"QMC early evaluation of the Mobidiag CarbaR+ test"

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Introduction

Carbapenemase producing organisms (CPO) are of major worldwide public health concern [1][2]. Rapid detection of these genes is vital to improve patient care, and to minimise onward transmission of infection. Standard diagnostic methods in many clinical laboratories are time consuming, and are limited in the range of Carbapenemase genes they detect [3]. As such, there is a demand in diagnostic laboratories for highly-sensitive, specific and rapid diagnostic systems for better management of risks associated with CPOs.

Aim: To evaluate the performance of Novodiag CarbaR+ panel (Version 1-0, Ref- NVD-CRB-012, LOT-00311048, October 2018)

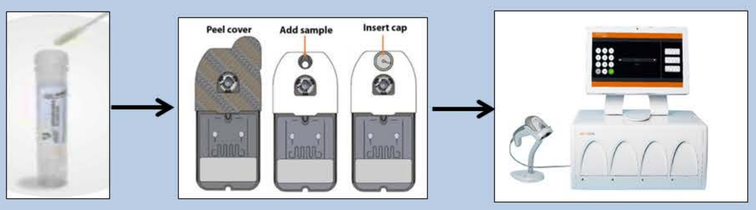
Type of evaluation (CarbaR +test)

Aspect 1: Testing of known Carbapenemase positive isolates to evaluate test performance

Aspect 2: Evaluation of performance against culture with simulated rectal swab specimens for the provided limit of detection (LOD) 1x, 3x and 10x

CarbaR+ test – An easy to run assay

1. Inactivation of sample in eNAT tubes (minimum 30 minutes)
2. Loading of sample on cartridge (600µl)
3. Cartridge run (80 minutes) on Novodiiag system



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Evaluation Methods

Aspect 1

70 different isolates from NUH pathogen bank were selected to evaluate the Carba R+ cartridge test performance.

Of these, 45 with defined carbapenemase genes, and 25 with unknown carbapenem resistance mechanisms.

Aspect 2

13 Carbapenemase possessing isolates tested positive in aspect 1 study, were selected to evaluate the performance of CarbaR+ in simulated rectal swab specimens.

Results

Aspect 1

Target genes	Isolate selected	Included in the Test panel	Detected during evaluation	Missed	Extra marker detected
KPC	7 isolates	Yes	9	None	2x KPC
OXA-48 like	13 isolates	Yes	13	None	
NDM	12 isolates	Yes	11	1x NDM	
VIM	3 isolates	Yes	3	None	
IMP	4 isolates	Yes	4	none	
OXA–type carbapenemase including OXA-23, 40, and OXA-51 group with unknown ISAbal promotor	5 isolates with 6 marker	Yes	4	2x OXA-51	1x OXA-51
IMI or SME	2 isolates	No	N/A	N/A	N/A
Others with unidentified genes but known Carbapenam resistant	25 isolates	Yes	21 negative	NONE	4x OXA-23
Total	47 total markers in isolates	45 studied	42 detected	3 missed	7 extra detected

Summary of marker detection in Aspect one study

42/45 target markers were detected

7 extra markers were detected which were not detected before

3 target markers were not identified by Novodiag CarbaR+.
These targets were also not detected by reference runs

Aspect 2

Isolate	Resistance Gene	Strain	MALDI ID	Detected targets on NOVODIAG CarbaR+	CFU/ml	Detected on 1XLOD	Detected on 3XLOD	Detected on 10XLOD
3	KPC	K. pneumoniae	2.28	KPC	69x10^6	Yes	Yes	Yes
4	KPC	K. pneumoniae	2.34	KPC	47x10^6	Yes	Yes	Yes
5	OXA-23	A. baumannii	2.38	OXA-23	58x10^6	Yes	Yes	Yes
6	OXA-40	A. baumannii	2.04	OXA-24	57x10^6	Yes	Yes	Yes
7[a]	OXA-23	A. baumannii	2.38	OXA-23/OXA-51	33.9x10^6	Yes OXA-23/missed OXA-51	YesX2	Yes
8	VIM	P. aeruginosa	2.43	VIM	44x10^6	Yes	Yes	Yes
9	VIM	P. aeruginosa	2.43	VIM	32x10^6	Yes	Yes	Yes
11	IMP	P. aeruginosa	2.51	IMP	71x10^6	No	No	Yes
26	OXA-48	E. coli	2.21	OXA-48/181	116x10^6	No	Yes	Yes
32	NDM-1	E. aerogenes	2.23	NDM	101x10^6	No	No	Yes
36	OXA-48	K. pneumoniae	2.4	OXA-48/181	77x10^6	Yes	Yes	Yes
38	IMP	P. aeruginosa	2.55	IMP	53x10^6	No	Yes®	Yes
43[b]	NDM-1	P. mirabilis	2.46	NDM	29.4x10^6	Yes	Yes	Yes
Total				14	Detected	9	12	14
Percentage						64%	86%	100%

Summary of detection rate in Aspect 2 study

Detection rate

1xLOD dilutions = 64%
3xLOD dilutions = 86%
10xLOD dilutions = 100%

Discussion

- Carbapenemase producing isolates could lose their plasmid in subsequent sub-culture if non-selective plates are used, resulting in unexpected test results.
- Unavailability of confirmatory test in our laboratory to rule out true negative/true positive results
- Presence of ISAbal promoter gene on isolate bearing OXA-51 marker is unknown. Novodiag Carba R+ only detects OXA-51 in presence of ISAbal promoter.
- Low detection rate on lower dilution, could be related to non-selective plate subsequent subculture (loss of plasmid).

	True Positive	True Negative	False Positive	False Negative	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
KPC	7	91	2	0	100	96.83	77.78	100
NDM	11	58	0	1	91.67	100	100	98.31
IMP	4	66	0	0	100	100	100	100
OXA-23[a]	3	63	4	0	100	94.03	42.86	100
OXA-24	1	69	0	0	100	100	100	100
OXA-48/181	13	57	0	0	100	100	100	100
OXA-51[b]	0	67	1	2	0	98.53	0	97.1
OXA-58[c]	0	70	0	0	N/A	100	N/A	100
VIM	3	67	0	0	100	100	100	100
MCR-1[c]	0	70	0	0	N/A	100	N/A	100

Analytical performance data for the Novodiag CarbaR+ Panel

[a] No method available to confirm gene presence.
[b] Only detected when the ISAb1 promoter is present.
[c] Not investigated in this study – no characterised strains available.

Conclusion

- The detection rate of Novodiag CarbaR+ test is very promising. It includes a wider range of Carbapenemase markers compared to a diagnostic assay e.g. Cepheid currently used by NUH. It has potential to improve diagnostic efficacy within a busy diagnostic laboratory.
- The assay is operator friendly, easy to run, interpret and requires minimum hands on time.
- Reliable test results with in-built internal control system.
- Single use, test specific cartridges are easy to identify with clear label test information and can be stored at room temperature
- eNAT tube chemical deactivation allows for safe specimen handling within the laboratory area, so can easily fit with laboratory demands and workflow.

Acknowledgements

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References

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