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Background and aims

Bloodstream infections (BSI) are serious infections and can lead to a state of septic shock where delay in adequate antibiotic therapy increases the risk of morbidity and mortality. In case of septic shock, current guidelines recommend empiric administration of broad-spectrum intravenous antibiotic therapy as soon as possible after recognition and within 1h for both sepsis and septic shock. Rapid antimicrobial susceptibility testing has been shown to reduce mortality, length of stay in hospitalization, time until alteration of antimicrobial therapy and the cost of hospitalization.

The aim of this study was to measure the clinical impact associated with rapid reporting of antimicrobial susceptibility test MHR-SIR results directly from blood cultures after 6-8 h of incubation on the same day that the bacteremia was detected.

Material and Methods

Case-control study conducted between June 2015 and June 2018 at the Hospital Paris Saint-Joseph

Inclusion criteria: Presence of an active infection defined as positive blood culture and clinical definition of sepsis caused by at least *Enterobacteriaceae* or *Staphylococcus aureus* and requirement of an empirical antibiotic therapy. All patients were screened daily for eligibility.

Exclusion criteria:

- 1) infections related to bacteria other than *Enterobacteriaceae* or *Staphylococcus aureus* and
- 2) moribund patient or a patient in palliative care in whom clinical decide to not introduce antibiotic therapy.

This study included two periods:

Period 1: From June 2015 to December 2016 followed a conventional strategy with the standard method of disk diffusion with a 16-24h of incubation according to the recommendations of EUCAST

Period 2: From January 2017 to June 2018 following MHR-guided adaptation therapy

Microbiological procedures:

Blood cultures were collected on BacT/ALERT bottles and incubated in Virtuo (bioMérieux, La Balme-les-Grottes, France). Once the blood culture was flagged positive, Gram stain was performed, followed by identification by mass spectrometry with MALDI-TOF MS Andromas® (Beckman Coulter, Villepinte, France) directly on blood culture pellets using the AMUST®, as recommended by the manufacturer's instructions.

AST was performed from positive blood samples by direct inoculation as recommended by the British Society for Antimicrobial Chemotherapy 23 on MHR-SIR agar (i2a, Montpellier, France) and incubated for 6-8 h. A panel of 32 antibiotic disks were tested for *Enterobacteriaceae* and 16 antibiotic disks for *Staphylococcus aureus*.

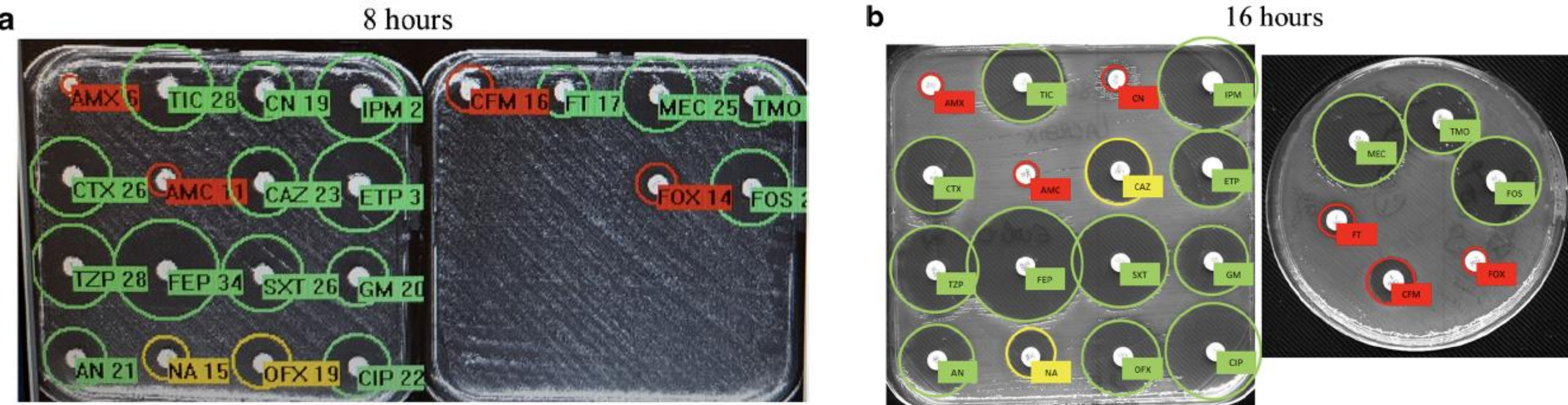


Figure 1. Automatic photos of an AmpC hyperproducer *Escherichia coli* strain isolated from urine sample on MHR-SIR (a) and standard MH (b) after respectively 8-and 16-h incubation.

Results and discussion

From June 2015 to June 2018, 330 patients were included in the study. Patient's characteristics are presented in table 1

	Conventional strategy (n=163)	MHR-guided adaptation therapy (n=167)	P-value
Sex ratio (M/F)	88/75	91/76	1
Median age	72.5 [59.8 – 83.2]	72.7 [60.5 - 82]	1
Source of infections			
Urinary tract infections	55 (33.7)	74 (44.3)	0.06
Intra-abdominal infections	35 (25.1)	33 (19.8)	0.78
Catheter related infections	22 (13.5)	15 (9)	0.22
Skin and soft tissue infections	11 (6.7)	10 (6)	0.82
Respiratory tract infections	6 (3.7)	9 (5.4)	0.59
Bone and joint infections	13 (8)	11 (6.6)	0.39
Infective endocarditis	13 (8)	8 (4.8)	0.26
Primary bacteraemia	8 (4.9)	7 (4.1)	0.77
Isolated bacteria			
<i>Enterobacteriaceae</i>	118 (72.4)	133 (79.6)	0.15
<i>Staphylococcus aureus</i>	45 (27.6)	34 (20.4)	0.1
Mean time between positivity of blood cultures and adaptation of antibiotic therapy	18h ± (3h40)	7h ± (2h30)	< 0.01

Table 1. Characteristics of patients included in the study

MHR-SIR disk diffusion method allowed early reading for the most important pathogens isolated from positive blood cultures such as *Enterobacteriaceae* and *Staphylococcus aureus* accounting for 50% of all blood culture isolates in our laboratory in the period 2015 to 2017.

Rapid method by MHR-SIR directly from blood cultures allows a significantly more effective de-escalation of treatment than the conventional technique.

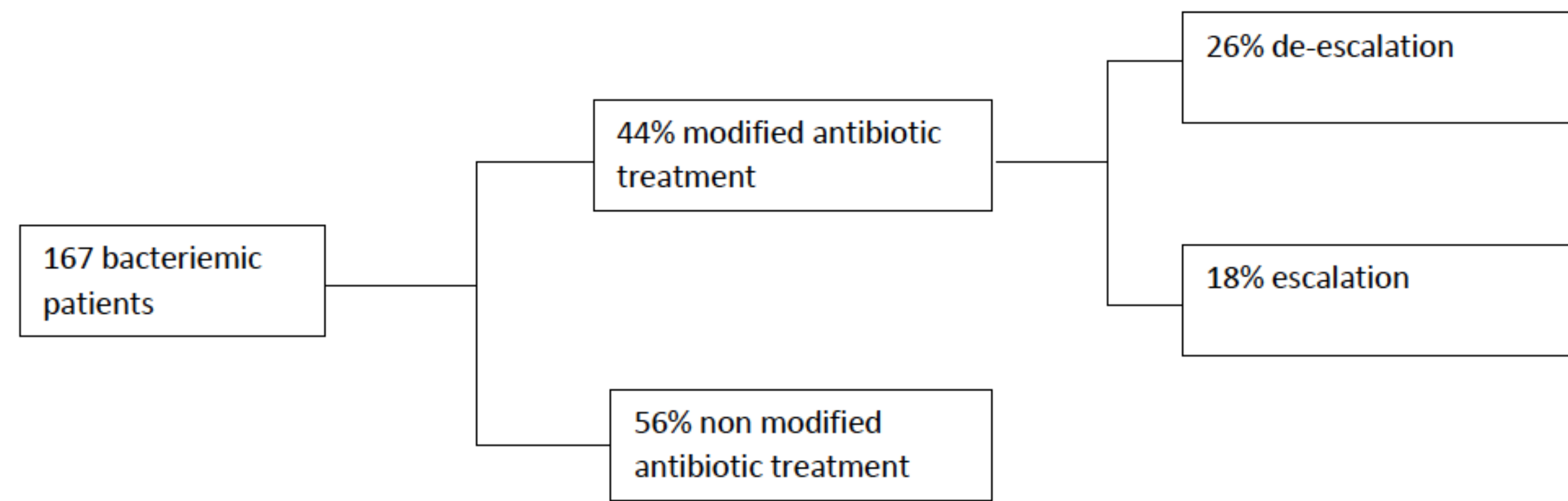


Figure 2. Antibiotic therapies modification according to MHR-SIR results

Conclusion

This study based on rapid AST MHR-SIR showed a significant time saving (11h) on the appropriateness of antibiotics prescription and demonstrated a significant impact at very moderate cost (6 USD) including the choice and reduction of the spectrum of antibiotic therapy. It represented an added value when combine with the efficient action in real time by the antimicrobial stewardship team.