.082	1.966	.917	4.213
CCI score[a]	–	–	0.002	1.156	1.054	1.267
Katz Index	–	–	0.001	0.704	0.625	0.792
Constant			0.001	0.033		

[a] The day when blood cultures are taken, Katz Index: Independence score in activities of daily living; CCI: Charlson Comorbidity Index.

Table 5
Susceptibility profiles of common pathogens to frequently used antibiotics.

Gram negatives	CRO	TZP	MEM	CIP	GN	COL	TGC	SXT
E. coli (n = 196)	85/167[a]	132/164	176/181	65/186	157/183	17/18	69/74	98/184
	50.9%	80.0%	97.2%	34.9%	85.8%	94.4%	93.2%	53.3%
K. pneumoniae (n = 79)	26/69	24/57	41/63	30/74	42/73	17/20	8/9	32/71
	37.7%	42.1%	65.1%	40.5%	57.5%	85%	88.9%	45.1%
A. baumannii (n = 7)	0/7	0/7	1/6	0/7	3/7	1/1	NA	1/7
	0%	0%	16.7%	0%	42.9%	100%		14.3%
P. aeruginosa (n = 20)	NA	3/17	14/17	2/18	12/19	1/1	NA	NA
		17.6%	82.4%	11.1%	63.2%	100%		
Gram positives	**FOX/OX**	**VAN**	**LZD**	**CLI**	**GN**	**TET**	**DAP**	**SXT**
S. aureus (n = 86)	54/83	65/65	51/51	52/72	34/43	41/46	25/25	66/70
	65.1%	100%	100%	72.2%	79.1%	89.1%	100%	94.3%
CNS (n = 50)	21/50	43/43	33/35	18/43	20/29	14/33	18/23	30/43
	42.0%	100%	94.3%	41.9%	69.0%	42.4%	78.3%	69.8%
E. faecium (n = 15)	NA	13/15	13/13	NA	5/10	NA	NA	NA
		86.7%	100.0%		50.0%			
E. faecalis (n = 37)	NA	30/30	29/29	NA	11/20	NA	NA	NA
		100.0%	100.0%		55.0%			
S. pneumoniae (n = 12)	NA	10/10	7/8	5/11	1/3	1/5	NA	2/6
		100.0%	87.5%	45.5%	33.3%	20.0%		33.3%
Streptococci (n = 32)	NA	20/21	12/12	14/22	4/4	NA	NA	NA
		95.2%	100.0%	63.7%	100.0%			

CIP: ciprofloxacin; CLI: clindamycin; CNS: Coagulase negative staphylococcus; COL: colistin; CRO: ceftriaxone; DAP: Daptomycin; FOX: cefoxitin; GN: gentamicin; LZD: linezolid; MEM: meropenem; NA: not applicable; OX: oxacillin; SXT: trimethoprim-sulfamethoxazole; TET: tetracycline; TGC: tigecycline; TPZ: piperacillin-tazobactam; VAN: vancomycin.
[a] Susceptible/tested.

ters, a SOFA score ≥5, and platelet count <50,000/μL reflecting thrombocytopenia, were strongly associated with mortality [16]. Furthermore, higher CCI scores, reflecting greater comorbidity burden, were associated with increased mortality, whereas higher Katz ADL Index scores, indicating more independence in daily activities, were protective. Moreover, our data revealed substantial antimicrobial resistance, with methicillin resistance observed in one-third of *S. aureus* isolates and over half of coagulase-negative staphylococci. Vancomycin resistance in *E. faecium* was 13.3%. Meropenem resistance rates were 34.9%, 83.3%, and 17.6% among *K. pneumoniae, A. baumannii*, and *P. aeruginosa* isolates, respectively, indicating a considerable burden for the management of these infections.

Contrary to previous studies that reported higher sepsis mortality in men [17,18], our findings suggested a non-significant trend toward increased mortality among women. Accordingly, after adjustment for other variables age was not a strong independent predictor of mortality. Rather, poor functional status, comorbidities, and severe infection were significantly associated with higher infection-related mortality in this study. According to our data, patients with more severe underlying conditions as indicated by higher CCI scores and those with greater illness severity, reflected by an elevated SOFA score of 5 or above, had higher risks for death. Conversely, better functional status, as measured by a higher Katz ADL Index score, was associated with a reduced risk of mortality. Moreover, consistent with earlier research [19], platelet counts less than 50,000 were associated with increased mortality in BSIs. Thus, these findings likely reflect greater infection severity or impending sepsis, rather than acting as independent predictors beyond chronological age. Consequently, our findings underscore the pivotal influence of baseline health status and acute illness severity on mortality outcomes among older adults with CA-BSIs rather than the age.

The literature demonstrates a predominance of Gram-negative bacteria over Gram-positive bacteria in the older adult population, consistent with the shift toward Gram-negative pathogens observed, particularly in females [20,21]. In our study, three-fifths of the identified causative agents were Gram-negative bacteria and two-fifths were Gram-positives, indicating that Gram-negative organisms continue to predominate in community-onset BSIs among older adults. *E. coli* was the most common pathogen detected in one-third of the patients followed by *S. aureus, K. pneumoniae*, Coagulase-negative Staphylococci, and *P. aeruginosa* in descending order. Previous reports indicate that *E. coli* bacteremia is associated with a favorable prognosis among both immunocompetent [22] and immunocompromised [23] patients. A similar trend was observed in our study of older adults with CA-BSIs, although it did

not reach statistical significance. In contrast, *S. aureus*, the second most common cause of CA-BSI, demonstrates significantly higher mortality in older adults, with approximately one-third of isolates resistant to methicillin, requiring anti-Gram-positive agents such as glycopeptides. It was reported that older adults faced a threefold higher risk of death from MRSA bacteremia compared with younger adults [24] with adults over 80 exhibiting the greatest vulnerability [25]. Early evidence also indicates the occurrence of community-onset MRSA outbreaks in Europe [26]. Consequently, *S. aureus*, and MRSA in particular, remains a frequent pathogen in older adults, underscoring the importance of careful antimicrobial management. On the other hand, *S. pneumoniae*, once famously called "the captain of the men of death" by Sir William Osler [27], was identified in fewer than 2% of CA-BSI cases. Pneumococcal bacteremia now appears to be a rare occurrence in older adults, likely due to the widespread availability of pneumococcal vaccination [28]. Additionally, as the study was conducted during the summer months (June-September), seasonal bias may have been introduced, potentially leading to underrepresentation of respiratory pathogens that are more prevalent in winter, such as *S. pneumoniae*.

In this study, the most common underlying infections as the possible sources of CA-BSI were urinary tract infections followed by pneumonia, intra-abdominal infections, and skin and soft tissue infections. A previous study reported that, among elderly patients hospitalized with urinary tract infections, the presence or absence of bacteremia did not affect outcomes such as in-hospital mortality or length of stay [29]. Accordingly, we could not show the effect of urinary tract infections on mortality. In our study, pneumonia as the likely source of bacteremia was independently linked to higher mortality. This finding aligns with previous research showing that pneumonia-associated BSI was associated with significantly shorter survival than BSI without pneumonia [30]. Bacteremia of unknown origin accounted for approximately 29.5% of cases and was associated with high mortality in older adults. In routine medical practices bacteremia from an unknown course is not a rare entity [31]. Potential causes include undetected sources causing ineffective source control, unusual presentations that complicate early diagnosis, rapid disease progression, or early death that prevents the full diagnostic evaluation [9]. These findings highlight the importance of early clinical suspicion, prompt evaluation, and timely empiric therapy, along with efforts to identify and control the infection source [32].

According to our data, the susceptibility patterns showed that community-acquired Gram-negative BSIs, particularly *E. coli* and *K. pneumoniae*, have high resistance to ceftriaxone and ciprofloxacin, making these relatively unreliable for empiric therapy in many settings. Meropenem and gentamicin retain good activity and may be preferred when BSI is suspected. Although tigecycline has good *in vitro* activity, it is not a reliable choice in severe infections since clinical failure and development of septic shock were significantly higher with tigecycline [33]. For Gram-positive pathogens, *S. aureus* and CoNS remain uniformly susceptible to glycopeptides, supporting their use in empiric coverage when MRSA or MR-CoNS are a concern. Overall, empiric therapy should prioritize agents with reliable activity such as carbapenems for severe Gram-negative infections and vancomycin or linezolid for severe Gram-positive coverage until culture results allow for targeted treatment.

Although the univariate analysis showed that guided treatment decreased mortality, we could not disclose the efficacy of either empirical or guided treatment in the final multivariate model. The lack of significant differences in the efficacy of empirical treatment strategies (none, monotherapy, or combination therapy) and guided therapeutic approaches (appropriate empirical therapy, necessary modification, or unnecessary escalation) for BSIs in older adults are likely influenced by several overlapping clinical factors. Advanced frailty, multimorbidity, and pre-existing organ dysfunction often dominate outcomes regardless of antibiotic strategy, while atypical presentations and cognitive impairment frequently delay diagnosis and limit the potential impact of timely treatment. In addition, challenges in achieving effective source control, the high prevalence of multidrug-resistant organisms like MRSA, variability in dosing or administration, and confounding by indication, where sicker patients receive more intensive therapy, may have all obscured true treatment effects.

This study has several limitations. First, it was not population-based, and although centers were encouraged to enroll consecutive eligible patients, variations in case ascertainment across sites may have introduced selection bias. Another limitation of this study is the absence of systematically collected data on vasopressor use and oxygen support across participating centers, largely due to variability in clinical practices. Instead, surrogate indicators of disease severity such as the SOFA score, platelet count, and MAP were used in the analysis. Another constraint of the study is the short follow-up period, which was restricted to 30 days. Moreover, detailed pathogen-specific resistance profiles (e.g., carbapenem-resistant Enterobacterales, vancomycin-resistant Enterococci, MRSA, and MR-CNS) were not incorporated as independent variables in the model. Instead, treatment adequacy was assessed based on receipt of at least one antimicrobial agent with confirmed *in vitro* activity according to AST results, which may not fully capture the differential impact of specific resistance mechanisms on clinical outcomes. But the strengths of our study included its prospective and multicenter design, and the large number of cases analyzed. Additionally, the statistical model demonstrated good performance, correctly identifying 91.1% of survivors and 55.1% of non-survivors.

Conclusion

In conclusion, our study found that mortality in older adults with CA-BSIs was influenced by multiple factors, including clinical indicators such as elevated SOFA scores, thrombocytopenia, and a high comorbidity burden; the causative pathogen; the type and identification of the underlying infection; and poorer functional status. These findings underscore the importance of early risk stratification and comprehensive clinical assessment in this vulnerable population.

Data availability

The data presented in this study are available on request from the corresponding author.

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Author contributions

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Ethical approval

The study was approved by the Ethics Committee of Haydarpaşa Numune Training and Research Hospital, University of Health Sciences, Istanbul (approval no: 67, dated 13 May 2024).

Declaration of competing interest

The authors have no competing interests to declare.

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