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Preliminary evaluation of KarbaDiag, a new rapid test for the detection of carbapenemase in bacterial colonies

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PRELIMINARY EVALUATION OF KARBADIAG, A NEW RAPID TEST FOR THE DETECTION OF CARBAPENEMASE IN BACTERIAL COLONIES

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Introduction

The antimicrobial resistance crisis clearly highlights the need for rapid diagnostic tests to quickly identify resistant bacteria and treat the patients accordingly.
Carbapenem-resistant Enterobacterales (CRE) are one of the most critical Antibiotic-resistant bacteria classified by WHO.
The present study reports performance evaluation of KarbaDiag, a new rapid test for CRE detection using clinical isolates.

Methods & Materials

Source organisms: A total of 212 clinical isolates were collected from various European and American hospitals in 2019 and 2020, including 19 carbapenemase- negative isolates (9%) and 193 (91%) carbapenem-resistant Enterobacterales (CRE) with various carbapenemase types. These were collected from various infection sources including respiratory, urinary tract, intra-abdominal and chorionic villus sampling.
Antimicrobial Assay: Molecular analysis was performed on all isolates and MIC determination on discordant results using CLSI guidelines (1).
Rapid diagnostic test KarbaDiag: The isolates were cultivated on blood agar for 24h at 37°C and analysed with KarbaDiag rapid test. KarbaDiag is a new rapid test based on lateral flow assay technology for the detection of five carbapenemase types including KPC-, NDM, IMP, VIM and OXA- 48. The test gives a results in 15 minutes, differentiate the type of carbapenemase and can reduce the time for AMR classification after cultivation of isolates.

Results

Figure 1: Test Procedure

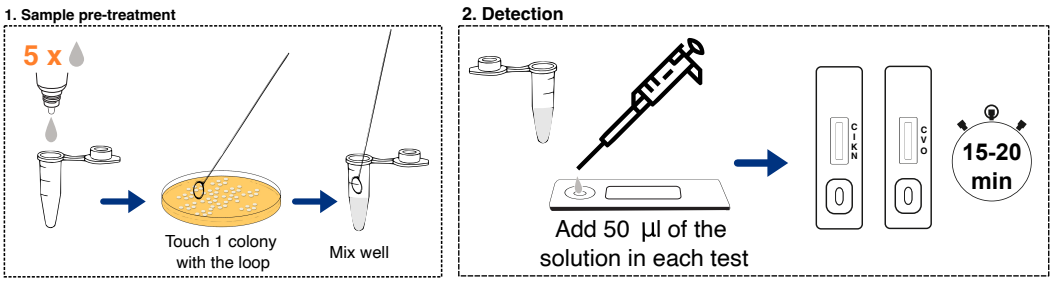


Figure 2: Positive control of the test

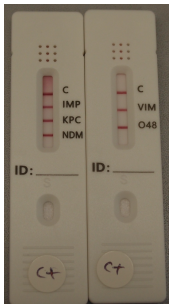
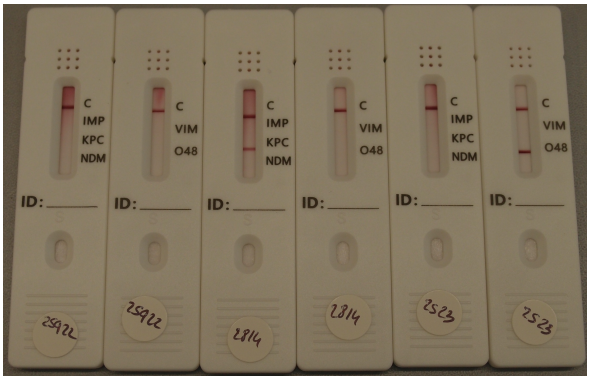
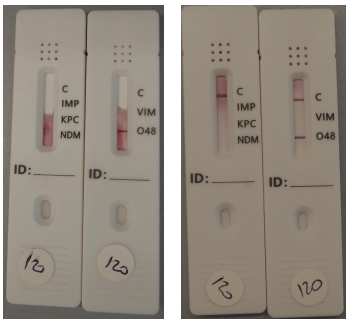


Figure 3: Examples of test results using ATCC reference strains



ATCC 25922 (negative control); ATCC 2814 (KPC-3 positive); ATCC 2523 (OXA-48 positive)

Figure 4: Optimization of sample preparation for mucous colonies



Klebsiella pneumoniae with OXA-232(c) gene was tested using the normal preocedure and a specific procedure for mucous colonies

Table 1: Carbapenemase variants detected during this study

Carbapenemase Type	Variants detected (previous study)	Variants detected (this study)
KPC	KPC-1, KPC-2, KPC-3, KPC-74	KPC-2, KPC-3, KPC-4, KPC-27
OXA	OXA-23 OXA-163, OXA-181, OXA-232	OXA-48(c), OXA-48 Type(u) OXA-181(c), OXA-232(c) OXA-244(c)
NDM	NDM-1, NDM-5, NDM-7	NDM-1, NDM-2, NDM-5, NDM-6, NDM-7
IMP	IMP-1, IMP-3, IMP-4, IMP-6, IMP-10, IMP-25, IMP-26, IMP-30, IMP-34, IMP-38, IMP-40, IMP-42	IMP-1, IMP-4, IMP-6, IMP-7, IMP-10, IMP-26
VIM	VIM-1, VIM-2, VIM-4, VIM-5, VIM-9, VIM-10	VIM-1, VIM-2

Table 2: KarbaDiag Rapid test results compared to genetic and MIC analysis

KPC	+	-	**Sensitivity**	**100%**	(CI95%: 87-100%)
+	32	0	**Specificity**	**100%**	(CI95%: 97-100%)
-	0	180	**PPV**	**100%**	(CI95%: 87-100%)
			NPV	**100%**	(CI95%: 97-100%)
OXA	+	-	**Sensitivity**	**98%**	(CI95%: 90-100%)
+	58	2	**Specificity**	**99%**	(CI95%: 95-100%)
-	1	149	**PPV**	**97%**	(CI95%: 87-99%)
			NPV	**99%**	(CI95%: 96-100%)
NDM	+	-	**Sensitivity**	**97%**	(CI95%: 89-99%)
+	65	1	**Specificity**	**99%**	(CI95%: 95-100%)
-	2	139	**PPV**	**98%**	(CI95%: 91-100%)
			NPV	**99%**	(CI95%: 94-100%)
IMP	+	-	**Sensitivity**	**93%**	(CI95%: 66-100%)
+	14	0	**Specificity**	**100%**	(CI95%: 98-100%)
-	* 1	190	**PPV**	**100%**	(CI95%: 73-100%)
			NPV	**99%**	(CI95%: 97-100%)
VIM	+	-	**Sensitivity**	**100%**	(CI95%: 85-100%)
+	29	0	**Specificity**	**100%**	(CI95%: 97-100%)
-	0	183	**PPV**	**100%**	(CI95%: 85-100%)
			NPV	**100%**	(CI95%: 97-100%)

* IMP-8 variants were not detected using the rapid test and were excluded of the table

Conclusions

KarbaDiag exhibited high diagnostic performance for KPC, OXA, NDM, IMP and VIM type carbapenemase with sensitivity and specificity greater than 90%. For NDM and OXA types, 2 isolates for both types showed positive genetic analysis but the MIC determinations were negative, indicating that the carbapenemase was not expressed in these conditions. Regarding the IMP-8 variant, not detected using the test, it is a low prevalent variant and mostly detected in Asian isolates (2). These preliminary data are encouraging and suggest that of the KarbaDiag rapid test may prove useful in the detection of the majority of carbapenemase variants.

References

1. CLSI, 2018. *Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically. 11th ed.* CLSI Standard M07. CLSI, Wayne, PA, USA
2. Matsumura et al. (2017), *Global molecular epidemiology of IMP-producing Enterobacteriaceae.* Antimicrob Agents Chemother, 61 :e02729-16.

Acknowledgments

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