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Zohra Chaudhry
Henry Ford Health System

Hind Hadid
Henry Ford Health System

Mary B. Perri
Henry Ford Health System

Marcus J. Zervos
Henry Ford Health System

Indira Brar
Henry Ford Health System

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Increasing incidence of multi-drug resistant organisms (MDROs): An emerging global concern

Zohra Chaudhry MD, Hind Hadid MD, Mary B Perri MT, Marcus Zervos MD, Indira Brar MD
Infectious Disease, Henry Ford Health System, Detroit, Michigan

Introduction:

- With massive efflux of civilians from violence-stricken countries, the high rates of colonization with multidrug-resistant organisms (MDROs) amongst the refugees is an emerging global concern.
- Our case report describes two Middle Eastern patients
 - suffered severe traumatic injuries in their home countries,
 - subsequently developing chronic wounds.
- Upon arrival to the United States, the patients sought treatment in our institution for wound infection with MDRO

Objectives:

1. Describe the patients' clinical characteristics and risk factors for MDRO colonization.
2. Elucidate the susceptibility pattern of bacterial isolates from our patients, highlighting how our experimental studies helped choosing antibiotic therapy.
3. Describe the treatment and clinical outcome of the patients.

Materials and Methods:

- Clinical data was collected from the patients' charts
- Identification (MALDI-TOF[®] MS, bioMerieux, Inc., Durham, NC) and susceptibility (Vitek-2[®], bioMerieux, Inc., Durham, NC) of the organisms from the wound performed as part of routine identification/susceptibility test in the clinical microbiology laboratory.
- MICs performed by manual microbroth dilution according to Clinical and Laboratory Standards Institute (CLSI) guidelines.
- Time kill curves used to determine in vitro synergy of *Pseudomonas aeruginosa* isolate in antibiotic combinations:
 - ½ x MIC meropenem plus ½ x MIC colistin,
 - ½ x MIC meropenem plus ½ x MIC colistin plus ½ x MIC rifampin, and
 - ½ x MIC meropenem plus ½ x MIC ceftazidime/avibactam utilizing a starting inoculum of 10⁵ CFU/ml.

Materials and methods:

- Mueller Hinton II broth (Becton, Dickenson and Co., Sparks, MD) was used (Table 1).
- Antibiotics prepared at 100X concentration being tested in two or three tubes:
 - with each ½ x MIC antibiotic alone,
 - a synergy tube with combination of two or three ½ x MIC antibiotics and
 - growth control tube
- Samples were serially diluted at 0, 4 and 24 hours and
- plated on TSA II agar (Becton, Dickinson, and Co., Sparks, NC).

	MIC Mero	MIC Mero used	MIC Col	MIC Col used	MIC Rif	MIC Rif used	MIC Ceft/avi	MIC Ceft/avi used	Synergy
102053	16	8	1	0.5					No
102053	16	8	1	0.5	32	16			Yes
102053	16	8					32	16	No

(Table 1)

Materials and methods:

- Time kill curves were constructed by plotting colony counts over time,
- With synergy being defined as:
 - ≥ 2 -log₁₀ decrease in CFU/ml between the combination and its most active constituent after 24hrs,
 - the number of surviving organisms in the presence of combination must be ≥ 2 log₁₀ CFU/ml below the starting inoculum

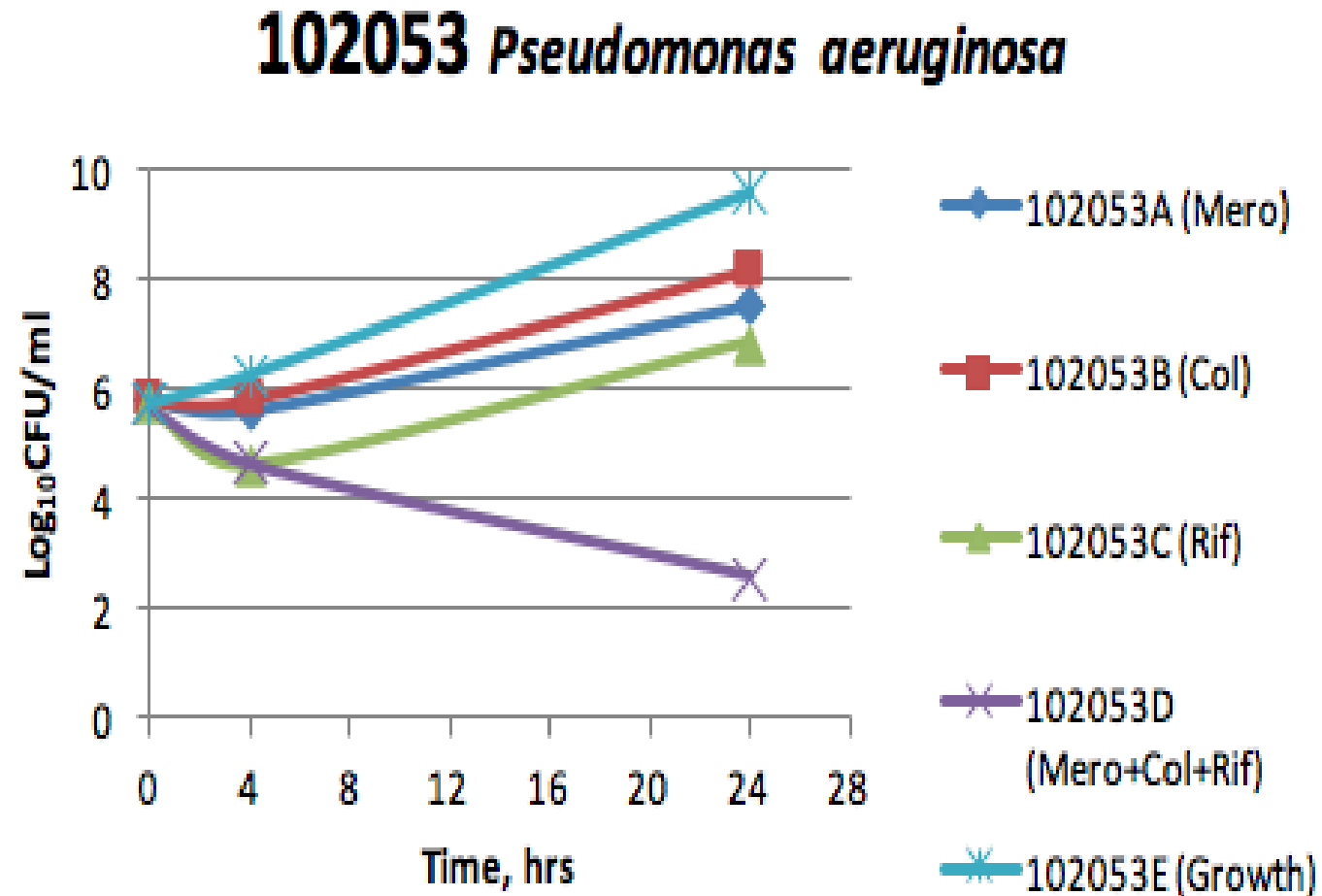


Figure 1: Time kill synergy curve of synergistic combination of meropenem, colistin and rifampin

Results:

- Patient 1 came from Syria
- Patient 2 from Yemen
- Both patients' wound infections were healthcare-associated,
 - with underlying chronic osteomyelitis
- Both had multiple risk factors for MDRO, including multiple prior surgeries and antibiotic courses.

Results:

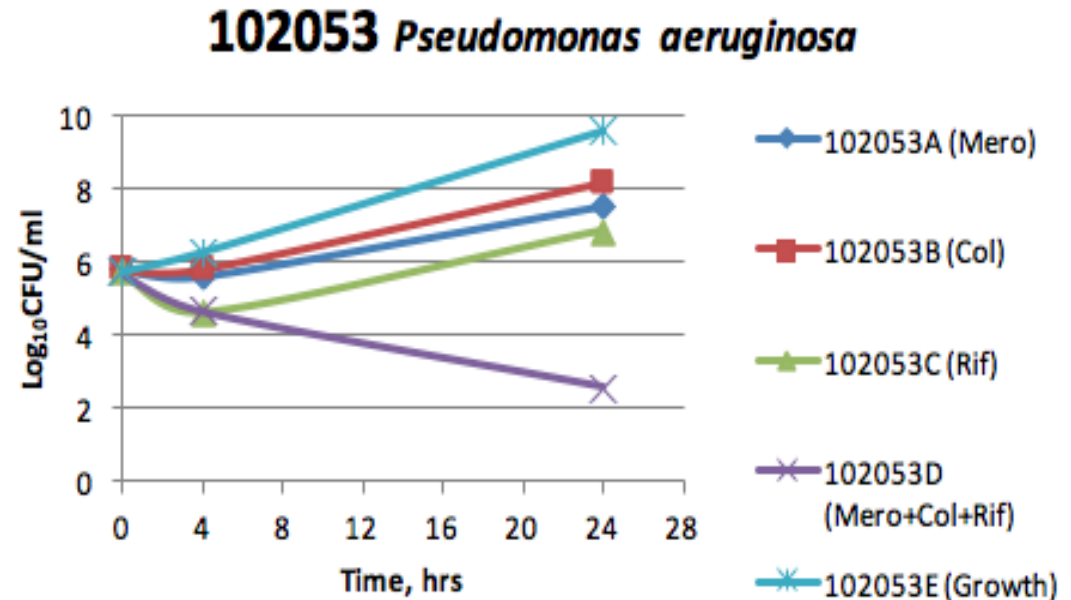
- Patient 1 culture grew:
 - CRE *Klebsiella*
 - MDR *Morganella*, and
 - on a later date, ESBL *Escherichia coli*.
- Patient 2 culture grew:
 - CRE *Pseudomonas aeruginosa*, sensitive only to colistin (Figure 2).

Culture & Susceptibility		
<i>PSEUDOMONAS AERUGINOSA</i>		
Antibiotic	Kirby Bauer	Microscan
Amikacin	Resistant	Resistant
Aztreonam	Resistant	Resistant
Cefepime	Resistant	>=64 Resistant
Ceftazidime Avibact	Resistant	Resistant
Ceftolozane Tazobactam	Resistant	Resistant
Ciprofloxacin	Resistant	>=4 Resistant
Colistin	Susceptible	0.5 Susceptible
Fosfomycin	Intermediate	96 Intermediate
Gentamicin	Resistant	>=16 Resistant
Meropenem	Resistant	>=16 Resistant
Piperacillin/Tazobactam	Resistant	Resistant
Tobramycin	Resistant	>=16 Resistant

(Figure 2).

Results:

- Patient 1 was treated with ceftazidime-avibactam
- Patient 2 received rifampin + meropenem + colistin,
 - the only antibiotic combination demonstrating in-vitro synergistic killing (Figure 1).
- Both patients required prolonged therapy up to to 6-weeks
- Doing well on follow up



Conclusions:

- Colonization with MDRO amongst Middle Eastern immigrants is an alarming phenomenon.
- In-vitro experiments with available antibacterial agents may assist in the choice of therapy for MDRO strains when conventional options are exhausted.

Questions?

Thank you!