

Analysis of Blood Cultures of Patients Presenting to the Emergency Department in a Tertiary Healthcare Hospital in Mumbai

Deepak Kishor Sharma¹, Sandeep B Gore²

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ABSTRACT

Aim and objectives: Analysis of blood cultures taken from patients attending emergency departments is an important exercise in determining the common pathogens prevalent in the region. The distribution of these infective pathogens keeps changing over time, and the rise in antimicrobial-resistant pathogens makes it difficult to routinely conduct effective empirical broad-spectrum antimicrobial therapy. This study aimed to analyse the results of blood cultures obtained from patients presenting to the Emergency Department of a Tertiary Healthcare Hospital in Mumbai and provide updated and detailed information on the distribution of causative pathogens in adult sepsis and study their antibiotic-susceptibility pattern.

Materials and methods: A hospital-based prospective cross-sectional study of 121 positive blood culture reports was conducted at the Department of Emergency Medicine, Fortis Hospital Mulund, Mumbai, which included all adult (age > 18 yrs) suspected sepsis patients arriving to the Emergency Department whose blood cultures were sent from the Emergency Department from January 2021 to December 2021.

Results: The study showed that mean age of the study cases was 59.3 years with 59.5% cases that belonged to the elderly age group with a male predominance (56.2% males–43.8% females). Overall, Gram-negative isolates were seen in 95% cases, while Gram-positive isolates were seen in only 1.7% cases. The most common organism isolated from cases with sepsis was *Escherichia coli* (45.5%) followed by *Klebsiella* (13.2%), *Salmonella* (10.7%), *Stenotrophomonas* (7.4%) and *Pseudomonas* (5%). Among Gram-positive organisms, *Staphylococcus aureus* was the most common organism isolated (1.7%). *Escherichia coli* isolates showed poor sensitivity towards fluoroquinolones and cephalosporins while good sensitivity towards aminoglycosides, carbapenems and combination drugs like Cefoperazone and Sulbactam and Piperacillin and Tazobactam. These findings suggest that Gram-negative organisms are the most common isolates observed in this study, with *E. coli* being the predominant pathogen followed by *Klebsiella*. High-level antimicrobial resistance was observed in sepsis cases for commonly used antimicrobials like fluoroquinolones and cephalosporins.

Keywords: Antibiotic stewardship, Blood culture, Emergency Department, Sepsis.

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INTRODUCTION

Sepsis is the combination of a known or suspected infection and an accompanying systemic inflammatory response. Sepsis, severe sepsis and septic shock are terms used to describe the body's systemic responses to infection. Severe sepsis is sepsis with acute dysfunction of one or more organ systems, and septic shock is a subset of severe sepsis. It is common and frequently fatal. Underlying illness, increased age and multisystem organ failure are major risk factors for mortality from sepsis.^{1,2}

The prognosis of the patient with severe sepsis is related to the number of dysfunctional organs. Progression from signs of the inflammatory response to sepsis/severe sepsis and septic shock is associated with incrementally higher mortality risk. The transition to serious illness may occur during the critical 'golden hours' when definitive recognition and treatment provide maximal benefit in terms of outcome. Therefore, early recognition of sepsis and its appropriate treatment is of paramount importance in reducing mortality.³

One of the essential facets of sepsis management to maximise survival rates is the rapid administration of appropriate antimicrobials. Several studies have reported that each hour's delay in the administration of appropriate antimicrobials is associated with a measurable increase in mortality in patients with sepsis or

^{1,2}Department of Emergency Medicine, Fortis Hospital Mulund, Mumbai, India

Corresponding Author: Deepak Kishor Sharma, Department of Emergency Medicine, Fortis Hospital Mulund, Mumbai, India, Phone: +91 8779299053, e-mail: dr.sharma3539@gmail.com

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septic shock.⁴ Further, failure to initiate appropriate empiric therapy in patients with sepsis and septic shock has been associated with a substantial increase in mortality.^{5,6}

Based on this evidence, the Surviving Sepsis Campaign (SSC) guidelines strongly recommend that empiric broad-spectrum therapy be conducted with one or more antimicrobials as soon as possible after the recognition of sepsis or septic shock, to cover

all likely pathogens, including bacterial, fungal or viral coverage⁷ ideally within 1 hour of sepsis recognition.⁸

However, the distribution of causative pathogens has changed over time,⁹ and the global rise in antimicrobial-resistant pathogens has made it difficult to routinely conduct empiric broad-spectrum antimicrobial therapy.^{9,10} To optimise the accurate selection of initial antimicrobial agents, clinicians should consider the various factors associated with the causative pathogens, including:

- Patient pre-existing comorbidities,
- Prior knowledge of pathogens known to colonise the patient,
- Prior antibiotic exposures and
- The local pattern of causative pathogens, antibiotic resistance and zoonotic pathogens.^{11,12}

Furthermore, there is no one-size-fits-all empiric antimicrobial therapy for sepsis because the typical pathogen profile varies according to the anatomical site of infection. Although there are multiple lines of evidence related to the causative pathogens in paediatric sepsis,^{13,14} there are only limited reports in adult sepsis. Blood cultures taken from patients attending emergency departments are an important antibiotic stewardship tool, which directly influences patient management.¹⁵

Therefore, updating knowledge on the current distribution of causative pathogens in adult sepsis is required to initiate appropriate antimicrobial therapy. The aims of this study were to provide updated and detailed information on the distribution of causative pathogens in adult sepsis and study their antibiotic-susceptibility pattern.

AIM AND OBJECTIVES

Aim

To find out the common pathogens/microbes and their respective antimicrobial drug susceptibility in suspected sepsis patients presenting to the Emergency Department.

Objectives

- To study the clinical spectrum of sepsis cases presenting to Emergency Department.
- To study the microbiological profile of sepsis cases presenting to Emergency Department.
- To study the antimicrobial drug-susceptibility pattern of isolated organisms in sepsis cases.

MATERIALS AND METHODS

Study Area

Emergency Department, Fortis Hospital Mulund, Mumbai.

Study Population

All suspected sepsis patients arriving at the Emergency Department whose blood cultures are being sent from the ER.

Study Design

A hospital-based cross-sectional study.

Sample-size Calculation

The sample size was calculated using the following formulae:

$$n = (Z\alpha/2)^2 * p(1 - p)/E^2$$

n – sample size.

$Z\alpha/2$ – Z value at 5% error (1.96).

P – prevalence of septicaemia (taken as 28%).

E – allowable error (taken as 10%).

$$n = \frac{(1.96)^2 * 0.28 * 0.72}{(0.05)^2}$$

N – 80 (approx.)

So, by rounding off, we will be taking 121 subjects.

Consecutive type of non-probability sampling will be followed for the selection of study subjects. A total of 121 patients fulfilling the eligibility criteria were taken for study after taking informed consent.

Study Duration

18 months.

Inclusion Criteria

- Age >18 years.
- Both genders.
- Blood cultures reported positive for growth of organism.

Exclusion Criteria

- Limitation of sustained life care or post cardiopulmonary arrest resuscitation status at the time of sepsis diagnosis.
- Pregnant and lactating females.

METHODOLOGY

- As per predefined, inclusion and exclusion criteria patients were included in the study.
- All these patients were evaluated thoroughly by clinical, radiological and laboratory methods.
- Most of the patients in the study sample were from the Mumbai region barring a few who were referred from other regions such as Kalyan, Thane and Navi Mumbai.
- These patients were provisionally diagnosed to have sepsis in the ER, barring a few who were diagnosed elsewhere and referred here.
- Blood cultures were collected from peripheral veins, other sites were excluded because these could confound the results.
- Each patient was started on empirical therapy as per the current protocol.
- Susceptibility testing was done by Kirby–Bauer disc diffusion method and interpreted according to the Clinical and Laboratory Standards Institute (CLSI) guidelines – 2012.
- Empirical upgradation of antibiotics or change in antibiotics was done as per the culture sensitivity report.

Statistical Analysis

All the data were noted down in a pre-designed study proforma. Qualitative data were represented in the form of frequency and percentage. Quantitative data were represented using mean \pm SD. SPSS Version 21.0 was used for most analyses, and Microsoft Excel 2010 for graphical representation.

RESULTS

Mean age of the study cases was 59.3 years with 59.5% cases that belonged to elderly age group (Fig. 1).

Male predominance was seen among cases of suspected sepsis with 56.2% males–43.8% females (Fig. 2).

The most common organism isolated from cases with sepsis was *Escherichia coli* (45.5%) followed by *Klebsiella* (13.2%), *Salmonella* (10.7%), *Stenotrophomonas* (7.4%) and *Pseudomonas* (5%). Among

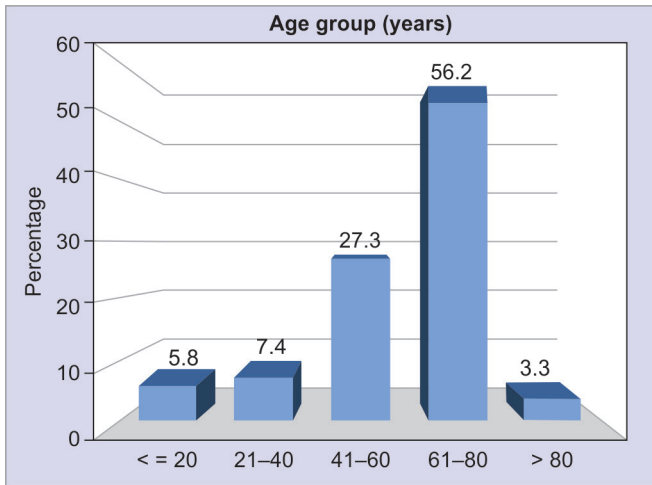


Fig. 1: Patients' age distribution

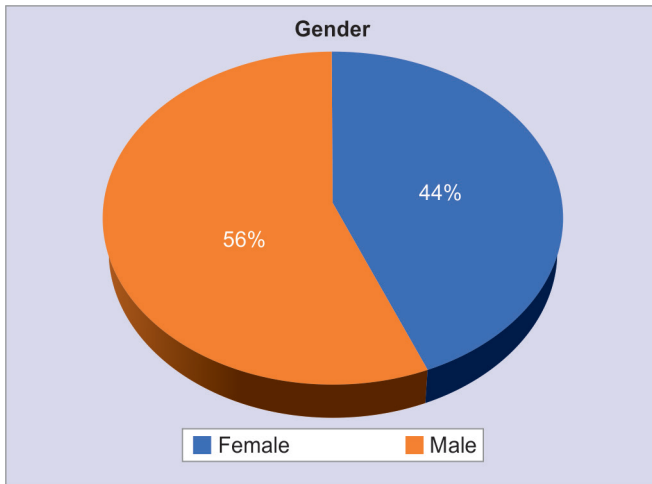


Fig. 2: Patients' gender distribution

Gram-positive organisms, *Staphylococcus aureus* was the most common organism isolated (1.7%) (Table 1).

Overall Gram-negative isolates were seen in 95% of cases, while Gram-positive isolates were seen in only 1.7% cases (Table 2).

DISCUSSION

Sepsis is the combination of a known or suspected infection and an accompanying systemic inflammatory response. The prognosis of the patient with severe sepsis is related to the number of dysfunctional organs. One of the essential facets of sepsis management to maximise survival rates is the rapid administration of appropriate antimicrobials. Several studies have reported that each hour's delay in the administration of appropriate antimicrobials is associated with a measurable increase in mortality in patients with sepsis or septic shock.⁴

Based on this evidence, the Surviving Sepsis Campaign (SSC) guidelines strongly recommend that empiric broad-spectrum therapy be conducted with one or more antimicrobials as soon as possible after the recognition of sepsis or septic shock, to cover all likely pathogens, including bacterial, fungal or viral coverage.⁷

However, the distribution of causative pathogens has changed over time,⁹ and the global rise in antimicrobial-resistant pathogens

Table 1: Distribution of study groups as per isolated organism

Organism	N	%
<i>E. coli</i>	55	45.5
<i>Klebsiella</i>	16	13.2
<i>Salmonella</i>	13	10.7
<i>Stenotrophomonas</i>	9	7.4
<i>Pseudomonas</i>	6	5.0
<i>Acinetobacter</i>	4	3.3
<i>Proteus mirabilis</i>	4	3.3
<i>Burkholderia</i>	3	2.5
<i>Achromobacter</i>	1	0.8
<i>Morganella morganii</i>	1	0.8
<i>Serratia fonticola</i>	1	0.8
<i>Shigella</i>	1	0.8
<i>Sphingomonas</i>	1	0.8
MRSA	1	0.8
<i>S. aureus</i>	1	0.8
Not detected	4	3.3
Total	121	100.0

Table 2: Distribution of study groups as per type of organism

Organism	N	%
Gram-positive	2	1.7
Gram-negative	115	95.0
Not detected	4	3.3
Total	121	100.0

has made it difficult to routinely conduct empiric broad-spectrum antimicrobial therapy.^{9,10} Therefore, updating knowledge on the current distribution of causative pathogens in sepsis is required to initiate appropriate antimicrobial therapy.

In this study, we thus aimed to find out the common pathogens/microbes and their respective antimicrobial drug susceptibility in suspected sepsis patients presenting to the Emergency Department. The study included 121 suspected sepsis patients arriving to Emergency Department whose blood cultures are being sent from the Emergency room (ER).

Demography

Mean age of the study cases was 59.3 years with 59.5% cases that belonged to elderly age group. Male predominance was seen among cases of suspected sepsis with 56.2% males–43.8% females.

The study by Todi S et al.¹⁶ had shown that sepsis is common in elderly age group (>50 years, 61%) and in males (57.71%). Peres Bota DP et al.,¹⁷ in a similar study observed the mean age as 59.76 years with male predominance (71% vs 29%). Dash et al.,¹⁸ in a similar study, observed the mean age of cases was 58.15 years, with male and female ratio as 1.63:1.

Thus, from the above observations, it was evident that sepsis mostly affects adult males after their fifth decade of life. The waning immunity in the elderly age group could be attributed to this observation.

Organisms Isolated

Overall, Gram-negative isolates were seen in 95% cases, while Gram-positive isolates were seen in only 1.7% cases. The most common

organism isolated from cases with sepsis was *E. coli* (45.5%) followed by *Klebsiella* (13.2%), *Salmonella* (10.7%), *Stenotrophomonas* (7.4%) and *Pseudomonas* (5%). Among Gram-positive organisms, *S. aureus* was the most common organism isolated (1.7%).

In the ANZICS study,¹⁹ Gram-negative isolates were seen in 90% of the cases with *E. coli* being the most common (29.3%) Gram-negative organism and methicillin-sensitive *S. aureus* (3.1%), the most common Gram-positive organism. Chatterjee S et al.²⁰ in their study observed that the majority of hospital-acquired infections were caused by Gram-negative organisms (73%). The commonly isolated microbes were *Acinetobacter baumannii* (21.2%), *Pseudomonas aeruginosa* (17%) and equal prevalence of *Klebsiella* and *E. coli* (15.4%). In the study by Kumalo et al.,²¹ observed 53.3% were for Gram-negative bacteria and 46.7% for Gram-positive bacteria. The predominant isolates were *E. coli* and *S. aureus* from the total isolate that constitutes for Gram-positive and Gram-negative organisms, respectively. Vendemiato AVR et al.²² observed prevalent microorganisms such as coagulase-negative *Staphylococcus* (15.87%), *E. coli* (13.0%), *S. aureus* (11.7%), *Klebsiella* (9.8%), *Enterobacter* (9.5%), *Acinetobacter* (9.2%), *Pseudomonas* (5.7%) and *Candida* (5.1%). Fuchs A et al.²³ in their study observed that Gram-positive cocci (GPC) and Gram-negative rods (GNR) were isolated in the same proportion of 44.4% ($n = 8$) each. In 11.1% of cases ($n = 2$), *Candida* spp. were isolated. The most common bacterial isolates were *S. aureus* ($n = 7$, 38.9%) and *E. coli* ($n = 4$, 22.2%).

The difference in microbiological profile across studies can be attributed to the difference in prevalent organisms in a particular area and region, which also varies on time-to-time basis. However, Gram-negative organisms were the predominant organisms causing sepsis across most studies.

Antimicrobial Susceptibility

The most common organism isolated from cases with sepsis was *E. coli* (45.5%) followed by *Klebsiella* (13.2%), *Salmonella* (10.7%), *Stenotrophomonas* (7.4%) and *Pseudomonas* (5%). Among Gram-positive organisms, *S. aureus* was the most common organism isolated (1.7%).

Over half of the *E. coli* and *Klebsiella* isolates showed poor sensitivity towards fluoroquinolones and cephalosporins while good sensitivity towards aminoglycosides, carbapenems and combination drugs like Cefoperazone-Sulbactam and PipTaz. *Salmonella* isolates showed good sensitivity towards cephalosporins and ampicillin and resistance towards fluoroquinolones and nalidixic acid. Out of the 9 isolates of *Stenotrophomonas*, 7 showed sensitivity towards TMP-SFX and 2 showed resistance. *Pseudomonas* isolates showed resistance towards fluoroquinolones and imipenem, while moderate sensitivity was observed towards aminoglycosides, cephalosporin and good sensitivity towards meropenem. The isolate of MRSA was sensitive only towards clindamycin while resistant to fluoroquinolones and beta-lactam antibiotics. A single isolate of *S. aureus* was sensitive towards clindamycin, oxacillin and TMP-SFX while resistant towards ampicillin and benzyl penicillin.

In the study by Kumalo et al.,²¹ they observed antimicrobial resistance levels for the Gram-negative organisms, causing adult sepsis that ranged from 14.3% to 85.7%. A single *P. aeruginosa* isolate was sensitive to ciprofloxacin and gentamicin. An isolate of *Enterobacter* species was sensitive to all drugs, except cephalothin. The ranges of resistance for Gram-positive isolates were from 0%

to 100%. All isolates of Gram positives showed resistance against penicillin-G (8/8, 100%), but they showed high susceptibility to most of the other antimicrobials tested: ceftriaxone (7/8, 87.5%), chloramphenicol (7/8; 87.5%), ciprofloxacin (7/8, 87.5%), amoxicillin-clavulanic acid (6/8, 75%), cephalothin (5/8, 62.5%) and erythromycin (5/8, 62.5%). From a total of six *S. aureus*, two (33.3%) were methicillin-resistant (MRSA) (cefoxitin disc used), whereas the remaining four of them (66.7%) were methicillin-sensitive (MSSA). Among *S. aureus* strains isolated from blood culture, 2/6, 33.3% were MRSA. In this study, 50% of *S. aureus* strains were MRSA. In general, ciprofloxacin was the effective drug against the tested Gram-positive and Gram-negative bacteria (86.7%, 13/15). But in this study, most of the organisms were resistant for ciprofloxacin.

Vendemiato AVR et al.²² revealed that 51% of the *S. aureus* isolates were MRSA. For *A. baumannii*, the ideal profile drugs were ampicillin-sulbactam and piperacillin/tazobactam, and for *P. aeruginosa*, they were piperacillin/tazobactam and ceftazidime. *Enterobacter* showed on average 32.5% and 35.7% resistance to beta-lactams and ciprofloxacin, respectively. When all Gram-negative bacteria were considered, the resistance to beta-lactams rose to 40.5%, and the resistance to ciprofloxacin rose to 42.3%.

Fuchs A et al.²³ in their study observed that 71.4% of the isolated strains of *S. aureus* were resistant to co-trimoxazole and 28.6% to clindamycin. Half of the isolated *S. aureus* strains were MRSA. Antimicrobial resistance in the isolated Gram-negative bacterial isolates was much more common. Enterobacteriales were frequently resistant to aminopenicillins combined with beta-lactamase-inhibitors (83.3%), 3rd-generation cephalosporins (66.7%), quinolones (66.7%) and sulphonamides (83.5%). Resistance to aminoglycosides (33.3%) and carbapenems ($n = 1$) was less frequent but still considerably high.

The results of the studies showed high-level antimicrobial resistance in sepsis cases for commonly used antimicrobials. The difference in microbiological-susceptibility profile across studies shows the importance of regular surveillance to determine the local prevalence of organisms and antimicrobial susceptibilities in order to guide the proper empirical management of adults' sepsis cases.

SUMMARY AND CONCLUSION

Summary

A hospital-based observational study was conducted at Emergency department, Fortis Hospital Mulund, Mumbai. The study aimed to find out the common pathogens/microbes and their respective antimicrobial drug susceptibility in suspected sepsis patients presenting to the Emergency Department. The study included 121 suspected sepsis patients arriving to the Emergency Department whose blood cultures are being sent from the Emergency room (ER) and reported positive for microbial infection. The following observations were made during the study:

- Mean age of the study cases was 59.3 years with 59.5% cases that belonged to elderly age group.
- Male predominance was seen among cases of suspected sepsis with 56.2% males-43.8% females.
- The most common organism isolated from cases with sepsis was *E. coli* (45.5%) followed by *Klebsiella* (13.2%), *Salmonella* (10.7%), *Stenotrophomonas* (7.4%) and *Pseudomonas* (5%). Among Gram-positive organisms, *S. aureus* was the most common organism isolated (1.7%).

- Overall, Gram-negative isolates were seen in 95% cases, while Gram-positive isolates were seen in only 1.7% cases.
- *E. coli* isolates showed poor sensitivity towards fluoroquinolones and cephalosporins, while good sensitivity towards aminoglycosides, carbapenems and combination drugs like Cefoperazone–Sulbactam and PipTaz.
- *Klebsiella* isolates also showed poor sensitivity towards fluoroquinolones and cephalosporins, while good sensitivity towards aminoglycosides, carbapenems and combination drugs like Cefoperazone–Sulbactam and PipTaz.
- *Salmonella* isolates showed good sensitivity towards cephalosporins and ampicillin and resistance towards fluoroquinolones and nalidixic acid.
- Out of the 9 isolates of *Stenotrophomonas*, 7 showed sensitivity towards TMP–SFX and 2 showed resistance.
- *Pseudomonas* isolates showed resistance towards fluoroquinolones and imipenem, while moderate sensitivity was observed towards aminoglycosides, cephalosporin and good sensitivity towards meropenem.
- The isolate of MRSA was sensitive only towards clindamycin, while resistant to fluoroquinolones and beta-lactam antibiotics.
- A single isolate of *S. aureus* was sensitive towards clindamycin, oxacillin and TMP–SFX, while resistant towards ampicillin and benzyl penicillin.

CONCLUSION

This study observed the microbiological profile and antibiotic-susceptibility pattern of adult sepsis cases. Gram-negative organisms are the most common isolates observed in this study with *E. coli* being the predominant pathogen followed by *Klebsiella*. High-level antimicrobial resistance was observed in sepsis cases for commonly used antimicrobials like fluoroquinolones and cephalosporins.

This knowledge is very necessary to treat sepsis cases empirically in the hospital settings. Hence, regular surveillance should be carried out to determine the local prevalence of organisms and antimicrobial susceptibilities in order to guide the proper management of adults' sepsis cases.

Post cardiac-sustained life care or post cardiopulmonary arrest resuscitation status at the time of sepsis diagnosis have been excluded from the study as these result in changes in the body that mimic sepsis-like syndrome and could act as a confounding factor in the study. Pregnant females have been excluded from the study as the evaluation and management of maternal sepsis are complicated because of physiological changes that occur during pregnancy.

ORCID

Deepak Kishor Sharma  <https://orcid.org/0009-0005-3162-6414>

Sandeep B Gore  <https://orcid.org/0009-0004-0585-2015>

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