Improved Detection of ESBL and AmpC Beta-Lactamase Producing Isolates of *Enterobacteriaceae* in Pediatric Patients with Bloodstream Infections Using Combined Genotypic and Phenotypic Antimicrobial Susceptibility Testing

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Background

AmpC and extended-spectrum β-lactamases (ESBL), present in *Enterobacteriaceae,* confer resistance to third-generation cephalosporins (3GC)

The detection of resistant AmpC and ESBL producing organisms in the clinical laboratory can be challenging

Currently, there are no recommendations regarding identification of AmpC in *Citrobacter*, *Enterobacter, Morganella* and *Serratia* spp. (CEMS organisms)

Aim

Increase the detection of AmpC and ESBL producing *Enterobacteriaceae* isolated in blood cultures from a pediatric population by combining genotypic with phenotypic antimicrobial susceptibility testing (AST)

Method

All first time *Enterobacteriaceae* isolates recovered from blood cultures of pediatric patients at CCHMC between January 1st 2017 and December 31st 2018

Phenotype

AST was performed using the Vitek-2 platform

- AmpC: Cefoxitin resistance **PLUS** (ceftriaxone OR ceftazidime resistance) using EUCAST standards
- ESBL: Ceftriaxone **OR** ceftazidime resistance using CLSI breakpoints

Genotype

Presence of AmpC and ESBL genes using Check-MDR CT103XL assay

Figure 1: AmpC- and ESBL- Producing Isolates Detected Using Phenotypic Method, Genotypic Method and Combined Testing

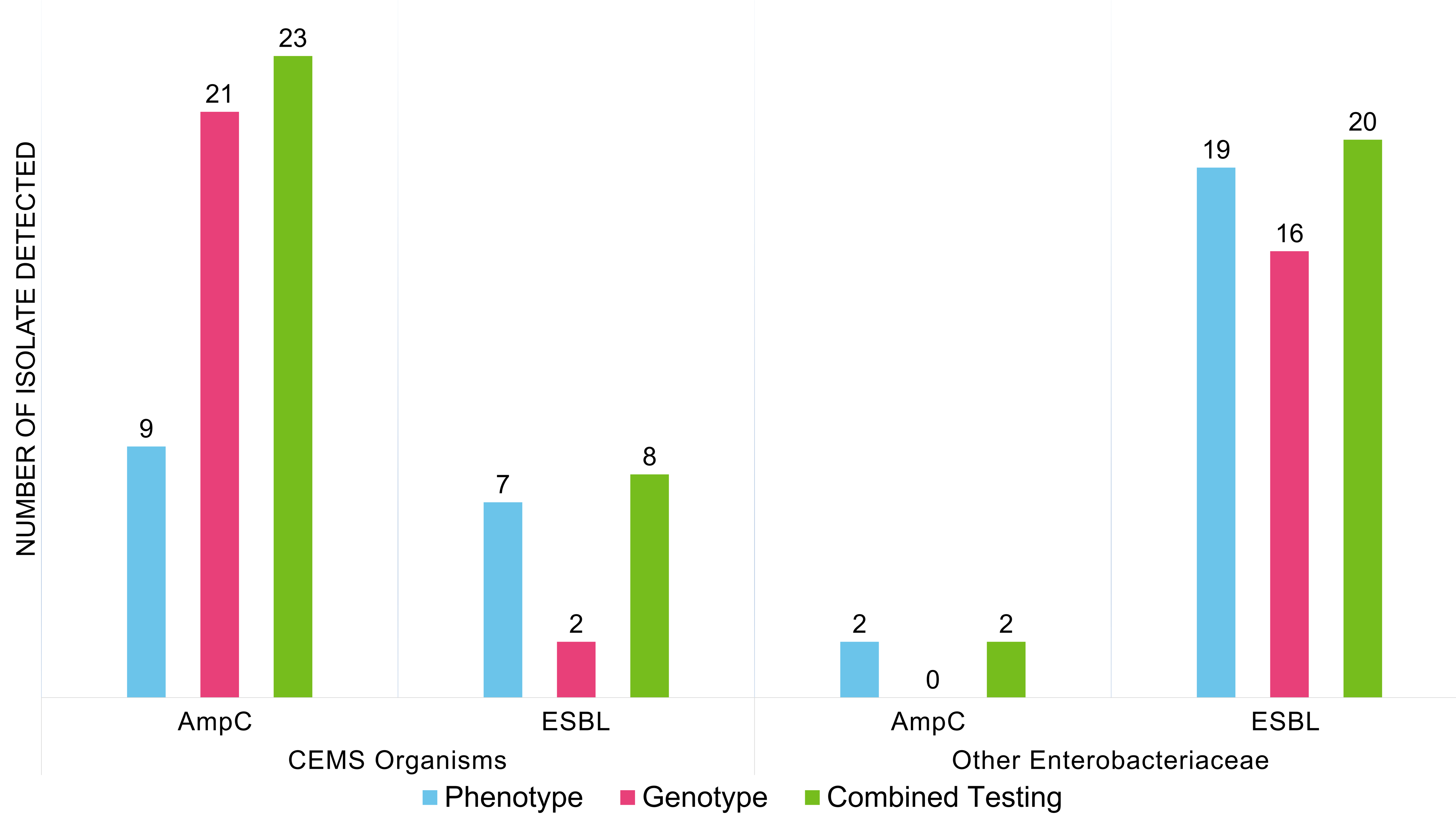

Table 1: Susceptibility of Isolates with Resistance Gene Detected but Failed to Meet Phenotypic Criteria

Organism	AmpC	ESBL	Cefoxitin	Ceftriaxone	Ceftazidime	Cefepime	Phenotypic AmpC	Phenotypic ESBL
Citrobacter freundii	CMY II		32 R	≤1 S	≤1 S	≤1 S		
Enterobacter cloacae complex	ACT/MIR		≤4 S	≤1 S	≤1 S	≤1 S		
Enterobacter cloacae complex	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter cloacae complex	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≤4 S	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		≥64 R	≤1 S	≤1 S	≤1 S		
Enterobacter species	ACT/MIR		8 S	≤1 S	≤1 S	≤1 S		
Morganella morganii	DHA		16 I	≤1 S	≤1 S	≤1 S		
Morganella morganii	DHA		≤4 S	2 S [a]	8 S [a]	≤1 S		
Escherichia coli		TEM 104K	≤4 S	≤1 S	≤1 S	≤1 S		
Serratia marcescens		SHV 238S+240K	16 I	4 S [a]	≤1 S	≤1 S	Yes	

[a]Resistant per EUCAST but not CLSI breakpoints

Results

170 isolates from 147 patients

Escherichia coli (n=83), *Klebsiella pneumoniae* (n=29), and *Enterobacter species* (n=21)

14 isolates with AmpC genes detected and 2 isolates with ESBL genes detected failed to meet phenotypic criteria

4 (19%) of 21 genotypic AmpC isolates were susceptible to cefoxitin and 3GC

Both genotypic ESBL *E. coli* and *S. marcescens* isolates were susceptible to 3GC.

Conclusion

16 (9.4%) additional resistant isolates were detected due to the addition of genotypic testing

Patients may have been treated with 3GC leading to possible treatment failure and poor outcomes

Combined testing could decrease treatment failure and be useful to monitor resistance prevalence

References

Paterson, David L., et al. "Outcome of cephalosporin treatment for serious infections due to apparently susceptible organisms producing extended-spectrum β-lactamases: implications for the clinical microbiology laboratory." *Journal of clinical microbiology* 39.6 (2001): 2206-2212.

Powell, Eleanor A., David Haslam, and Joel E. Mortensen. "Performance of the check-points check-MDR CT103XL assay utilizing the CDC/FDA antimicrobial resistance isolate bank." *Diagnostic Microbiology and Infectious Disease* 88.3 (2017): 219-221.