

Central Line-Associated Bloodstream Infection in Hospitalized Children: A Retrospective Cohort Study of Risk, Mortality, and Antimicrobial Resistance

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Abstract

Background

Central line-associated bloodstream infection (CLABSI) remains an important complication of central venous catheter use in children, particularly where antimicrobial resistance limits treatment options. We evaluated patient-level CLABSI risk, mortality-associated factors, bloodstream-isolate distribution, time to documented culture negativity, and multidrug resistance (MDR) in a mixed-ward pediatric cohort.

Methods

This retrospective cohort included hospitalized children younger than 18 years with central venous catheters at a tertiary pediatric referral hospital in Tehran, Iran, from 2021 to 2024. Modified Poisson regression estimated adjusted risk ratios for CLABSI. Among children with CLABSI, Firth penalized logistic regression evaluated mortality-associated factors, with bootstrap internal validation. Microbiological and resistance analyses were conducted at patient and isolate levels.

Results

Among 723 eligible children, 182 (25.2%) had at least one CLABSI and 128 (17.7%) died in hospital. Mortality among children with CLABSI was 22.0%. Compared with the PICU/general ICU, CLABSI risk was higher in the cardiac ICU/open-heart ICU (adjusted risk ratio [aRR], 1.35; 95% CI, 1.00–1.82) and lower in transplant/oncology (aRR, 0.57; 95% CI, 0.37–0.88). Femoral catheter placement (adjusted odds ratio [aOR], 3.04; 95% CI, 1.37–6.82) and each halving of platelet count (aOR, 1.51; 95% CI, 1.20–1.94) were associated with mortality. *Klebsiella* and *Staphylococcus epidermidis* predominated. MDR was detected in 82.0% of assessable children. Time to documented culture negativity differed across organism groups ($P = 0.002$).

Conclusions

CLABSI was common, and children with CLABSI had substantial in-hospital mortality and frequent antimicrobial resistance. Ward-specific surveillance, careful femoral-line use, early assessment of thrombocytopenia, and locally informed antimicrobial stewardship are priorities.

Background

Central venous catheters (CVCs) are indispensable in contemporary pediatric care, providing reliable access for vasoactive medications, antimicrobial therapy, parenteral nutrition, hemodynamic support, and prolonged treatment in critically ill, oncologic, surgical, and medically complex children. Their use, however, creates a direct pathway for bloodstream infection. Central line-associated bloodstream

infection (CLABSI) remains an important and potentially preventable healthcare-associated complication, with consequences that include clinical deterioration, prolonged hospitalization, additional antimicrobial exposure, increased resource use, and death [1, 2]. These consequences are particularly important in children, whose underlying diseases, vascular-access requirements, and physiological reserves differ substantially from those of adults.

The risk of CLABSI is not uniform across pediatric populations. It reflects the interaction of patient vulnerability, underlying disease, catheter type and duration, insertion circumstances, admission setting, and line-maintenance practices. Studies in pediatric intensive care have identified prolonged catheter exposure, parenteral nutrition, multiple catheters, transfusion, and selected chronic conditions as relevant risk markers, while the magnitude and composition of risk vary across intensive care, cardiac, neonatal, oncology, transplant, medical, and surgical settings [3–5]. Insertion and maintenance bundles have reduced CLABSI rates in many hospitals, but incomplete implementation and persistent between-center variation indicate that prevention cannot rely on uniform assumptions about risk [6–8]. Locally derived patient-level evidence is therefore needed to identify where preventive attention may be most useful within heterogeneous pediatric services.

The clinical importance of CLABSI also depends on the causative organism and its antimicrobial susceptibility. Gram-positive organisms associated with skin flora and biofilm formation remain prominent in catheter-related infection, whereas Gram-negative bacteria and fungi may present distinct therapeutic and source-control challenges. Antimicrobial resistance can narrow empirical treatment options, delay delivery of active therapy, complicate catheter management, and increase the need for coordinated microbiological surveillance and antimicrobial stewardship. Evidence from low- and middle-income countries shows marked regional variation in pediatric bloodstream pathogens and frequent resistance among Gram-negative isolates, yet surveillance remains uneven and many healthcare settings are underrepresented [9, 10]. Relatively few pediatric studies from the Middle East and comparable resource-constrained settings have examined patient-level CLABSI risk, mortality-associated factors, clinical characteristics, organism distribution, time to documented culture negativity, and multidrug resistance (MDR) within a single mixed-ward cohort.

This study therefore evaluated demographic and admission-ward factors associated with patient-level CLABSI risk among hospitalized children with CVCs. Among children with CLABSI, it also examined clinical, catheter-related, microbiological, and laboratory factors associated with in-hospital mortality using a parsimonious, internally validated analysis. Additional objectives were to characterize the distribution of bacterial and fungal bloodstream isolates, describe time to documented culture negativity, and quantify key antimicrobial non-susceptibility phenotypes and patient-level MDR prevalence.

Methods

Study design and setting

This retrospective, single-center observational cohort study was conducted at the Children's Medical Center of Tehran University of Medical Sciences, a tertiary pediatric referral hospital in Tehran, Iran, from January 2021 through December 2024. The hospital provides intensive, cardiac, neonatal, oncologic, transplant, medical, and surgical pediatric services. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology guidance [11].

Participants and analytical units

The source population comprised hospitalized children younger than 18 years who had a central venous catheter during the study period. Neonates and children younger than 1 month were eligible. Records with a documented age of 18 years or older were excluded. Cultures obtained before the catheter had satisfied the prespecified infection-eligibility interval were not classified as CLABSI.

The unique child was the primary analytical unit. Each child contributed once to the patient-level cohort and was classified as having CLABSI if at least one eligible CLABSI record was identified. The mortality analysis was restricted to children with CLABSI, with one index patient-level record retained per child. For children with repeated eligible records, the index record was selected according to the lowest recorded age in months, followed by the shortest admission-to-culture interval and, when ties remained, the original record order. The analysis of time to documented culture negativity was also performed at the patient level using the selected index infection record. Organism distribution and antimicrobial-susceptibility analyses were conducted at the isolate-record level. Repeated eligible isolates from the same child were retained in these descriptive analyses. Patient-level MDR prevalence was the primary resistance analysis. The first MDR-eligible isolate per child was used in a sensitivity analysis, while all eligible isolate records were retained in a secondary descriptive analysis.

Definitions and outcomes

A CVC was defined as an intravascular catheter terminating at or near the heart or in a major vessel and used for infusion, withdrawal of blood, or hemodynamic monitoring. CLABSI was identified using an operational definition adapted from the Centers for Disease Control and Prevention/National Healthcare Safety Network surveillance framework [12]. To be eligible, the positive blood culture had to occur at least 48 hours after catheter insertion. An event was considered eligible when a recognized bloodstream pathogen was isolated from at least one blood culture or when the same common commensal was recovered from at least two separately collected blood cultures within 48 hours, with no documented alternative source explaining the bloodstream isolate.

The primary infection outcome was binary patient-level CLABSI status. Because central-line days and person-time denominators were unavailable, the outcome was expressed as patient-level occurrence or risk rather than incidence density. The secondary clinical outcome was all-cause in-hospital death during the index hospitalization.

Time to documented culture negativity was defined as the interval between the initial positive bloodstream culture and the first subsequently documented negative blood culture in the index CLABSI episode. The original interval was recorded in hours and converted to days by division by 24. This post-infection outcome was analyzed descriptively and was not included as a baseline mortality predictor. Comparisons among Gram-positive bacteria, Gram-negative bacteria, and fungi were exploratory because biological clearance patterns and follow-up culture practices may differ across these groups.

Data collection and quality assurance

Demographic, admission, catheter-related, clinical, laboratory, microbiological, and outcome data were abstracted from routinely collected hospital and laboratory records. Variables included age, sex, admission ward, underlying disease, catheter insertion setting and site, intervals from admission and catheter insertion to positive culture, mechanical ventilation, inotropic support, laboratory measurements around infection recognition, organism identification, antimicrobial-susceptibility results, and in-hospital outcome. Age was categorized as younger than 1 year, 1–4 years, 5–11 years, and 12–17 years. Admission wards were grouped as PICU/general ICU, cardiac ICU/open-heart ICU, transplant/oncology, NICU/neonatal open-heart ICU, general medical wards, and surgical ward.

Data-quality procedures included duplicate-identifier, range, plausibility, temporal-consistency, laboratory-consistency, and susceptibility-coding checks. Documented transcription or unit errors were corrected according to predefined audit rules; unresolved impossible values were set to missing, whereas clinically plausible extreme values were retained. Five initially missing mortality outcomes were resolved as alive after source-record review and were treated as data corrections rather than imputations. Analyses used available complete observations for the variables included in each model; multiple imputation was not performed.

Microbiological and antimicrobial-resistance analyses

Organism identification and antimicrobial-susceptibility results were obtained from microbiology records. Laboratory interpretations were accepted as recorded because minimum inhibitory concentrations, inhibition-zone diameters, and the exact breakpoint edition were unavailable. Results were classified as susceptible, intermediate, or resistant; intermediate and resistant categories were combined as non-susceptible. Each organism–antibiotic proportion used only isolates for which the relevant agent had been tested. Detailed table and heatmap cells were restricted to combinations with at least five tested isolates, and exact binomial 95% confidence intervals were calculated for principal proportions.

Prespecified phenotypes included third-generation cephalosporin non-susceptibility among Enterobacterales; carbapenem non-susceptibility among Enterobacterales, *Klebsiella*, *Pseudomonas*, and *Acinetobacter*; oxacillin resistance among coagulase-negative staphylococci; vancomycin non-

susceptibility among *Enterococcus*; and trimethoprim–sulfamethoxazole non-susceptibility among *Stenotrophomonas*.

MDR was defined as non-susceptibility to at least one agent in at least three evaluable antimicrobial categories, following the framework proposed by Magiorakos et al [13]. A *Staphylococcus aureus* isolate was classified as MDR if it met the three-category MDR definition or was recorded as oxacillin resistant, consistent with the predefined MRSA rule. An isolate or patient was considered assessable only when the observed testing panel permitted classification under the organism-specific rules. “MDR not detected” indicated that MDR was not demonstrated within the observed evaluable panel and did not imply complete susceptibility. Isolates with insufficient category coverage were classified as not classifiable and were excluded from the assessable MDR denominator. Extensively drug-resistant and pandrug-resistant classifications were not calculated because category coverage was incomplete. Fungal isolates were excluded from the bacterial MDR framework.

Statistical analysis

Categorical variables were summarized as counts and percentages and continuous variables as medians and interquartile ranges. All tests were two-sided, with a significance level of 0.05.

Patient-level CLABSI status was analyzed using modified Poisson regression with a log link and HC0 robust standard errors to estimate adjusted risk ratios directly [14]. The prespecified model included sex, four-level age group, and six-level admission ward, with male sex, infancy, and PICU/general ICU as reference categories. Robust Wald tests evaluated multi-category variables. Standardized adjusted risks and 95% confidence intervals for age and ward categories were obtained through marginal standardization.

The mortality analysis was restricted to unique children with CLABSI. Because the number of deaths and several covariate patterns were limited, Firth penalized logistic regression was used to reduce sparse-data bias and separation-related instability [15]. The primary model included age per 5-year increase, sex, oncologic/hematologic/immunologic disease versus other conditions, femoral versus non-femoral catheter site, Gram-negative versus other organisms, and platelet count. Platelet count was transformed as the negative base-2 logarithm so that a one-unit increase represented a halving of the platelet count. Mechanical ventilation and inotropic support were excluded from the primary model because their timing relative to infection onset was unavailable. A secondary augmented model incorporated concurrent mechanical ventilation and inotropic support as a recorded severity marker.

Model performance was internally evaluated using 500 bootstrap resamples. Optimism-corrected area under the receiver operating characteristic curve, Brier score, and calibration slope were calculated, and bootstrap distributions were used to assess coefficient stability and consistency of effect direction [16].

Exploratory continuous clinical and laboratory variables were compared between survivors and nonsurvivors using Wilcoxon rank-sum tests with rank-biserial correlations. Holm adjustment was

applied for multiple comparisons. Separate age- and sex-adjusted Firth models were fitted for each variable, with effects expressed using clinically interpretable units specified in Supplementary Table S3.

Time to documented culture negativity was summarized using medians and interquartile ranges. The Kruskal–Wallis test compared organism groups, and the Wilcoxon rank-sum test compared survival groups. Resistance and MDR proportions were accompanied by exact binomial confidence intervals. The exploratory association between patient-level MDR status and mortality was evaluated using Fisher's exact test and an unadjusted odds ratio with a 95% confidence interval.

Analyses were performed in R version 4.6.0 using the sandwich, lmtest, logistf, emmeans, boot, and ggplot2 packages.

Use of generative artificial intelligence

Grammarly was used to support English-language editing, including grammar, spelling, clarity, and readability. All scientific content, analyses, numerical results, references, interpretations, and final manuscript text were reviewed and verified by the authors. Grammarly did not make autonomous scientific decisions and is not listed as an author.

Results

Study cohort and patient-level outcomes

The source dataset contained 724 unique patient identifiers. One patient with a recorded age of 228 months was excluded because the age exceeded the prespecified pediatric range, leaving 723 eligible children. Neonates and children younger than 1 month were retained. The median age was 24 months (IQR, 7–72), and 424 children (58.6%) were male. Overall, 182 of 723 children had at least one eligible CLABSI, corresponding to a patient-level proportion of 25.2%, while 541 had no eligible infection. In-hospital death occurred in 128 children (17.7%): 40 of 182 children with CLABSI (22.0%) and 88 of 541 children without CLABSI (16.3%) (Table 1).

Table 1
Characteristics, CLABSI, and in-hospital mortality among eligible children

Characteristic	Category	Total, n	CLABSI, n (%)	In-hospital deaths, n (%)
Overall	All eligible children	723	182 (25.2%)	128 (17.7%)
Sex	Male	424	108 (25.5%)	80 (18.9%)
	Female	299	74 (24.7%)	48 (16.1%)
Age group	Infant (< 1 year)	237	74 (31.2%)	38 (16.0%)
	Young child (1–4 years)	248	56 (22.6%)	45 (18.1%)
	Child (5–11 years)	173	43 (24.9%)	32 (18.5%)
	Adolescent (12–17 years)	65	9 (13.8%)	13 (20.0%)
Admission ward	PICU/general ICU	315	80 (25.4%)	88 (27.9%)
	Cardiac ICU/open-heart ICU	130	46 (35.4%)	21 (16.2%)
	Transplant/oncology	175	25 (14.3%)	14 (8.0%)
	NICU/neonatal open-heart ICU	57	14 (24.6%)	3 (5.3%)
	General medical wards	38	12 (31.6%)	1 (2.6%)
	Surgical ward	8	5 (62.5%)	1 (12.5%)
<i>Note. Values are n or n (%). Infection and mortality are reported at the patient level.</i>				

The patient-level CLABSI proportions were 25.4% in the PICU/general ICU, 35.4% in the cardiac ICU/open-heart ICU, 14.3% in transplant/oncology, 24.6% in the NICU/neonatal open-heart ICU, 31.6% in general medical wards, and 62.5% in the surgical ward. The surgical estimate was based on eight children.

Detailed infection and mortality proportions with exact confidence intervals are presented in Supplementary Table S1 in Additional file 1.

Characteristics of children with CLABSI

Among the 182 children with CLABSI, 142 survived and 40 died during hospitalization. Compared with survivors, children who died had longer median intervals from catheter insertion to positive culture [13.0 days (IQR, 7.0–23.0) versus 10.0 days (IQR, 6.0–16.0)] and from admission to positive culture [26.0 days (IQR, 18.5–42.0) versus 17.5 days (IQR, 10.0–30.0)]. Median platelet count was lower among children who died [$71 \times 10^3/\text{mm}^3$ (IQR, 31–186) versus $178 \times 10^3/\text{mm}^3$ (IQR, 76–316)]. Femoral catheters were present in 19 of 40 children who died (47.5%) and 31 of 142 survivors (21.8%), while concurrent mechanical ventilation and inotropic support was recorded in 33 deaths (82.5%) and 45 survivors (31.7%). Gram-negative organisms were identified in 65.0% of children who died and 54.9% of survivors (Table 2).

Table 2
Selected characteristics of children with CLABSI according to in-hospital survival

Characteristic	Overall (N = 182)	Survived (n = 142)	Died (n = 40)
Age, months	17.0 (5.0–60.0)	16.5 (5.0–61.0)	19.5 (4.0–60.0)
Catheter insertion to positive culture, days	11.0 (6.0–18.0)	10.0 (6.0–16.0)	13.0 (7.0–23.0)
Admission to positive culture, days	20.0 (11.0–35.0)	17.5 (10.0–30.0)	26.0 (18.5–42.0)
White blood cell count, cells/mm ³	8500 (5200–12900)	8900 (5250–13000)	6600 (3355–12400)
Platelet count, 10 ³ /mm ³	150 (59–299)	178 (76–316)	71 (31–186)
Hemoglobin, g/dL	9.6 (8.4–11.5)	9.8 (8.6–11.5)	9.4 (7.6–10.8)
Oncologic, hematologic, or immunologic disease	46 (25.3%)	33 (23.2%)	13 (32.5%)
Femoral catheter	50 (27.5%)	31 (21.8%)	19 (47.5%)
Gram-negative organism	104 (57.1%)	78 (54.9%)	26 (65.0%)
Concurrent mechanical ventilation and inotropic support	78 (42.9%)	45 (31.7%)	33 (82.5%)
<i>Note. Values are median (interquartile range) or n (%). The timing of organ support relative to infection onset was unavailable.</i>			

Detailed distributions by underlying disease, catheter insertion setting, catheter site, organ-support pattern, and organism group are provided in Supplementary Table S2. In exploratory laboratory analyses, platelet count was the only measure that retained evidence of association with mortality after Holm adjustment. Each halving of the platelet count was associated with higher odds of death in a separate age- and sex-adjusted model (OR, 1.62; 95% CI, 1.29–2.07; Holm-adjusted $P < 0.001$). Other laboratory measures did not retain evidence of association after multiplicity adjustment (Supplementary Table S3).

Factors associated with CLABSI and mortality

In the adjusted modified Poisson model, admission ward was associated with patient-level CLABSI risk (global robust Wald $P < 0.001$). Compared with the PICU/general ICU, risk was higher in the cardiac ICU/open-heart ICU (adjusted RR, 1.35; 95% CI, 1.00–1.82; $P = 0.047$) and lower in transplant/oncology (adjusted RR, 0.57; 95% CI, 0.37–0.88; $P = 0.012$). The surgical ward had an adjusted RR of 2.59 (95% CI, 1.48–4.52; $P < 0.001$), although this estimate was based on eight children. Sex and age group were not clearly associated with CLABSI risk (Table 3). Standardized adjusted risks by ward and age group are presented in Supplementary Figures S1 and S2, respectively, in Additional file 2.

In the primary Firth mortality model, femoral catheter placement was associated with higher odds of death (adjusted OR, 3.04; 95% CI, 1.37–6.82; $P = 0.006$), as was each halving of platelet count (adjusted OR, 1.51; 95% CI, 1.20–1.94; $P < 0.001$). Age, sex, underlying disease group, and Gram-negative infection were not clearly associated with mortality (Table 3). In the secondary augmented model, concurrent mechanical ventilation and inotropic support was associated with higher odds of death (adjusted OR, 15.60; 95% CI, 5.86–49.83; $P < 0.001$). Femoral catheter placement and platelet-count halving remained associated with mortality. Organ support was treated as a secondary recorded severity marker because its timing relative to infection onset was unavailable (Supplementary Figure S3).

All 500 bootstrap samples were completed. The optimism-corrected AUC, Brier score, and calibration slope were 0.708, 0.156, and 0.859 for the primary model and 0.851, 0.126, and 0.897 for the augmented model, respectively (Supplementary Table S4).

Microbiological findings and antimicrobial resistance

The microbiological analysis included 189 isolate records from 182 children. The leading organisms were *Klebsiella* (40/189, 21.2%), *Staphylococcus epidermidis* (37/189, 19.6%), *Candida* (22/189, 11.6%), *Pseudomonas* (20/189, 10.6%), *Serratia* (19/189, 10.1%), and *Enterococcus* (17/189, 9.0%) (Fig. 1).

Third-generation cephalosporin non-susceptibility was observed in 66 of 66 tested Enterobacterales isolates. Carbapenem non-susceptibility occurred in 36 of 64 Enterobacterales isolates (56.2%), including 29 of 37 *Klebsiella* isolates (78.4%), 10 of 20 *Pseudomonas* isolates (50.0%), and 8 of 10 *Acinetobacter* isolates (80.0%). Oxacillin resistance was recorded in 37 of 37 coagulase-negative staphylococcal isolates, and vancomycin non-susceptibility occurred in 13 of 16 *Enterococcus* isolates (81.2%). One of eight *Stenotrophomonas* isolates was non-susceptible to trimethoprim–sulfamethoxazole. Patient-level MDR prevalence was 82.0% among assessable children (Fig. 2). Detailed organism–antibiotic findings are provided in Supplementary Table S5.

Among 101 children with an MDR-eligible organism, 100 were assessable and one was not classifiable. MDR was detected in 82 of 100 assessable children (82.0%; 95% CI, 73.1%–89.0%). In the first-isolate analysis, MDR was identified in 62 of 67 Enterobacterales, 9 of 10 *Acinetobacter*, 8 of 19 *Pseudomonas*, and 3 of 4 *S. aureus* isolates. The all-isolate analysis identified MDR in 82 of 101 assessable records (81.2%). Mortality occurred in 21 of 82 children with MDR and 3 of 18 without detected MDR (unadjusted OR, 1.71; 95% CI, 0.42–10.14; $P = 0.550$), providing no statistically clear evidence of an association (Supplementary Table S6).

Time to documented culture negativity

Time to documented culture negativity was available for 16 of 20 children with fungal infections, 98 of 104 with Gram-negative infections, and all 58 with Gram-positive infections. Median times were 5.5 days (IQR, 4.0–7.0), 5.0 days (IQR, 4.0–6.0), and 3.0 days (IQR, 3.0–5.0), respectively (Kruskal–Wallis $P = 0.002$). The median was 4.0 days (IQR, 3.0–6.0) among survivors and 5.0 days (IQR, 3.0–6.0) among

children who died ($P = 0.756$) (Supplementary Table S7). Individual distributions are shown in Supplementary Figure S4. Full non-susceptibility matrices are presented in Supplementary Figures S5 and S6.

Discussion

Approximately one quarter of the children with central venous catheters experienced at least one central line-associated bloodstream infection (CLABSI), and more than one fifth of children with CLABSI died during hospitalization. Infection risk differed across admission wards, while femoral catheter placement and lower platelet count were associated with mortality in the primary adjusted analysis. The microbiological profile included Gram-negative bacteria, Gram-positive bacteria, and fungi, with frequent antimicrobial non-susceptibility and multidrug resistance (MDR). Time to documented culture negativity also varied by organism group. These findings describe a clinically complex population in which infection prevention, early recognition of deterioration, and selection of effective antimicrobial therapy are closely interconnected.

The observed 25.2% represents the proportion of children who developed at least one CLABSI and should not be equated with incidence rates expressed per 1,000 central-line days. Consequently, direct numerical comparison with most surveillance reports is limited. Differences among pediatric studies may reflect referral complexity, ward composition, duration and type of vascular access, line-use intensity, surveillance procedures, and prevention practices. Recent pediatric intensive care data continue to identify longer catheter exposure and specific clinical treatments as relevant risk markers even where prevention measures are well established [4]. Multicenter evidence also indicates that greater maintenance-bundle reliability is associated with lower CLABSI rates [8]. Line-days, utilization ratios, bundle adherence, staffing, and catheter-access frequency were unavailable in the present study, however, and cannot explain the observed variation directly.

The higher adjusted risk in the cardiac ICU/open-heart ICU is clinically plausible given the repeated procedures, prolonged intensive care, frequent vascular access, and physiological instability encountered in children with complex cardiac disease. Multicenter cardiac critical-care data have similarly shown that catheter exposure is concentrated in high-risk subgroups and that longer line duration is an important potentially modifiable factor [17]. Conversely, the lower adjusted risk in transplant/oncology should not be interpreted as a protective effect of that clinical setting. Specialized line-care procedures, differences in exposure time or surveillance, patient selection, and residual confounding may have contributed. The surgical-ward estimate was based on only eight children and therefore has limited precision and generalizability.

All-cause in-hospital mortality among children with CLABSI was 22.0%, but not every death can be attributed directly to CLABSI. Femoral catheter placement was associated with approximately threefold higher odds of mortality. This finding may reflect anatomical and maintenance-related factors, but femoral access may also be selected during urgent resuscitation or in patients with greater baseline instability. A pediatric surgical cohort likewise reported an association between femoral catheterization

and catheter-related bloodstream infection, although the clinical setting and outcome differed from those of the present analysis [18]. Confounding by indication and unmeasured illness severity therefore cannot be excluded.

Each halving of platelet count was associated with higher mortality. Thrombocytopenia may reflect systemic inflammation, coagulation activation, platelet consumption, organ dysfunction, hematologic disease, or the severity of sepsis rather than a direct causal pathway. Pediatric septic-shock studies have also associated low platelet counts with mortality, organ failure, transfusion requirements, and fewer intensive-care-free days [19]. In this cohort, platelet count was the only laboratory measure that retained evidence of association after correction for multiple exploratory comparisons, supporting further evaluation of platelet count as a routinely available severity marker rather than establishing it as a disease-specific prognostic test.

Concurrent mechanical ventilation and inotropic support had a strong association with mortality and improved the optimism-corrected discrimination of the augmented model. Its timing relative to infection onset was unknown, however. Organ support could have preceded the infection, represented contemporaneous physiological instability, or followed deterioration caused by infection or another complication. It was therefore appropriately treated as a secondary recorded severity marker rather than a baseline causal risk factor. The primary model showed moderate discrimination, whereas the augmented model performed better after inclusion of this marker. Both models underwent internal bootstrap correction only and should be viewed as analyses of prognostic structure, not as externally validated bedside prediction tools.

The organism distribution was consistent with the mixed case profile of a tertiary pediatric hospital. *Klebsiella* and other Gram-negative organisms were prominent, while *Staphylococcus epidermidis*, *Enterococcus*, and *Candida* also accounted for appreciable proportions. Earlier surveillance from the same Iranian referral environment similarly identified *Klebsiella*, *Serratia*, *Pseudomonas*, and other Gram-negative organisms as important causes of pediatric bloodstream infection [20, 21]. Coagulase-negative staphylococci remain relevant catheter-associated pathogens because of skin colonization and biofilm formation, although retrospective surveillance must carefully distinguish infection from contamination. The presence of *Candida* is also clinically credible in a population containing critically ill and immunocompromised children with prolonged catheter exposure; pediatric hematology cohorts have documented the particular importance of candidemia in children with hematologic disease and stem-cell transplantation [22]. These findings nevertheless represent one referral hospital and should not be regarded as nationally representative.

The recorded resistance patterns suggest that empirical and definitive treatment options may be limited in this setting. As recorded in the laboratory data, all tested Enterobacterales were non-susceptible to third-generation cephalosporins, and carbapenem non-susceptibility was frequent among *Klebsiella*, *Acinetobacter*, and *Pseudomonas*. Oxacillin resistance among coagulase-negative staphylococci and vancomycin non-susceptibility among *Enterococcus* were also common. High resistance among

pediatric bloodstream isolates has been reported previously in Iran and other resource-constrained settings, although the magnitude varies with organism selection, laboratory methods, and tested denominators [9, 20, 21, 23]. These patterns support empirical treatment policies informed by current local antibiograms, rapid review of culture results, prompt modification of inactive therapy, and stewardship measures intended to preserve effective last-line agents. Percentages in this study applied only to tested isolates; untested organism–antibiotic combinations cannot be presumed susceptible.

MDR was detected in 82.0% of assessable children, although classification depended on the antimicrobial categories represented in the recorded testing panel. “MDR not detected” therefore did not establish complete susceptibility, and one patient could not be classified. Mortality was numerically higher among children with MDR, but the confidence interval was wide and the small non-MDR group limited power. Pediatric studies have likewise produced inconsistent estimates of the relationship between resistance and mortality: some have reported poorer outcomes with resistant Gram-negative infection, whereas a large Japanese multicenter study found no statistically clear increase in all-cause mortality despite less frequent effective empirical coverage [24, 25]. Organism heterogeneity, underlying disease, severity, source control, and timing of active therapy may modify this relationship and were not sufficiently captured here.

The distribution of time to documented culture negativity differed across organism groups, with higher median values for Gram-negative and fungal infections than for Gram-positive infections. This exploratory global comparison should not be interpreted as evidence of pairwise differences or differential treatment effectiveness. Clearance depends on organism biology, biofilm formation, catheter removal, antimicrobial activity, immune status, source control, and the timing and frequency of follow-up cultures. Fungi were appropriately retained as a clinically distinct descriptive group, but candidemia has different management and surveillance practices from bacterial bloodstream infection. Missing clearance data were also proportionally more frequent among fungal infections.

Strengths of this study included the mixed-ward pediatric cohort, use of the unique child as the primary analytical unit, separation of patient- and isolate-level analyses, direct estimation of infection risk ratios, penalized mortality modeling, bootstrap internal validation, and detailed data auditing. The study was limited by its retrospective single-center design; absence of central-line days, utilization data, and prevention-process measures; residual confounding; sparse ward and organism subgroups; uncertain timing of organ support; use of all-cause mortality; nonuniform susceptibility panels and unavailable breakpoint editions; repeated isolates in descriptive analyses; missing culture-negativity observations; and lack of external validation. The findings support ward-specific surveillance, review of femoral-line use and maintenance, prompt assessment of thrombocytopenia and clinical deterioration, and regular updating of local antibiograms. Prospective multicenter studies using catheter-day denominators, standardized microbiological methods, treatment-timing data, and infection-prevention measures are needed.

Conclusions

In this mixed-ward pediatric cohort, one quarter of children with CVCs had at least one CLABSI, and in-hospital mortality among children with CLABSI was 22.0%. Femoral catheter placement and lower platelet count were associated with mortality, while antimicrobial non-susceptibility and MDR were frequent among assessable bacterial infections. Ward-specific surveillance, careful evaluation of femoral catheter use, and antimicrobial policies informed by current local susceptibility data may support prevention and management. Prospective multicenter studies using catheter-day denominators and standardized microbiological and infection-prevention data are needed.

Abbreviations

AUC

Area under the receiver operating characteristic curve

CI

Confidence interval

CLABSI

Central line-associated bloodstream infection

CVC

Central venous catheter

HCO

Heteroskedasticity-consistent type 0

ICU

Intensive care unit

IQR

Interquartile range

MDR

Multidrug resistance

MRSA

Methicillin-resistant *Staphylococcus aureus*

NICU

Neonatal intensive care unit

OR

Odds ratio

PICU

Pediatric intensive care unit

RR

Risk ratio

Declarations

Ethics approval and consent to participate

All methods were conducted in accordance with relevant institutional and national guidelines and regulations and with the ethical principles of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of the Children's Medical Center, Tehran University of Medical Sciences (approval code: IR.TUMS.CHMC.REC.1403.055). The requirement for informed consent to participate was waived by the same committee because the study involved the retrospective analysis of routinely collected clinical data.

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available because they contain potentially identifiable clinical information and are subject to institutional data-protection requirements. De-identified data may be available from the corresponding authors on reasonable request and following approval by the relevant institutional authorities.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HT contributed to study conceptualization and design, data collection and curation, formal analysis, and preparation of the initial manuscript. BP contributed to methodology, statistical interpretation, and critical revision of the manuscript. MS contributed to laboratory data acquisition, microbiological interpretation, and critical revision. RHS contributed to clinical data collection, data validation, and manuscript revision. MF contributed to study design, statistical analysis, interpretation of the findings, preparation of tables and figures, and drafting and revision of the manuscript. SM supervised the study, contributed to clinical interpretation, and critically revised the manuscript. All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work.

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Not applicable.

Authors' information

Not applicable.

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Table 3

Table 3 is available in the Supplementary Files section.

Figures

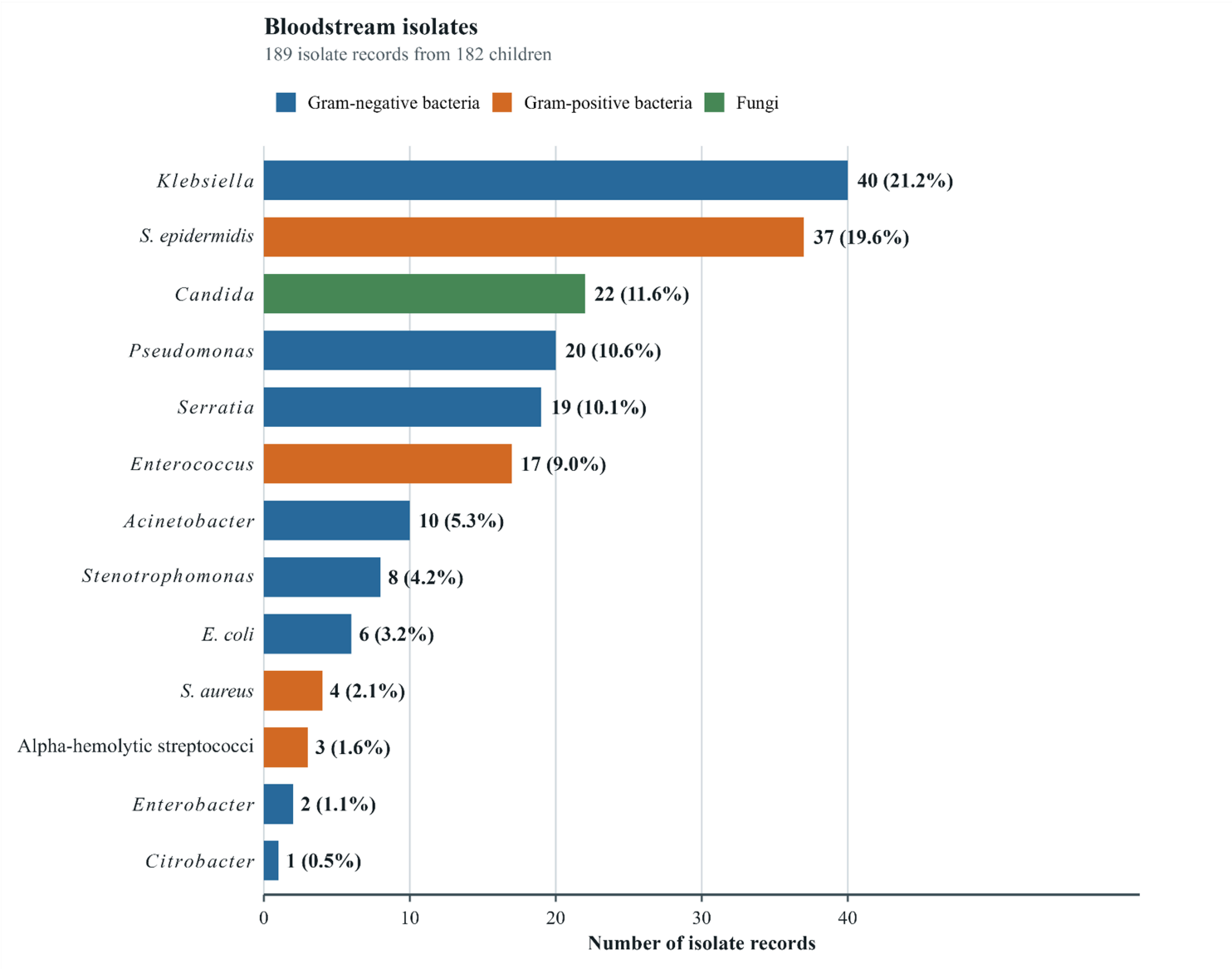


Figure 1

Distribution of bloodstream isolates. Bars show the number and percentage of 189 isolate records obtained from 182 children. Colours indicate Gram-negative bacteria, Gram-positive bacteria, and fungi.

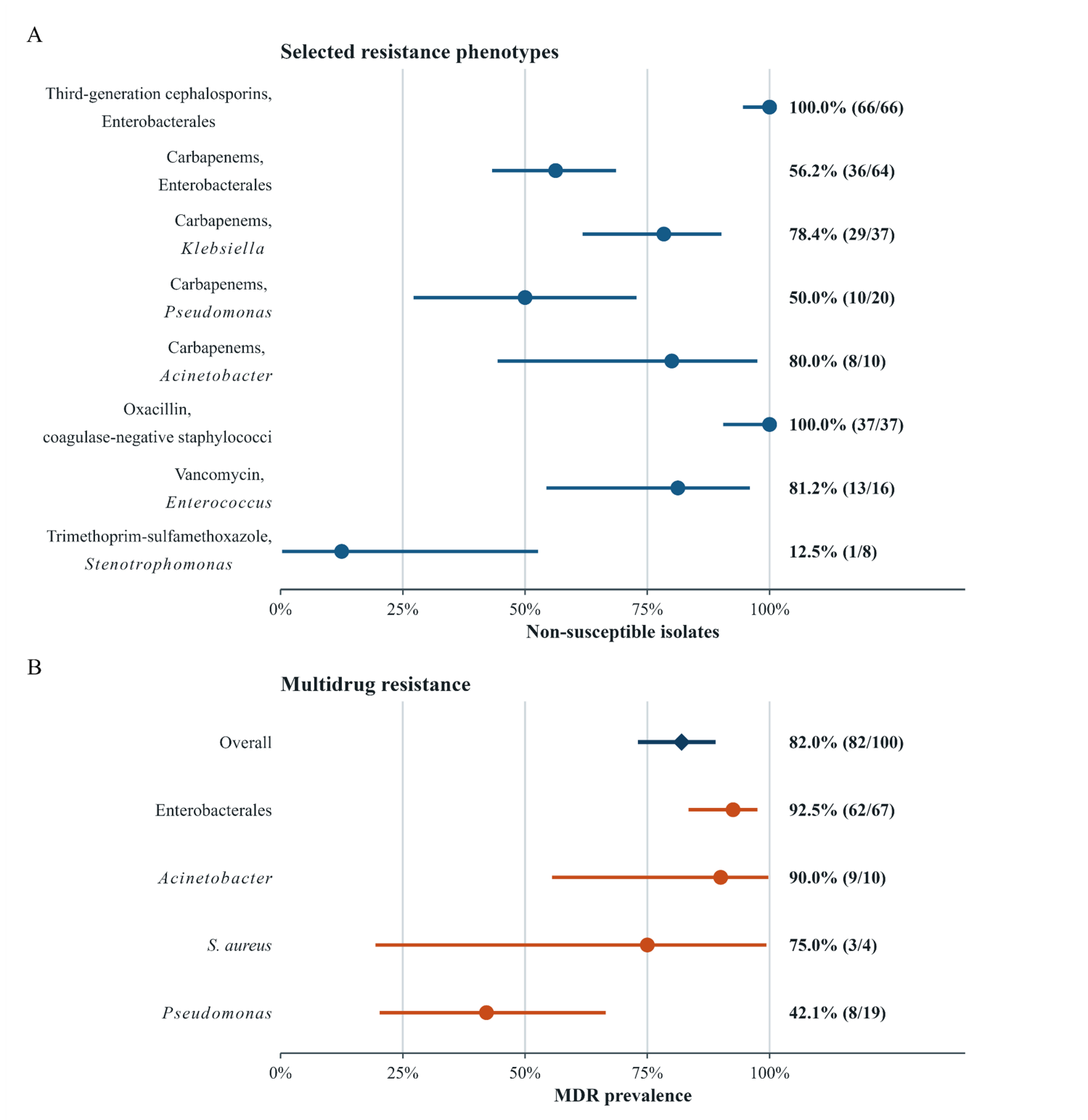


Figure 2

Key antimicrobial-resistance findings. (A) Selected organism-specific non-susceptibility phenotypes. (B) Multidrug-resistance prevalence among assessable patients and by organism group using the first MDR-eligible isolate per patient. Points show estimates, horizontal lines show exact 95% confidence intervals, and labels show percentages with numerators and denominators. MDR, multidrug resistance.

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