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A Multicenter Evaluation of Pathogen Distribution in Patients Hospitalized With Culture-Positive Pneumonia in the United States

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BACKGROUND

- Pneumonia affects >6 million patients each year in the United States and is associated with significant morbidity and mortality
- The microbiological diagnosis of community-acquired bacterial pneumonia (CABP) has proven difficult with standard culture methods and can vary by clinical setting, complicating the selection of appropriate empiric antimicrobial treatment

OBJECTIVE

- The objective of this study was to describe the epidemiology of bacteria in patients with culture-positive CABP who received empiric antibiotic therapy and were admitted to acute-care hospitals in the United States

METHODS

- We analyzed first positive bacterial respiratory isolates for patients with primary or secondary *International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM)* codes for pneumonia and treated with empiric antibiotic therapy who were discharged from 68 acute-care hospitals in the BD Insights Research Database (Becton, Dickinson and Company, Franklin Lakes, NJ, USA) **(Table 1)**
- Admissions were further classified as follows, based on distribution of ICD-10-CM codes **(Table 2)**: community-acquired pneumonia (CAP) A (unspecified bacteria or bacteria included within the spectrum of activity for lefamulin), CAP B (acute lower respiratory tract infections), CAP C (viral), CAP D (Gram-negative bacteria outside of spectrum of activity for lefamulin), and multiple categories
- Gram-positive (GP), Gram-negative (GN), and other respiratory bacterial pathogens in CAP A and CAP B were included if collected within 3 days of admission and were further categorized as collected in an intensive care unit (ICU) or non-ICU setting
- Respiratory cultures and urine antigen were used to identify *Streptococcus pneumoniae* and *Legionella pneumophila*, and respiratory cultures and serologies were used to identify *Mycoplasma pneumoniae*

METHODS (continued)

- Healthcare-associated (HCA) episodes were defined as admitted from another acute-care facility, skilled nursing facility, long-term acute-care hospital, rehabilitation center, or hospice, admission in the prior 30 days, presence of a dialysis ICD-10-CM Z99.2 (dependence on renal dialysis) or cancer comorbidity as identified in the Agency for Healthcare Research and Quality Clinical Classifications Software comorbidity classification
- The Fisher's exact test was used to test for significance

Table 1. US Hospital Characteristics

	BD Facilities, *n* (%) *n*=68	CMS, % *n*=4656
Region		
Northeast	5 (7.4)	12.3
South	32 (47.1)	37.9
Midwest	26 (38.2)	29.9
West	5 (7.4)	19.9
Urban/rural		
Urban	62 (91.2)	59.2
Rural	6 (8.8)	40.8
Medical school affiliation		
Major	4 (5.9)	9.3
Limited	12 (17.6)	13.7
Graduate	2 (2.9)	2.7
No affiliation	50 (73.5)	74.3
Number of beds		
<100	12 (17.6)	51.0
100–300	27 (39.7)	29.3
>300	29 (42.6)	19.7

BD=Becton, Dickinson and Company; CMS=Centers for Medicare & Medicaid Services (USA).

RESULTS

- Of 1875 CAP A and CAP B admissions with pathogens identified by serology or respiratory cultures collected within 3 days of admission and treated with empiric antibiotic therapy, 1035 (55.2%) were in the ICU and 634 (33.8%) had HCA risk factors **(Tables 2 and 3)**
- Overall, 61.9%, 37.1%, and 9.1% were positive for GP, GN or other bacterial pathogens, respectively. *Staphylococcus aureus* (43.9%) *S. pneumoniae* (19.0%), *Haemophila influenzae* (9.9%), and *Pseudomonas aeruginosa* (9.2%) were the most common bacterial pathogens, representing 81.9% of all episodes

RESULTS (continued)

- Methicillin-resistant *S. aureus* (MRSA) represented 55.4% of *S. aureus* episodes and 24.3% of all culture-positive episodes
- *S. aureus* (52.8% vs 32.8%; *P*<0.0001) and MRSA (27.9% vs 19.8%; *P*<0.0001) were more common in the ICU vs non-ICU setting; *S. pneumoniae* (21.4% vs 17.0%; *P*=0.0178) and *M. pneumoniae* (7.7% vs 2.2%; *P*<0.0001) were more common in the non-ICU setting **(Table 4)**
- MRSA (29.2% vs 21.8%; *P*<0.0001) was more common in those with HCA vs. non-HCA status, and *S. pneumoniae* (21.4% vs 14.82; *P*<0.0001) was more common in non-HCA vs HCA status **(Table 5)**

Table 2. Pathogen Distribution by CAP Categories in Admissions Treated With Empiric Antibiotic Therapy

Pathogen	CAP A	CAP B	CAP C	CAP D	Multiple	Overall
Total admissions, *n* (%)	1683 (53.2)	192 (6.1)	21 (0.7)	588 (18.6)	677 (21.4)	3161 (100)
Gram-positive	1106 (65.7)	75 (39.1)	11 (52.4)	28 (4.8)	348 (51.4)	1568 (49.6)
S. aureus	774 (46.0)	48 (25.0)	7 (33.3)	24 (4.1)	241 (35.6)	1094 (34.6)
MSSA	353 (21.0)	14 (7.3)	5 (23.8)	13 (2.2)	97 (14.3)	482 (15.2)
MRSA	421 (25.0)	34 (17.7)	2 (9.5)	11 (1.9)	144 (21.3)	612 (19.4)
S. pneumoniae	328 (19.5)	28 (14.6)	4 (19.0)	4 (0.7)	112 (16.5)	476 (15.1)
Gram-negative	578 (34.3)	126 (65.6)	8 (38.1)	575 (97.8)	398 (58.8)	1685 (53.3)
A. baumannii (complex)	30 (1.8)	5 (2.6)	—	20 (3.4)	12 (1.8)	67 (2.1)
E. coli	61 (3.6)	6 (3.1)	—	96 (16.3)	42 (6.2)	205 (6.5)
E. aerogenes	11 (0.7)	2 (1.0)	—	14 (2.4)	5 (0.7)	32 (1.0)
E. cloacae	20 (1.2)	2 (1.0)	1 (4.8)	24 (4.1)	10 (1.5)	57 (1.8)
H. influenzae	150 (8.9)	34 (17.7)	4 (19.0)	8 (1.4)	70 (10.3)	266 (8.4)
K. oxytoca	5 (0.3)	2 (1.0)	—	16 (2.7)	3 (0.4)	26 (0.8)
K. pneumoniae	59 (3.5)	8 (4.2)	1 (4.8)	81 (13.8)	43 (6.4)	192 (6.1)
L. pneumophila	48 (2.9)	—	—	3 (0.5)	6 (0.9)	57 (1.8)
M. catarrhalis	29 (1.7)	16 (8.3)	—	16 (2.7)	25 (3.7)	86 (2.7)
M. morganii	4 (0.2)	1 (0.5)	—	5 (0.9)	3 (0.4)	13 (0.4)
P. mirabilis	36 (2.1)	5 (2.6)	—	21 (3.6)	14 (2.1)	76 (2.4)
P. aeruginosa	135 (8.0)	38 (19.8)	2 (9.5)	285 (48.5)	164 (24.2)	624 (19.7)
S. marcescens	19 (1.1)	6 (3.1)	1 (4.8)	33 (5.6)	18 (2.7)	77 (2.4)
S. maltophilia	31 (1.8)	12 (6.3)	—	17 (2.9)	25 (3.7)	85 (2.7)
Other	86 (5.1)	2 (1.0)	2 (9.5)	0 (0.0)	16 (2.4)	106 (3.4)
M. pneumoniae	86 (5.1)	2 (1.0)	2 (9.5)	0 (0.0)	16 (2.4)	106 (3.4)

CAP=community-acquired pneumonia; CAP A=unspecified bacteria or bacteria included within the spectrum of activity for lefamulin; CAP B=acute lower respiratory tract infections; CAP C=viral; CAP D=Gram-negative bacteria outside of spectrum of activity for lefamulin; MRSA=methicillin-resistant *Staphylococcus aureus*; MSSA=methicillin-sensitive *Staphylococcus aureus*.

RESULTS (continued)

Table 3. Pathogen Category Distribution by ICU vs Non-ICU Status for CAP A and B Admissions Treated With Empiric Antibiotic Therapy

Culture Type, *n* (%)	ICU	Non-ICU	Total
Total	1035 (55.2)	840 (44.8)	1875*
Monomicrobial GP	567 (54.8)	384 (45.7)	951 (50.7)
Monomicrobial GN	224 (21.6)	251 (29.9)	475 (25.3)
Mixed GN and GP	81 (7.8)	53 (6.3)	134 (7.2)
Polymicrobial GN	51 (4.9)	36 (4.3)	87 (4.6)
Monomicrobial other	22 (2.1)	64 (7.6)	86 (4.6)
Polymicrobial GP	59 (5.7)	15 (1.8)	74 (4.0)
3+ (GN, GP, and other)	31 (3.0)	37 (4.4)	68 (3.6)

CAP=community-acquired pneumonia; CAP A=unspecified bacteria or bacteria included within the spectrum of activity for lefamulin; CAP B=acute lower respiratory tract infections; GN=Gram-negative; GP=gram-positive; ICU=intensive care unit.
*ICU status unevaluable in 2 admissions.

Table 4. Pathogen Distribution by ICU vs Non-ICU Admission Status for CAP A and B Admissions Treated With Empiric Antibiotic Therapy

Pathogen	ICU	Non-ICU	Total	*P* Value
Total admissions, *n* (%)	1035 (55.2)	840 (44.8)	1875* (100.0)	—
MRSA	289 (27.9)	166 (19.8)	455 (24.3)	<0.0001
MSSA	258 (24.9)	109 (13.0)	367 (19.6)	<0.0001
S. pneumoniae	176 (17.0)	180 (21.4)	356 (19.0)	0.0178
H. influenzae	91 (8.8)	93 (11.1)	184 (9.8)	0.1017
P. aeruginosa	87 (8.4)	86 (10.2)	173 (9.2)	0.1737
M. pneumoniae	23 (2.2)	65 (7.7)	88 (4.7)	<0.0001
E. coli	29 (2.8)	38 (4.5)	67 (3.6)	0.0598
K. pneumoniae	38 (3.7)	29 (3.5)	67 (3.6)	0.9006
L. pneumophila	22 (2.1)	26 (3.1)	48 (2.6)	0.1896
M. catarrhalis	23 (2.2)	22 (2.6)	45 (2.4)	0.6497
S. maltophilia	13 (1.3)	30 (3.6)	43 (2.3)	0.001
P. mirabilis	24 (2.3)	17 (2.0)	41 (2.2)	0.7516
S. marcescens	16 (1.5)	9 (1.1)	25 (1.3)	0.423
E. cloacae	11 (1.1)	11 (1.3)	22 (1.2)	0.6699
A. baumannii	19 (1.8)	3 (0.4)	22 (1.2)	0.0039
L. pneumophila	5 (0.5)	13 (1.5)	18 (1.0)	0.0293
E. aerogenes	9 (0.9)	4 (0.5)	13 (0.7)	0.4057
A. baumannii/haemolyticus	10 (1.0)	3 (0.4)	13 (0.7)	0.1618
K. oxytoca	3 (0.3)	4 (0.5)	7 (0.4)	0.7073
M. morganii	5 (0.5)	0 (0.0)	5 (0.3)	0.0690

CAP=community-acquired pneumonia; CAP A=unspecified bacteria or bacteria included within the spectrum of activity for lefamulin; CAP B=acute lower respiratory tract infections; ICU=intensive care unit; MRSA=methicillin-resistant *Staphylococcus aureus*; MSSA=methicillin-sensitive *Staphylococcus aureus*.
*ICU status unevaluable in 2 admissions.

RESULTS (continued)

Table 5. Pathogen Distribution by Non-HCA vs HCA Admission Status for CAP A and B Admissions Treated With Empiric Antibiotic Therapy

Pathogen	HCA	Non-HCA	Total	*P* Value
Total admissions, *n* (%)	634 (33.8)	1241 (66.2)	1877 (100.0)	—
MRSA	185 (29.2)	271 (21.8)	456 (24.3)	0.0005
MSSA	118 (18.6)	249 (20.0)	367 (19.6)	0.4986
S. pneumoniae	90 (14.2)	266 (21.4)	356 (19.0)	0.0001
H. influenzae	59 (9.3)	126 (10.1)	185 (9.9)	0.6234
P. aeruginosa	69 (10.9)	104 (8.4)	173 (9.2)	0.0769
M. pneumoniae	26 (4.1)	62 (5.0)	88 (4.7)	0.4209
E. coli	29 (4.6)	38 (3.1)	67 (3.6)	0.1137
K. pneumoniae	26 (4.1)	41 (3.3)	67 (3.6)	0.4300
L. pneumophila	11 (1.7)	37 (3.0)	48 (2.6)	0.1227
M. catarrhalis	10 (1.6)	35 (2.8)	45 (2.4)	0.1112
S. maltophilia	16 (2.5)	27 (2.2)	43 (2.3)	0.6275
P. mirabilis	14 (2.2)	27 (2.2)	41 (2.2)	1.0000
S. marcescens	7 (1.1)	18 (1.4)	25 (1.3)	0.6719
E. cloacae	8 (1.3)	14 (1.1)	22 (1.2)	0.8223
A. baumannii	7 (1.1)	15 (1.2)	22 (1.2)	1.0000
L. pneumophila	5 (0.8)	13 (1.0)	18 (1.0)	0.8029
E. aerogenes	7 (1.1)	6 (0.5)	13 (0.7)	0.1448
A. baumannii/haemolyticus	7 (1.1)	6 (0.5)	13 (0.7)	0.1448
K. oxytoca	4 (0.6)	3 (0.2)	7 (0.4)	0.2353
M. morganii	2 (0.3)	3 (0.2)	5 (0.3)	1.0000

CAP=community-acquired pneumonia; CAP A=unspecified bacteria or bacteria included within the spectrum of activity for lefamulin; CAP B=acute lower respiratory tract infections; HCA=healthcare-associated; MRSA=methicillin-resistant *Staphylococcus aureus*; MSSA=methicillin-sensitive *Staphylococcus aureus*.

CONCLUSIONS

- Based on a representative and contemporary sample of patients with a causative organisms identified by serology or culture presenting to a hospital for treatment, the epidemiology of CABP in the United States may be changing
- Gram-positive pathogens were the most common organisms identified, with *S. aureus* and MRSA identified most frequently regardless of setting or HCA status
- Assessing the bacteriology of CABP is a critical consideration for clinicians and formulary committees when determining the most appropriate empiric antibacterial therapy

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