Utility of Previous Culture Results for Guiding Empirical Treatment of Sepsis in The Emergency Department

Saleh Alhaidar, Adel Korairi, Abdullah Alshehri, Ali Aldufairi, and Maya Othman

Abstract—**Background: Sepsis is a serious medical condition and a major cause of morbidity and mortality, and poses challenges in terms of recognition and management. Although studies have investigated the early identification of sepsis and early use of broad-spectrum antibiotics, no clear criteria exist to identify those patients needing additional coverage for resistant organisms.**

Aims: This study aims to evaluate the utility of previous positive blood or urine culture results in predicting the presence of resistant organisms in septic patients in the emergency department (ED).

Methods: This retrospective observational study was conducted at King Fahad Medical City (KFMC), a tertiary care centre in Riyadh, Saudi Arabia, between March and August 2021. Patients aged 18 years or older, who visited the ED at KFMC during the study period, were included if they had a positive blood or urine culture and met the sepsis definition. Result: A total of 133 patients were enrolled (mean age 61.6 [18.3] years), of whom approximately half were male (67, 50.4%). We found that previous colonisation with resistant organisms was more likely in patients with resistant organisms at the time of the enrolled visit (n = 17, 77.3%) than in patients with non-resistant organisms (n = 22, 19.8%, p < .05). Therefore, one statically significant predictor of a current resistant organism is a prior colonisation with a resistant organism (OR = 13.8; 95% CIs 3.6, 51.9; p < .05).

Conclusion: Previous cultures, from within the last 12 months, are useful predictors of current resistant organisms, and are therefore essential in guiding empirical antibiotic treatment in septic patients in the ED. Further more extensive and prospective cohort studies on this subject are now needed to mitigate the burden of sepsis on healthcare systems worldwide.

Index Terms—**Antibiotics, Emergency, Sepsis**

I. Introduction

Sepsis is a serious medical condition and a major cause of morbidity and mortality.[1] The recognition and management of sepsis, as well as antibiotic choices for its treatment, continue to pose challenges — especially in the emergency department (ED), due to limited data and short clinical courses. It is established, however, that early initiation of antibiotics can reduce mortality and limit complications.[2]

Although extensive studies and guidelines have investigated the role of early identification and early broad-spectrum antibiotics for sepsis,[2,3] no clear criteria exist to identify patients who need additional coverage for resistant organisms. Some suggest a review of previous cultures to guide empirical treatment; however, the available evidence is limited. Some studies are based on throat swabs in intensive care unit (ICU) settings, with no blood cultures included.[4] Others included screening swabs taken a few days before infection onset.[4–7] In addition, most of the included patients in previous studies were in ICU settings, rather than in ED settings.[5–7] Some of the studies investigated specific Gram classes but not all organisms.[8–10]

We hypothesise that positive blood or urine culture results from within the previous 12 months can

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predict the presence of resistant organisms in septic ED patients. Therefore, this study aims to evaluate the utility of previous positive blood or urine culture results as predictors of current resistant organisms in septic patients in the ED.

II. METHODS

Study design and patient selection:

This retrospective observational study was conducted at King Fahad Medical City (KFMC), a tertiary care centre in Riyadh, Saudi Arabia. Patients aged 18 years or older, who visited the ED at KFMC between March and August 2021, had a positive blood or urine culture, and met the sepsis definition, were included. Patients with microbiology reports older than 12 months, as well as any patients discharged from the ED, were excluded. A total of 133 patients were enrolled. If a patient had multiple visits that met the inclusion criteria during the study period, only the most recent visit was included.

We defined sepsis as documented bacteraemia or bacteriuria and a positive systemic inflammatory response syndrome (SIRS) or positive Lactate-enhanced-qSOFA (LqSOFA) in the absence of alternative conditions.[11–14] Prior antibiotic exposure is any receipt of antibiotics within 90 days preceding the enrolled visit.[8,15,16] An infection was deemed hospital-acquired if the patient was previously admitted in the 90-day period preceding the enrolled visit.[8] Immunosuppressive therapy is the current use, or use within 30 days preceding the enrolled visit, of the following medication: corticosteroids, cyclosporine A, tacrolimus, rapamycin, cyclophosphamide, azathioprine, mycophenolate mofetil, methotrexate, etanercept, infliximab, daclizumab, basiliximab, chlorodeoxyadenosine, fludarabine, or alemtuzumab.[17] Cancer treatment therapy is any exposure to chemotherapy, radiation therapy, or hormonal therapy during or preceding the enrolled visit by 14 days.[18] An immunocompromised patient is any patient with the following conditions: neutropenia, splenectomy, haematopoietic stem cell transplant, solid organ transplant, or HIV-AIDS.[17]

Data sources:

Subjects were identified automatically from the electronic medical record, and two trained data collectors obtained the following variables from the same record.

Study variables:

Age, gender (male/female), comorbidities (cardiopulmonary disease, medical disease, oncological diseases, neurological disease, rheumatological and immunological diseases, infectious disease, surgical disease, none), prior antibiotic exposure, admission diagnosis (medical/surgical), community-acquired infection, hospital-acquired infection, ICU admission, immunosuppressive therapy, cancer treatment therapy, immunocompromised, organisms identified in the enrolled visit (blood or urine), prior microbiology results (blood, urine).

Data management and analysis plan:

The analysis used the Statistical Package for Social Sciences (SPSS) version 25.0 (IBM-SPSS, Armonk, New York, USA). Descriptive statistics were reported as mean and standard deviation for continuous variables and as frequency and percentages for categorical variables. An independent samples t-test was used to compare means for two groups, and analysis of variance was used for three or more groups. The chi-square test was used to determine significant association between categorical groups. A logistic regression analysis was carried out to determine the significant factors associated with current resistance. p-values ≤ 0.05 were considered statistically significant.

Ethical considerations:

All obtained data were treated with strict confidentiality, and any identifying information was excluded from all reports or published documents. Approval was obtained from the Research Ethics Board at KFMC.

III. RESULTS

A total of 133 patients were enrolled (mean age 61.6 [18.3] years), about half of whom were male (n = 67, 50.4%). The patients were divided into two groups, the first consisting of patients with non-resistant organisms at the time of the enrolled visit (n = 111, 83.5%), and the second group consisting of those with resistant organisms at the time of the enrolled visit (n = 22, 16.5%). No significant differences in age, gender or comorbidities were found between the two groups; however, the second group was less likely to have cardiopulmonary diseases (n = 14, 63.6%) than those with non-resistant organisms (n = 92, 82.9%) $p < 0.05$. Patients with

resistant organisms were more likely to have prior antibiotic exposure (n = 21, 95.5%) than those with non-resistant organisms (n = 99, 89.2%), although this was not statistically significant (p = 0.36). Furthermore, all those in the second group had hospital-acquired infections (n = 22, 100%) and were more likely to have had ICU admissions (n = 19, 86.4%) than patients with non-resistant organisms (n = 77, 69.4%). Overall, the study population consisted of sick patients with an ICU admission rate of 72.2%, 60% receiving immunosuppression therapy, and almost a third receiving cancer treatment (n = 37, 27.8%). In addition, 9.8% were identified as immunocompromised. Notably, previous colonisation with resistant organisms was more likely in patients with resistant organisms during the enrolled visit (n = 17, 77.3%) than in those with non-resistant organisms (n = 22, 19.8%, p< 0.05). (Table 1).

Table 2. shows the odds ratios (OR) and 95% confidence intervals (CI) of predictors of a resistant organism at the time of the enrolled visit. The only statistically significant predictor is previous colonisation with a resistant organism (OR = 13.8; 95% CI 3.6, 51.9; p < 0.05). Figure 1. reports the prevalence of resistant organisms.

IV. Discussion

Reviewing culture results, either blood or urine, from the previous 12 months is crucial in assessing and managing septic patients. Reviewing previous cultures along with historical data such as prior antibiotic exposure, history of recent hospitalisation, and comorbidities can help to identify those patients more likely to develop sepsis secondary to a resistant organism.

The results of this study demonstrate that prior colonisation with a resistant organism is a strong predictor of a current resistant organism in the same patient. The study also found that patients with resistant organisms are less likely to be suffering from cardiopulmonary disease.

All of the patients in our study who developed resistant organisms had a history of recent hospitalisation, their infection was considered hospital-acquired, and they had a higher rate of exposure to antibiotics. This information highlights the importaance of identifying these factors when assessing septic patients and selecting antimicrobial agents; it should also alert the healthcare systems to the real need for efforts aimed at fighting and decreasing hospital-acquired infections.

Multiple factors are advised to guide the administration of empirical antibiotics, one of which is local hospital susceptibility.[2,19,20] Thus, the predictive utility of previous cultures should be paramount in clinical practice, alongside other factors, to avoid unnecessary antibiotic administration and to ensure that appropriate antibiotics are received in the shortest possible time — even before culture results — as these patients' condition is usually critical. Early appropriate antibiotics are essential, as advised by the guidelines.[2]

Although this is an essential outcome of the study, it is crucial to highlight that this study's population is unique, as it was conducted in a tertiary centre with 38% of the population being oncology and sicker patients. Nevertheless, it is unlikely that this fact affected the results or their application.

Although the literature review was limited on this subject, some studies discussed the utility of previous cultures and examined other risk factors for predicting resistant organisms. For example, MacFadden's study concluded that "prior resistant culture results are useful in the selection of empiric therapy for bloodstream infections due to confirmed Gram-negative pathogens".[8] Other studies found that a history of detected methicillin-resistant Staphylococcus aureus on cultures was highly specific for subsequent infection with Staphylococcus aureus.[9] When assessing patients with current infection, it is helpful to review the previous microbiological data and cultures and recommend empirical antibiotic coverage for the identified resistant organisms.[21,22]

A limitation of this study is that it is a retrospective observational study conducted in a single centre with a relatively small sample size.

V. Conclusion

Cultures taken within 12 months prior to the current infection, are useful in predicting current resistant organisms, and are therefore essential in guiding empirical antibiotic treatment of sepsis in the ED. More in-depth studies are needed on this topic to lower the impact of sepsis on global health- care systems.

Table 1. Demographic and clinical variables among septic patients with occurrence of resistant organisms in blood or urine culture (N=133)

Variables	**Patients with non-resistant organisms (current) N=111**	**Patients with resistant organisms (current) N=22**	***p-value***	**All patients (current) n=133**
Age, mean (SD)	61.9 ± 18.7	60.5 ± 19.5	0.7*	61.6 ± 18.3
Gender				
Male	57 (51.4%)	10 (45.5%)	0.6	67 (50.4%)
Female	54 (48.6%)	12 (54.5%)		66 (49.6%)
Mean number of comorbidities	2.75 ± 1.5	2.45 ± 1.4	0.3*	2.70 ± 1.5
Comorbidities				
Cardiopulmonary	92 (82.9%)	14 (63.6%)	0.04	106 (79.7%)
Medical disease	93 (83.8%)	17 (77.3%)	0.4	110 (82.7%)
Oncological	42 (37.8%)	9 (40.9%)	0.7	51 (38.3%)
Neurological	56 (50.5%)	12 (54.5%)	0.7	68 (51.1%)
Rheumatological	12 (10.8%)	0	0.1	12 (9.0%)
Infectious	47 (42.3%)	7 (31.8%)	0.3	54 (40.6%)
Surgical disease	54 (48.6%)	10 (45.5%)	0.7	64 (48.1%)
Admission diagnosis				
Medical	106 (95.5%)	20 (90.9%)		126 (94.7%)
Surgical	5 (4.5%)	2 (9.1%)	0.3	7 (5.3%)
Prior antibiotic exposure	99 (89.2%)	21 (95.5%)	0.3	120 (90.2%)
Community-acquired infection	10 (9.0%)	0	0.1	10 (7.5%)
Hospital-acquired infection	101 (91.0%)	22 (100%)	0.1	123 (92.5%)
Current ICU admission	77 (69.4%)	19 (86.4%)	0.1	96 (72.2%)
Immunosuppressive therapy	72 (64.9%)	12 (54.5%)	0.3	84 (63.2%)
Cancer treatment therapy	31 (27.9%)	6 (27.3%)	0.9	37 (27.8%)
Immunocompromised	10 (9.0%)	3 (16.7%)	0.5	13 (9.8%)
Previous colonisation with resistant organisms	22 (19.8%)	17 (77.3%)	< 0.001	39 (29.3%)
No previous colonisation with resistant organisms	89 (80.2%)	5 (22.7%)		94 (70.7%)

* tested by independent samples t-test; the rest by chi-square test

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Table 2. Odds ratios (95% CI) of predictors of antibiotic resistance from multi-variable logistic regression analysis

Variable	**B**	**OR (95% CI)**	***p*-value**
Age	0.01	1.01 (0.9, 1.06)	0.6
Gender	-0.3	0.6 (0.1, 2.2)	0.5
Number of comorbidities	1.3	0.2 (0.003, 22.74)	0.5
Cardiopulmonary disease	2.3	0.09 (0.010, 0.855)	0.03
Medical disease	2.7	15.6 (0.09, 248.5)	0.2
Oncological disease	0.7	2.0 (0.01, 274.6)	0.7
Neurological disease	1.7	5.6 (0.04, 690.2)	0.4
Rheumatological disease	17.4	0 (0)	0.9
Infectious disease	0.4	1.5 (0.01, 211.2)	0.8
Surgical disease	1.6	5.1 (0.03, 757.0)	0.5
Admission diagnosis	0.2	1.3 (0.08, 21.5)	0.8
Prior antibiotic exposure	0.3	1.4 (0.1, 18.9)	0.7
Community-acquired infection	18.7	0 (0)	0.9
Current ICU admission	0.7	2.1 (0.3, 12.4)	0.3
Immunosuppressive therapy	0.8	0.4 (0.1, 1.8)	0.2
Cancer treatment therapy	0.8	2.2 (0.2, 22.2)	0.4
Immunocompromised	1.4	4.4 (0.5, 38.3)	0.1
Previous colonisation with resistant organisms	2.6	13.8 (3.6, 51.9)	< .001

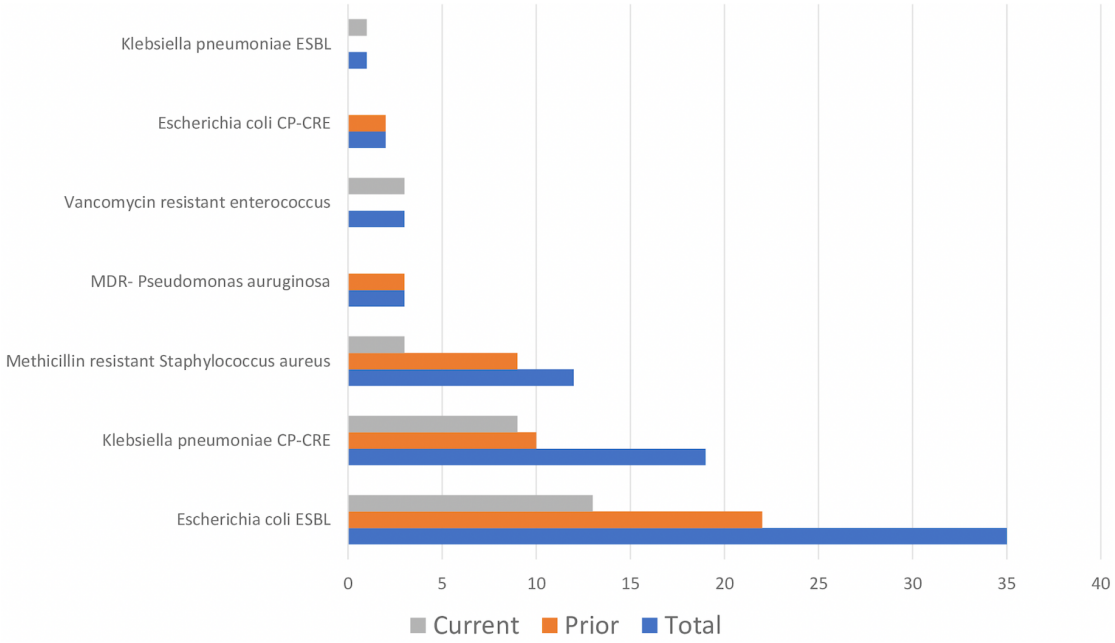

Figure 1. The prevalence of resistant organisms.

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