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Evaluation of MIC Test Strips (MTS) gradient-diffusion system for susceptibility testing of NDM-1 positive *Klebsiella pneumoniae* and *Escherichia coli*

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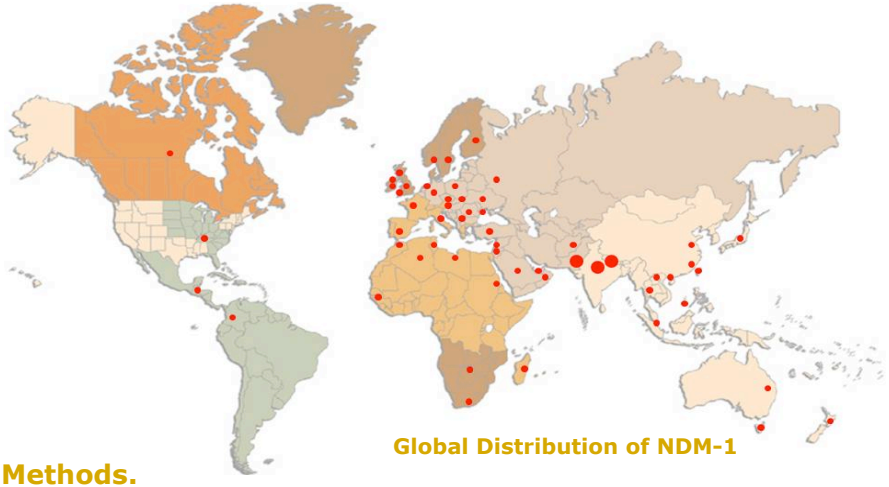
Introduction.

The rapid dissemination of NDM-1 positive Enterobacteriaceae is unprecedented among resistance genotypes (Figure). NDM-1 positive *Klebsiella pneumoniae* and *Escherichia coli* are highly resistant to most antimicrobials and represent particular challenges for antibiotic treatment. Due to the limited treatment options, accurate determination of minimum inhibitory concentrations (MICs) to those few antibiotics active is becoming increasingly important to guide the therapy. Herein we evaluated the performance of a new gradient-diffusion system for MIC determination (MTS) of NDM-1 positive *K. pneumoniae* and *E. coli* non-clonal isolates.



Global Distribution of NDM-1

Methods.

72 NDM-1 positive *K. pneumoniae* and *E. coli* non-clonal isolates (19 *Escherichia coli* and 53 *Klebsiella pneumoniae*) collected from 4 different countries and tested in triplicate for reproducibility. MICs of fosfomycin, nitrofurantoin, rifampicin and colistin were determined in parallel by MIC Test Strips (MTS) (Liofilchem, Italy) and by agar dilution (AD) method on MH agar. Results were interpreted according to EUCAST v 2.0 clinical breakpoints. MIC agreement between the two methods was defined as ±1 log2 dilution difference in MIC. Interpretive error rate for MTS vs. AD was calculated as follows: a major error was assumed if the isolate was classified as resistant by one method and as susceptible by another; a minor error was considered if the isolate was categorized as intermediate by one method and as either susceptible or resistant by another.

Results.

A total of 852 antibiotic-isolate combinations were evaluated (Table 1) and compared (Table 2). Overall agreement of MIC values was above 90%, with a specific agreement ranging from 88.9% to 94.4%. The major interpretive error rates ranged from 0% to 10.6% (Table 2). The reproducibility from performing the MTS in triplicate was 96.5% when taken as ±1 log2 dilution difference in MIC.

Table 1. MICs for fosfomycin, nitrofurantoin, rifampicin and colistin with NDM-1 positive *Klebsiella pneumoniae* (KP) and *Escherichia coli* (EC) using MTS.

Cardiff #	Genus/species	MTS-Rif	MTS-Nit	MTS-Fos	MTS-Col
10K	Klebsiella	>256	256	1.5	0.5
13	*E. coli*	6	>512	1.5	1.5
14	E. coli	>256	>512	2	0.75
15	Klebsiella	6	48	8	1
19k	Klebsiella	>256	>512	12	0.75
20K	Klebsiella	>256	>512	16	0.75
21	Klebsiella	>256	>512	12	0.5
25	Klebsiella	>256	>512	32	0.75
26	E. coli	>256	>512	2	0.5
29	E.coli	>256	16	1.5	1
3	E. coli	6	>512	1.5	0.75
30	E.coli	6	24	0.75	1.5
31	E. coli	8	>512	1.5	0.75
32	C. freundii	8	>512	16	1
34	Klebsiella	16	128	8	1
35	Klebsiella	>256	>512	12	0.75
43	Klebsiella	6	64	6	0.75
45	E. coli	8	24	1	0.75
5	E. coli	6	48	0.75	0.125
54	Klebsiella	8	128	8	1
57	Pr. rettgeri	4	32	1.5	1
60	E.coli	8	32	2	1
62K	Klebsiella	>256	256	8	0.75
8	Klebsiella	>256	>512	12	1
HR2	Klebsiella	6	48	8	1
L5	Klebsiella	8	>512	4	0.75
L23	Klebsiella	2	12	1	0.5
33-5	Klebsiella	8	>512	2	1
KI	Klebsiella	6	96	64	1
HR1	Klebsiella	4	48	8	0.75
17	Klebsiella	>256	>512	16	0.75
IR22	E. coli	8	256	2	0.75
IR11K	Klebsiella	>256	512	12	0.75
IR16	Klebsiella	8	192	16	0.75
IR15II	Klebsiella	6	>512	6	1

Table 2. Comparative performance of MIC determination by MTS and AD methods for NDM-1 positive *Klebsiella pneumoniae* (KP) and *Escherichia coli* (EC).
NA = not applicable.

Abx	% MIC Agreement			% Interpretative Errors			
				Major		Minor	
	KP	EC	Total	KP	EC	KP	EC
Fos	90.6	89.5	90.3	7.5	5.3	NA	NA
Rif	88.7	89.5	88.9	8.3	10	NA	NA
Nitro	96.2	94.7	94.4	5.7	5.3	NA	NA
Col	98.1	89.5	95.3	0	0	0	0

Abx: Antibiotic; Fos: fosfomycin; Nitro: nitrofurantoin; Rif: rifampicin and Col: colistin

Conclusions. The MTS method demonstrated overall good agreement with the AD method both in terms of MIC agreement and accurate classification of isolates into susceptibility categories. Importantly we could not find any major or minor errors when testing with colistin. Accordingly, it can be recommended for NDM-1 positive Enterobacteriaceae.

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