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BLOOD-CULTURE POSITIVITY, BACTERIAL ISOLATES AND EMPIRICAL-THERAPY CONCORDANCE IN ADULTS WITH SUSPECTED SEPSIS PRESENTING TO THE EMERGENCY DEPARTMENT OF A TERTIARY CARE HOSPITAL IN KARACHI

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Abstract

Objective: *To determine the blood-culture positivity rate and frequency distribution of clinically significant bacterial isolates among adults with suspected sepsis presenting to the emergency department (ED), and to describe empirical-therapy concordance.*

Study Design: *Descriptive cross-sectional study.*

Setting: *Emergency Department, Jinnah Postgraduate Medical Centre (JPMC), Karachi.*

Period: *December 2024 to March 2025 (four months).*

Material & Methods: *One hundred and eighty-two adults with suspected sepsis (acute SOFA ≥2) who had routine ED blood cultures were enrolled by non-probability purposive sampling. Episodes were classified as no growth, clinically significant bacteria, probable contaminant or yeast. Data were analysed in SPSS version 26 using exact binomial confidence intervals, chi-square/Fisher exact tests and binary logistic regression ($p < 0.05$).*

Results: *Mean age was 56.5 ± 17.0 years and 50.5% were female. Clinically significant bacteria were isolated in 68 patients, giving a positivity rate of 37.4% (95% CI 30.3–44.8%); the contamination rate was 2.7%. Of 70 isolates, 61.4% were Gram-negative. Staphylococcus aureus (30.0%), Klebsiella pneumoniae (18.6%) and Acinetobacter species (15.7%) predominated. Empirical therapy was concordant in 20 of 40 assessable patients (50.0%), and in only 42.9% of Gram-negative episodes. Diabetes (adjusted OR 0.46, 95% CI 0.23–0.94) and increasing age (adjusted OR 0.98 per year) were independently associated with lower culture positivity.*

Conclusion: *More than one-third of adults with suspected sepsis in our ED had culture-confirmed bacteraemia, predominantly Gram-negative, and half of assessable patients received discordant empirical therapy, supporting a locally derived ED antibiogram and stewardship-guided empirical regimens.*

INTRODUCTION

Sepsis is life-threatening organ dysfunction caused by a dysregulated host response to infection, and it remains one of the leading causes of death worldwide. The Global Burden of Disease Study estimated 166 million sepsis cases and 21.4 million sepsis-related deaths in 2021, with the heaviest burden in low- and middle-income countries.[1] International guidelines recommend that blood cultures be obtained before antimicrobials and that effective therapy be started within one hour in patients with probable sepsis or septic shock, because delay and inappropriate cover both increase mortality.[2]

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Antimicrobial resistance (AMR) now threatens this strategy: bacterial AMR was associated with 4.71 million deaths in 2021 and is projected to be associated with 8.22 million deaths annually by 2050.[3] *S. aureus*, *Escherichia coli* and *K. pneumoniae* are among the leading bacterial causes of death globally.[4] The World Health Organization reported in 2025 that one in six laboratory-confirmed bacterial infections was resistant to treatment, rising to one in three in the Eastern Mediterranean and South-East Asian Regions, and that more than 55% of *K. pneumoniae* isolates were resistant to third-generation cephalosporins.[5] Pakistani data mirror this picture. In 580 critically ill adults with suspected septicaemia, Zahra et al. reported blood-culture positivity of 29.4%, dominated by *K. pneumoniae* (31.8%), *Acinetobacter* species (23.8%) and *E. coli* (13.2%), with multidrug resistance in 86.7% of Gram-negative isolates.[6] A Karachi laboratory series found positivity of 36% and meropenem resistance of 85% in *Acinetobacter*.[7] In a Quetta intensive care unit, 91% of Gram-negative isolates produced extended-spectrum β-lactamase and 58% were carbapenem-resistant.[8] Extensively drug-resistant (XDR) *Salmonella* Typhi, which is resistant to ceftriaxone, is also now established in Pakistan.[9,10] However, most local series are laboratory-based and include all submitted cultures rather than a defined ED population with sepsis, and few report collection quality or whether the antibiotic given in the ED actually covered the organism isolated.[11,12] This matters because inappropriate empirical therapy roughly doubles the odds of death in bacteraemia.[13]

Empirical antibiotics for sepsis in our ED are chosen before culture results are available, and resistance patterns change over time and between hospitals. This study was therefore conducted to determine the blood-culture positivity rate and the frequency distribution of clinically significant bacterial isolates among adults with suspected sepsis presenting to the ED of JPMC, Karachi. Secondary aims were to describe blood-culture collection quality, empirical-therapy concordance and factors associated with culture positivity.

MATERIAL & METHODS

This descriptive cross-sectional study was conducted in the Emergency Department of Jinnah Postgraduate Medical Centre, Karachi, over four months from December 2024 to March 2025, after approval from the Research Evaluation Unit of the College of Physicians and Surgeons Pakistan and the institutional ethical review committee of JPMC. The sample size was calculated with the WHO formula for a single proportion using a blood-culture positivity of 29.4%,[6] 95% confidence and 7% absolute precision, giving 163 participants; after allowing 10% for incomplete records, 182 patients were enrolled by non-probability purposive sampling.

Inclusion criteria were age ≥18 years of either sex, suspected or documented infection with an acute increase of ≥2 points in the Sequential Organ Failure Assessment (SOFA) score at initial ED assessment (baseline assumed zero),[2] at least one blood-culture set collected in the ED as part of routine care, and written informed consent from the patient or a legally acceptable surrogate.

Exclusion criteria were trauma or burns as the principal reason for presentation, transfer after >48 hours of continuous admission elsewhere, blood culture collected only after ED transfer or >24 hours after the index assessment, repeat enrolment during the same illness, specimen rejection by the laboratory, and refusal or withdrawal of consent.

Data collection procedure: Trained ED residents recorded demographics, suspected source, comorbidities, antibiotic exposure in the preceding 30 days, hospital admission in the preceding 90 days, indwelling devices, initial vital signs, lactate, SOFA score and ED disposition on a structured proforma. Two blood-culture sets (aerobic and anaerobic bottles, 10 mL per bottle considered adequate) were drawn from separate peripheral venepuncture sites after skin and septum disinfection, and the timing relative to the first ED antibiotic was recorded. Cultures were processed in the JPMC Microbiology Laboratory, and isolates were identified and tested according to CLSI M100.[14] A recognised pathogen in any bottle was considered clinically significant; coagulase-negative staphylococci or other skin commensals grown from a single set without a device source were classified as probable contaminants after joint review by the microbiologist and ED consultant. Culture-positive bacterial sepsis was defined as at least one clinically significant bacterial isolate. Empirical therapy was considered concordant when every

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clinically significant isolate was reported susceptible to at least one antibacterial given in the ED, and not assessable when no empirical agent had been tested against an isolate.

Data analysis: Data were analysed using IBM SPSS Statistics version 26. Normality was assessed with the Shapiro-Wilk test; age, systolic blood pressure and temperature were normally distributed and reported as mean ± SD, and other continuous variables as median (interquartile range, IQR). Categorical variables were reported as frequencies and percentages. Blood-culture positivity was calculated for all 182 participants with an exact (Clopper-Pearson) 95% confidence interval (CI) and compared with the parent-study rate using an exact binomial test. Organism distribution used clinically significant isolates as the denominator, including both organisms from polymicrobial episodes. Groups were compared with the chi-square or Fisher exact (Fisher-Freeman-Halton for larger tables) test, the independent-samples t-test or the Mann-Whitney U test, and Kruskal-Wallis test as appropriate. Variables with $p < 0.20$ on univariate analysis were entered into a binary logistic regression model (Enter method), and results were expressed as odds ratios (OR) with 95% CI; model fit was assessed with the Hosmer-Lemeshow test and the area under the receiver-operating characteristic curve (AUC). Missing lactate values were not imputed. A two-sided p-value <0.05 was considered significant.

RESULTS

Of the 182 patients, 90 (49.5%) were male and 92 (50.5%) were female, with a mean age of 56.5 ± 17.0 years (range 18–92); 78 (42.9%) were older than 60 years. Suspected sources were evenly distributed, and 100 (54.9%) patients had at least one comorbidity, most often diabetes mellitus (31.9%). The median SOFA score was 4 (IQR 3–6), qSOFA was ≥2 in 86.3% and lactate was ≥4 mmol/L in 33 of 153 patients tested (21.6%). Eighteen patients (9.9%) died in the ED (Table-I).

Table-I. Demographic and clinical characteristics of patients with suspected sepsis (n=182)

Characteristic	n (%) / mean ± SD / median (IQR)
Age (years), mean ± SD	56.5 ± 17.0
Age group (years)	
18–40	33 (18.1)
41–60	71 (39.0)
>60	78 (42.9)
Female sex	92 (50.5)
Suspected source of infection	
Respiratory	31 (17.0)
Skin/soft tissue	31 (17.0)
Intra-abdominal	30 (16.5)
Urinary	28 (15.4)
Other	30 (16.5)
Unknown	32 (17.6)
Comorbidities*	
Diabetes mellitus	58 (31.9)
Chronic kidney disease	27 (14.8)
COPD	16 (8.8)
Liver disease	13 (7.1)

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Characteristic	n (%) / mean ± SD / median (IQR)
Malignancy	13 (7.1)
Immunosuppression	5 (2.7)
Any comorbidity	100 (54.9)
Antibiotic exposure in preceding 30 days	56 (30.8)
Hospital admission in preceding 90 days	36 (19.8)
Indwelling line/prosthetic device	28 (15.4)
SOFA score, median (IQR)	4 (3–6)
Systolic BP (mmHg), mean ± SD	102.1 ± 15.5
Lactate (mmol/L), median (IQR) (n=153)	3.2 (2.6–3.9)
qSOFA ≥2	157 (86.3)
Hypotension (SBP <90 mmHg)	41 (22.5)
Fever (≥38.0 °C)	112 (61.5)
ED disposition	
Ward	70 (38.5)
HDU/ICU	43 (23.6)
Transferred	29 (15.9)
Left against medical advice	22 (12.1)
Died in ED	18 (9.9)

**Multiple responses possible. BP: blood pressure; COPD: chronic obstructive pulmonary disease; SOFA: Sequential Organ Failure Assessment.*

Blood cultures were drawn before the first ED antibiotic in 127 (69.8%) patients, two sets were obtained in 143 (78.6%) and blood volume was adequate in 160 (87.9%); all three criteria were met in 85 (46.7%). The median time from arrival to the first antibiotic was 90.5 minutes (IQR 55.0–118.8), and only 56 (30.8%) patients received an antibiotic within one hour. Clinically significant bacteria were isolated in 68 patients, giving a blood-culture positivity rate of 37.4% (95% CI 30.3–44.8%), which was higher than the 29.4% reported in the parent study (exact binomial p = 0.022). Five episodes (2.7%) grew probable contaminants, all coagulase-negative staphylococci (Table-II).

Table-II. Blood-culture collection quality and final episode status (n=182)

Variable	n (%)	95% CI (%)
Collection quality		
Culture drawn before first ED antibiotic	127 (69.8)	
Two separately drawn sets	143 (78.6)	
Adequate blood volume (10 mL/bottle)	160 (87.9)	
All three criteria met	85 (46.7)	
First antibiotic within 1 hour of arrival	56 (30.8)	
Arrival to culture collection (min), median (IQR)	82.0 (43.5–109.2)	
Arrival to first antibiotic (min), median (IQR)	90.5 (55.0–118.8)	

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Variable	n (%)	95% CI (%)
Final episode status		
No growth	108 (59.3)	51.8–66.5
Clinically significant bacteria (positivity)	68 (37.4)	30.3–44.8
Probable contaminant	5 (2.7)	0.9–6.3
Yeast only	1 (0.5)	0.0–3.0
Polymicrobial (of 68 positives)	2 (2.9)	
Time to positivity (h), median (IQR)*	24.5 (15.5–34.5)	

*95% CI by the exact (Clopper-Pearson) method. *Culture-positive episodes (n=68).*

Seventy clinically significant isolates were recovered, including two polymicrobial episodes. Gram-negative bacteria accounted for 43 (61.4%) isolates and Gram-positive bacteria for 27 (38.6%). *S. aureus* was the single most frequent organism, followed by *K. pneumoniae* and *Acinetobacter* species; Enterobacterales together formed 40.0% of isolates (Table-III, Figure-1). The median time to positivity was 24.5 hours (IQR 15.5–34.5) and did not differ between Gram-positive and Gram-negative episodes (p = 0.529).

Table-III. Distribution of clinically significant bacterial isolates (n=70)

Organism	n (%)	95% CI (%)
Gram-negative	**43 (61.4)**	**49.0–72.8**
Klebsiella pneumoniae	13 (18.6)	10.3–29.7
Acinetobacter species	11 (15.7)	8.1–26.4
Escherichia coli	5 (7.1)	2.4–15.9
Enterobacter species	5 (7.1)	2.4–15.9
Salmonella Typhi	5 (7.1)	2.4–15.9
Pseudomonas aeruginosa	4 (5.7)	1.6–14.0
Gram-positive	**27 (38.6)**	**27.2–51.0**
Staphylococcus aureus	21 (30.0)	19.6–42.1
Coagulase-negative staphylococci*	5 (7.1)	2.4–15.9
Enterococcus faecalis	1 (1.4)	0.0–7.7
Organism group		
Enterobacterales	28 (40.0)	28.5–52.4
Non-fermenting Gram-negative bacilli	15 (21.4)	12.5–32.9

*Denominator is isolates; both organisms from the two polymicrobial episodes are counted. *Grown in ≥2 sets and adjudicated as pathogens.*

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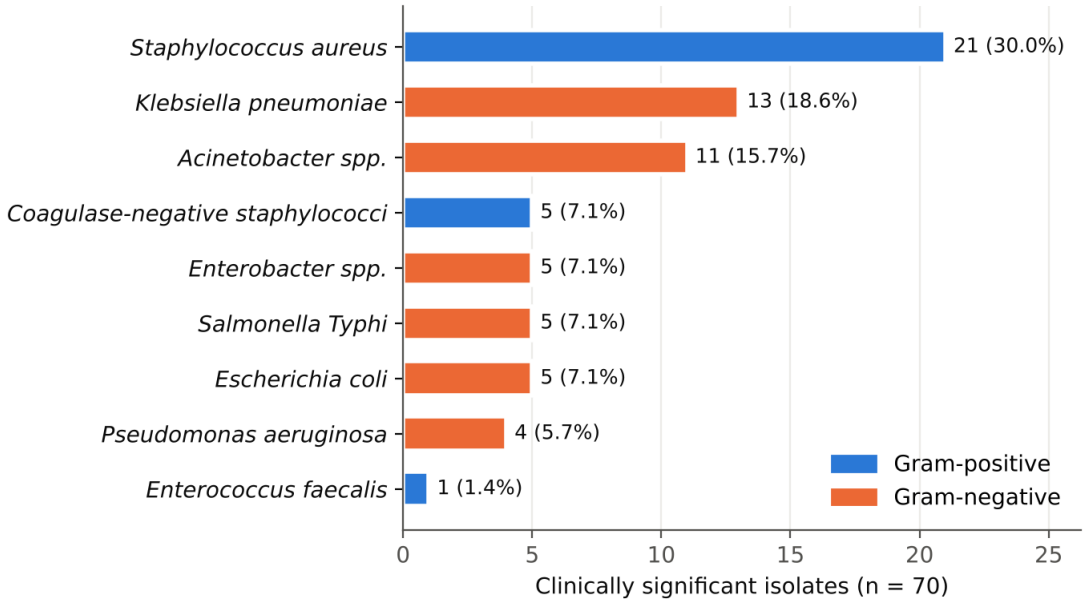


Figure-1. Distribution of clinically significant bacterial isolates (n=70)

Ceftriaxone (31.9%), piperacillin-tazobactam (25.8%) and meropenem (24.7%) were the commonest initial ED antibiotics, and vancomycin was added in 32 (17.6%) patients. Among the 68 culture-positive patients, concordance could be assessed in 40 (58.8%); in the remaining 28 no empirical agent had been tested against at least one isolate, including 16 of 19 monomicrobial *S. aureus* episodes. Empirical therapy was concordant in 20 of 40 assessable patients (50.0%; 95% CI 33.8–66.2%). Concordance was 100% in Gram-positive episodes but 42.9% in Gram-negative episodes (p = 0.047), and was lowest with ceftriaxone monotherapy (25.0%) (Table-IV, Figure-2).

Table-IV. Empirical-therapy concordance among assessable culture-positive patients (n=40)

Variable	n	Concordant n (%)	Discordant n (%)	p-value
Episode Gram category				**0.047[a]**
Gram-positive only	5	5 (100.0)	0 (0.0)	
Gram-negative only	35	15 (42.9)	20 (57.1)	
Organism group				**0.169[b]**
S. aureus	3	3 (100.0)	0 (0.0)	
Coagulase-negative staphylococci	1	1 (100.0)	0 (0.0)	
Enterobacterales	27	12 (44.4)	15 (55.6)	
Non-fermenters	8	3 (37.5)	5 (62.5)	
Polymicrobial	1	1 (100.0)	0 (0.0)	
Empirical regimen				**0.624[b]**
Ceftriaxone	8	2 (25.0)	6 (75.0)	
Piperacillin-tazobactam	14	7 (50.0)	7 (50.0)	
Meropenem	8	4 (50.0)	4 (50.0)	
Ceftriaxone + vancomycin	1	1 (100.0)	0 (0.0)	

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Variable	n	Concordant n (%)	Discordant n (%)	p-value
Piperacillin-tazobactam + vancomycin	6	4 (66.7)	2 (33.3)	
Meropenem + vancomycin	3	2 (66.7)	1 (33.3)	
Overall	**40**	**20 (50.0)**	**20 (50.0)**	

[a]Fisher exact test; [b]Fisher-Freeman-Halton exact test. Concordance was not assessable in 28 of 68 culture-positive patients (no empirical agent tested against at least one isolate).

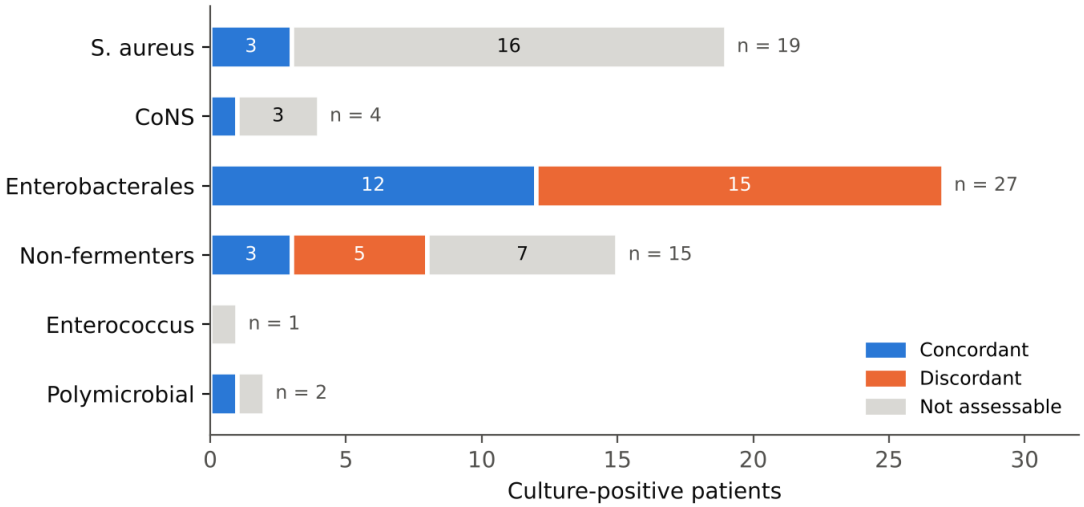


Figure-2. Empirical-therapy concordance by organism group among culture-positive patients (n=68)

On univariate analysis, diabetes mellitus was less frequent among culture-positive patients (22.1% vs 37.7%; p = 0.028), whereas suspected source (p = 0.647), prior antibiotic exposure, recent hospital admission, indwelling devices and culture-collection quality were not significantly associated with positivity. In multivariable regression, diabetes (adjusted OR 0.46, 95% CI 0.23–0.94; p = 0.033) and increasing age (adjusted OR 0.980 per year, 95% CI 0.961–0.998; p = 0.032) remained independently associated with lower odds of a positive culture (model χ^2 = 14.44, df = 5, p = 0.013; Hosmer-Lemeshow p = 0.324; AUC 0.668, 95% CI 0.589–0.746) (Table-V). ED death occurred in 1 of 68 (1.5%) culture-positive and 17 of 114 (14.9%) culture-negative patients (p = 0.003), while the combined rate of HDU/ICU admission or ED death was similar (32.4% vs 34.2%; p = 0.797).

Table-V. Factors associated with culture-positive bacterial sepsis (n=182)

Variable	Positive (n=68) n (%)	Negative (n=114) n (%)	p-value	Adjusted OR (95% CI)*
Age (years), mean ± SD	53.4 ± 17.5	58.3 ± 16.5	0.059	0.980 (0.961–0.998)
Female sex	36 (52.9)	56 (49.1)	0.618	—
Diabetes mellitus	15 (22.1)	43 (37.7)	0.028	0.46 (0.23–0.94)
Chronic kidney disease	13 (19.1)	14 (12.3)	0.209	—
COPD	8 (11.8)	8 (7.0)	0.274	—
Liver disease	7 (10.3)	6 (5.3)	0.240	—
Any comorbidity	38 (55.9)	62 (54.4)	0.844	—

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Variable	Positive (n=68) n (%)	Negative (n=114) n (%)	p-value	Adjusted OR (95% CI)*
Antibiotic exposure, preceding 30 days	17 (25.0)	39 (34.2)	0.193	0.56 (0.28–1.14)
Hospital admission, preceding 90 days	13 (19.1)	23 (20.2)	0.862	—
Indwelling device	12 (17.6)	16 (14.0)	0.514	—
Fever (≥38.0 °C)	37 (54.4)	75 (65.8)	0.127	0.68 (0.36–1.30)
qSOFA ≥2	58 (85.3)	99 (86.8)	0.769	—
Culture before first ED antibiotic	47 (69.1)	80 (70.2)	0.881	—
Two culture sets drawn	57 (83.8)	86 (75.4)	0.182	1.54 (0.69–3.44)
Adequate blood volume	61 (89.7)	99 (86.8)	0.566	—

*Univariate p-values from chi-square test (Fisher exact test for liver disease) or independent t-test (age). *Binary logistic regression including variables with p <0.20: age, diabetes, antibiotic exposure, fever and two-set collection; adjusted p-values: age 0.032, diabetes 0.033, antibiotic exposure 0.110, fever 0.247, two sets 0.294. Model $\chi^2 = 14.44$, $p = 0.013$; Nagelkerke $R^2 = 0.104$; Hosmer-Lemeshow $p = 0.324$; AUC = 0.668.*

DISCUSSION

This study found that more than one in three adults with suspected sepsis in our ED had culture-confirmed bacteraemia. The positivity rate of 37.4% is higher than the 29.4% reported by Zahra et al. in critically ill adults[6] and close to the 36% reported from a Karachi diagnostic laboratory.[7] It is considerably higher than the true-positive rate of 10.9% from an Australian ED benchmarking study,[11] and the much lower yields reported in paediatric emergency settings.[15] Our inclusion of only patients meeting a SOFA-based sepsis definition, and the fact that most patients had two adequately filled sets, probably explain the higher yield. A German multicentre ED study similarly found the highest pathogen detection (65.6%) when two or more sets were drawn before antibiotics.[12]

Gram-negative organisms accounted for 61.4% of isolates, consistent with the 66.3% reported by Zahra et al.[6] and lower than the 77% reported from an ICU in Quetta.[8] *K. pneumoniae* and *Acinetobacter* species were the leading Gram-negative organisms, as in other Pakistani series.[6,7] These organisms carry the greatest resistance burden locally: carbapenem-resistant *A. baumannii* is now highly prevalent in Pakistan and is often susceptible only to colistin or minocycline,[16,17] and recent hospital antibiograms show cephalosporin susceptibility below one-third in *K. pneumoniae*.[18] WHO surveillance places our region among those with the highest resistance worldwide.[5] The presence of *Salmonella* Typhi in 7.1% of isolates is also relevant, because XDR strains resistant to ceftriaxone are now established in Pakistan.[9,10]

S. aureus was the single most frequent organism (30.0%), which agrees with a Peshawar series in which *S. aureus* accounted for 37.5% of sepsis isolates.[19] Globally, *S. aureus* is associated with more deaths than any other bacterium in people older than 15 years.[4] Concordance could not be assessed in most *S. aureus* episodes because the β-lactam given in the ED was not on the reported susceptibility panel, and vancomycin was added in fewer than one in five patients. Routine reporting of methicillin status, and of the empirical agents actually used in the ED, would allow this gap to be measured.

Only half of assessable culture-positive patients received concordant empirical therapy, and concordance in Gram-negative bacteraemia was only 42.9%. Ceftriaxone monotherapy, the most commonly prescribed regimen, was concordant in only one in four assessable cases. In a Thai cohort of community-onset bloodstream infection, 30.1% of resistant infections received inactive empirical therapy.[20] The clinical consequences are substantial: a meta-analysis of 198 studies found that inappropriate empirical antibiotics roughly doubled mortality in adult bacteraemia (OR 2.06).[13] Our findings suggest that ceftriaxone alone may not be an adequate empirical choice for sepsis in our ED, and that empirical regimens should be guided by a regularly updated local antibiogram.[2,18]

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The contamination rate of 2.7% was below the widely used 3% benchmark[21] and the 3.4% reported by Hills et al.,[11] and two sets were drawn in 78.6% of patients compared with 45% in that Australian study.[11] However, 30% of cultures were drawn after the first antibiotic, and only 30.8% of patients received antibiotics within one hour, well short of guideline targets.[2] Although pre-antibiotic sampling markedly increases yield in other studies,[12,22] it was not associated with positivity in our data, possibly because the interval between antibiotic and sampling was short.

The lower culture positivity in patients with diabetes and in older patients was unexpected and was not a pre-specified hypothesis. It may reflect more frequent outpatient antibiotic use, non-bacterial or culture-negative causes of organ dysfunction in these groups, or residual confounding, and should be interpreted as exploratory. Similarly, the lower ED mortality among culture-positive patients is a disposition-level finding; early deaths may have included patients with non-bacterial causes of organ dysfunction, and in-hospital outcomes were not followed up.

This study has some limitations. It was a single-centre study using purposive sampling, which may limit generalisability. Isolate-level antimicrobial susceptibility results and resistance phenotypes such as ESBL production, carbapenem resistance and MRSA were not available in the analysed dataset, so organism-specific resistance rates could not be reported. Several subgroups were small, and concordance estimates based on fewer than 30 isolates should not alone guide empirical policy. Outcomes were limited to ED disposition. Larger multicentre studies with linked antibiogram and in-hospital outcome data are recommended.

CONCLUSION

More than one-third of adults presenting with suspected sepsis to our ED had culture-confirmed bacteraemia, mostly Gram-negative, with *S. aureus*, *K. pneumoniae* and *Acinetobacter* species predominating. Half of assessable patients received discordant empirical therapy, supporting an ED-specific antibiogram and stewardship-guided empirical regimens.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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