Poster #1652

National Differences in the Presentation and Management of Patients With Nosocomial Pneumonia Due to *Pseudomonas aeruginosa*

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INTRODUCTION

- Nosocomial pneumonia (NP), comprising hospital-associated pneumonia (HAP), ventilator-associated pneumonia (VAP), and healthcare-associated pneumonia (HCAP), is a prevalent hospital-acquired infection associated with increased morbidity, mortality, and prolongation of hospital stay.
- Recent trends show an increase in the prevalence of NP caused by multidrug-resistant (MDR) bacteria, most commonly *Pseudomonas aeruginosa* with documented resistance to β-lactams, carbapenems, aminoglycosides, and fluoroquinolones.[1-3]
- The therapeutic effectiveness of current therapies for NP, and especially VAP, is limited by the increasing prevalence of pathogens that express extended-spectrum β-lactamases (ESBLs), AmpC β-lactamases, or methicillin resistance, emphasizing the need for development of new and effective antimicrobials.[2]
- Prompt and adequate initial antimicrobial therapy has been shown to reduce mortality and improve morbidity associated with NP.[4]

OBJECTIVE

- This study evaluated regional differences in *P. aeruginosa* NP among hospitals in France, Germany, Italy, Spain, and the United States.

METHODS

Study Design

- This retrospective multicenter, hospital-based, medical record abstraction study collected data on hospitalized patients with a clinical diagnosis of NP comprising HAP, VAP, and HCAP, due to *P. aeruginosa*.
  - HAP was defined as pneumonia that occurred more than 48 hours after admission.
  - VAP was defined as pneumonia that occurred more than 48 hours after endotracheal intubation.
  - HCAP was defined as pneumonia that occurred in patients who were hospitalized in an acute care hospital for 2 or more days within 90 days of the infection; resided in a nursing home or long-term care facility; received recent intravenous antibiotic therapy, chemotherapy, or wound care within the past 30 days of the current infection; or attended a hospital or hemodialysis clinic.

METHODS (cont'd)

Inclusion Criteria

1. Age 18 years or older
2. Admitted for index hospitalization 36 months prior to study initiation at each site
3. Clinical diagnosis of NP defined as findings consistent with pneumonia on chest x-ray or computed tomography scan and either temperature >38.3°C or leukocytosis >10,000 cells/mm^3 or both
4. Microbiological cultures (qualitative or quantitative) obtained within the 24-hour period surrounding initiation of antibiotics
5. *P. aeruginosa* organism cultured from a respiratory specimen, including sputum, pleural puncture, flexible bronchoscopy with protected specimen brush, bronchoalveolar fluid, "mini-BAL" (bronchoalveolar lavage) or transbronchial biopsy, and tracheobronchial aspirate in intubated patients

Key Variable Definitions

- Susceptibility[5] was as described in medical records based on local laboratory results:
  - Resistant (R) was defined as resistant or intermediate susceptibility to 1 or 2 antibacterial drugs.
  - MDR was defined as resistant or intermediate susceptibility to at least 1 drug in ≥3 anti-pseudomonal classes.
  - All other infections were defined as susceptible (S).
- Appropriate therapy was defined as an antibiotic that was initiated within 24 hours of the diagnosis date and demonstrated in vitro activity.

RESULTS

Table 1. Patient Baseline Characteristics by Country

	France (n = 141)	Germany (n = 120)	Italy (n = 108)	Spain (n = 115)	United States (n = 178)
Number of sites	2	2	2	3	2
Age, y, mean (SD)	59 (16)	49 (17)	64 (15)	62 (15)	60 (16)
Gender, male, n (%)	108 (77)	70 (58)	79 (73)	84 (73)	109 (61)
Location prior to hospitalization, n (%)					
Home	6 (4)	44 (37)	79 (75)	93 (82)	103 (58)
Skilled nursing facility	23 (16)	1 (1)	0 (0)	5 (4)	16 (9)
Long-term care facility	8 (6)	5 (4)	4 (4)	2 (2)	8 (4)
Assisted living	4 (3)	2 (2)	0 (0)	1 (1)	0 (0)
Inpatient rehabilitation	0 (0)	33 (28)	1 (1)	2 (2)	11 (6)
Other	99 (71)	33 (28)	22 (21)	11 (10)	40 (22)
Unknown	1 (1)	2 (2)	2 (2)	1 (1)	0
Coexisting conditions, n/N (%)					
Sepsis	16/141 (11)	29/120 (24)	6/99 (6)	26/115 (23)	29/124 (23)
Acute coronary syndrome	14/141 (10)	14/120 (12)	6/98 (6)	5/114 (4)	37/114 (32)
Valvular heart disease	16/141 (11)	14/120 (12)	3/99 (3)	4/112 (4)	34/119 (29)
Hypertension	53/141 (38)	43/117 (37)	48/99 (48)	41/115 (36)	118/163 (72)
Venous thromboembolism	4/141 (3)	9/120 (8)	1/99 (1)	1/115 (1)	32/125 (26)
COPD/asthma	23/141 (16)	17/120 (14)	17/99 (17)	41/113 (36)	54/133 (41)
Other respiratory disease	19/141 (13)	73/117 (62)	10/99 (10)	24/111 (22)	49/119 (41)
Diabetes	24/140 (17)	48/119 (40)	28/108 (26)	31/110 (28)	61/121 (50)
Chronic kidney disease	14/141 (10)	46/119 (39)	12/108 (11)	25/99 (25)	44/126 (35)
Chronic liver disease	7/140 (5)	45/119 (38)	7/108 (6)	14/98 (14)	15/109 (14)
NP category, n (%)					
HAP	30 (21)	26 (22)	15 (14)	35 (30)	39 (22)
HCAP	11 (8)	59 (49)	3 (3)	22 (19)	96 (54)
VAP	100 (71)	35 (29)	90 (83)	58 (50)	43 (24)
Hospitalized in prior 6 months, n/N (%)	66/141 (47)	80/117 (68)	17/41 (41)	56/101 (55)	112/169 (66)
Antimicrobials in prior 30 days, n (%)	69 (49)	54 (45)	8 (7)	29 (25)	65 (37)
Admitted to ICU, n (%)	105 (74)	108 (90)	104 (96)	96 (83)	77 (43)

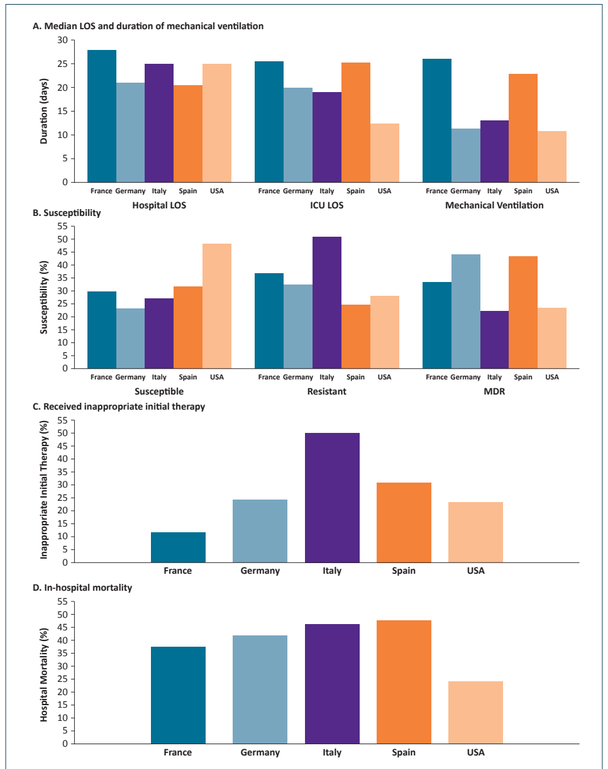
COPD = chronic obstructive pulmonary disease; ICU = intensive care unit.

Table 2. Antibiogram by Country

	No. Isolates (Susceptible %)				
Antibiotic	France	Germany	Italy	Spain	United States
Aminoglycoside	141 (77)	120 (58)	101 (75)	112 (59)	177 (79)
AP-PCN + β-lactamase Inhibitor	141 (65)	118 (47)	101 (70)	110 (64)	173 (79)
Carbapenem	139 (60)	119 (52)	107 (58)	112 (47)	177 (77)
AP Cephalosporin	140 (77)	120 (61)	101 (74)	111 (59)	178 (83)
Fosfomycin	138 (73)	42 (33)	11 (45)	N/A	N/A
Aztreonam	136 (70)	35 (14)	27 (11)	60 (53)	107 (52)
Ciprofloxacin	138 (67)	118 (61)	100 (75)	111 (52)	177 (76)
Colistin	15 (93)	68 (100)	102 (99)	81 (100)	100 (81)

Aminoglycoside: amikacin, gentamicin, tobramycin.
Antipseudomonal penicillin (AP-PCN) + β-lactamase inhibitor: piperacillin/tazobactam, ticarcillin/clavulanate.
Carbapenem: doripenem, imipenem/cilastatin, meropenem.
Antipseudomonal cephalosporin: cefepime, ceftazidime.

Figure 1. Patients' Outcomes by Country



LOS = length of stay after diagnosis of *P. aeruginosa* NP.

CONCLUSIONS

- NP due to *P. aeruginosa* imposes a substantial clinical and economic burden across countries. Local epidemiology and prevalence of resistance are major determinants of differences in resource utilization and clinical outcomes.
- Policies, guidelines, and treatment algorithms for *P. aeruginosa* NP must be tailored to reflect the regional differences in epidemiology and prevalence of resistance.

REFERENCES

1. Richards MJ, et al. *Crit Care Med.* 1999;27:887-892.
2. Joseph NM, et al. *Eur J Intern Med.* 2010;21:360-368.
3. Rea-Neto A, et al. *Crit Care.* 2008;12:R56.
4. Rello J. *Eur Respir Rev.* 2007;16:33-39.
5. Magiorakos AP, et al. *Clin Microbiol Infect.* 2012;18:268-281.

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