Detection of Gram Negative Resistance Markers Provided by a Syndromic Identification System

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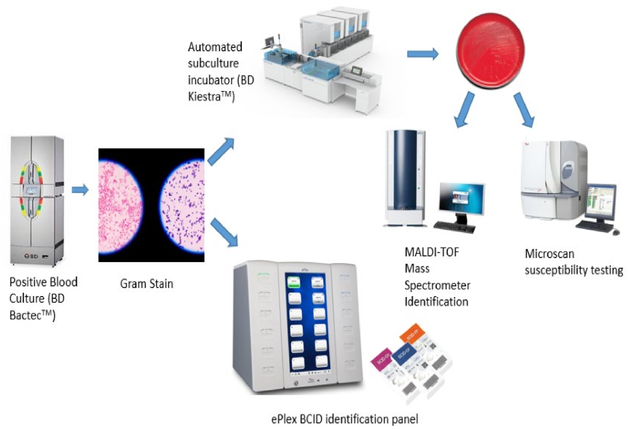
Background

Identification of pathogens from positive blood cultures is of highest importance in order to provide adequate therapy for bloodstream infections. With the risk of sepsis, the fast detection of antibiotic resistance genes is similarly important. The GenMark ePlex Blood Culture Identification Gram-Negative (BCID-GN) Panel, detects 21 gram-negative bacteria and 6 resistance genes. For this study, we focused on the accuracy of detection of the resistance genes on the BCID-GN panel compared to the phenotypical results of antimicrobial susceptibility testing (AST) on Microscan.

Methods

GenMark BCID panels were performed based on the gram stain of the first positive blood culture of each patient. Identification of all positive cultures was performed by MALDI-TOF, and susceptibility testing on Microscan. The comparative analysis of the detection of resistance markers (CTX-M, IMP, KPC, NDM, OXA and VIM) and AST by Microscan was performed using Northwell Health Laboratories Informatics Database.

Figure 1: Positive Blood Culture Workflow



RESULTS

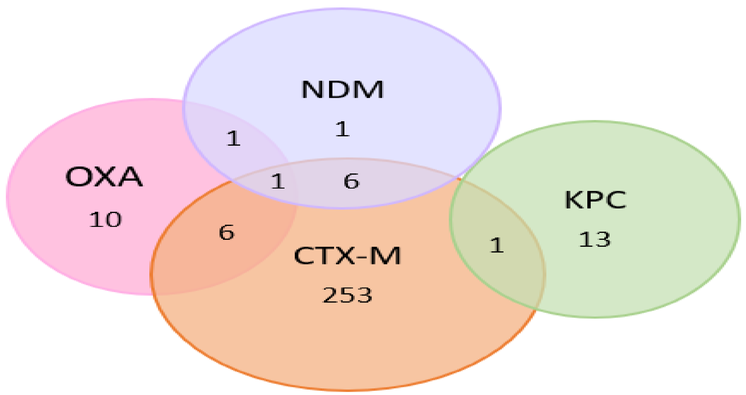
From January 4, 2021 to April 30, 2021, a grand total of 95,935 blood culture orders were received at Northwell Health Core Laboratory. There were 9,558 positives during the study period (10%). 5,228 were performed with all GenMark BCID panels, and a subset of 1,677 positives were tested with the BCID-GN panel only (32%). Enterobacteriaceae accounted for 1,381 positive bottles (82%). A total of 293 resistance genes were detected: 253 were CTX-M only. 40 results were linked with carbapenem resistance genes: 8 NDM, 14 KPC, and 17 OXA and one with a combination of NDM and OXA; no IMP or VIM. 14 carbapenem resistance markers were also linked with ESBL targets. 11 ESBL organisms were detected by culture only, suggestive of a different resistance mechanism than CTX-M. The overall pheno- and geno-typic concordance for ESBL was 93% (248 of 267).

Table 1: Distribution of Resistance Genes Among Different Isolates

Isolate	CTX-M	KPC	NDM	OXA
Escherichia coli	176	0	2	1
Klebsiella pneumoniae	51	14	3*	6*
Proteus mirabilis	32	0	0	1
Acinetobacter baumannii	0	0	0	10
Enterobacter cloacae complex	2	0	3	0
Salmonella typhi	2	0	0	0
Klebsiella variicola	2	0	0	0
Enterobacter aerogenes	1	0	0	0
Enterobacter cloacae	1	0	0	0
Citrobacter freundii complex	0	0	1	0
Total	267	14	9	18

*All Klebsiella pneumoniae with OXA / NDM have CTX-M resistance marker

Figure 2: Distribution of Resistance Genes



Summary

Table 2: Comparison of ESBL Detection between ePlex BCID and Microscan Susceptibility Testing

ePlex BCID CTX-M	ESBL Detection by Microscan		
	ESBL Organism	Non-ESBL Organism	Total
Det	264	3**	267
Not Det	11*	1399	1410
Total	275	1402	1677

*Due to phenotypic resistance mechanisms other than CTX-M

**Gene is detected by PCR, but it cannot encode a functional downstream actual resistance mechanism (CAP Magazine, May 2021)

Conclusions

The GenMark ePlex BCID-GN panel can accurately identify gram-negative resistance markers, such as ESBL and carbapenemases.

The high concordance of the GN panel to the Microscan for resistance markers indicates that the PCR based GenMark assay can provide fast and reliable results for improved antimicrobial stewardship.

95% of the circulating ESBL harboring organisms can be efficiently detected in blood by GenMark BCID with a fast turnaround time, providing physicians with reliable results to make effective treatment decisions for critical patients.