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A Multicenter Evaluation of Pathogen Distribution in Patients Admitted With Microbiologically-Confirmed Community-Acquired Bacterial Pneumonia (CABP) in the US

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ABSTRACT*

Background: Pneumonia affects >6 million patients each year in the United States and is associated with significant morbidity and mortality. The microbiological diagnosis of CABP has proven difficult with standard culture methods and can vary by clinical setting, complicating making the selection of appropriate empiric antimicrobial treatment difficult.

Materials/methods: We analyzed first positive bacterial respiratory isolates for patients from 68 acute care hospitals in the BD Insights Research Database (Franklin Lakes, NJ, US) discharged with primary or secondary ICD10 codes for pneumonia treated with empiric antibiotic therapy who did not have healthcare-associated (HCA) pneumonia risk factors at admission. Gram-positive (GP), Gram-negative (GN), and other respiratory bacterial pathogens were included, if collected within 3 days of admission and were further categorized as collected in an ICU or non-ICU setting in patients started on empiric antibiotic therapy. Respiratory cultures and urine antigen were used to identify *S. pneumoniae* and *L. pneumophila*, and respiratory cultures and serologies were used to identify *M. pneumoniae*. The Chi-square and Fisher's exact tests were used to assess statistical difference.

Results: A total of 1,243 admissions without HCA risk factors had positive serology or respiratory cultures collected within 3 days of admission and were treated with empiric antibiotic therapy. Of these admissions, 54.9% (681) were in the ICU. Overall, 55.1%, 29.5%, 6.8% and 8.4% were positive for GP only, GN only, mixed GN/GP, or other bacterial pathogens, respectively. *S. aureus* (41.9%), *S. pneumoniae* (21.4%), *H. influenzae* (10.1%), and *P. aeruginosa* (8.4%) were the most common bacterial pathogens, representing 81.8% of all episodes. MRSA represented 52.0% of *S. aureus* episodes and 21.8% of all culture positive episodes. *S. aureus* (51.5% vs. 30.0%; p<0.0001), MRSA (25.1% vs. 17.7%; p=0.0017), and *A. baumannii* (2.5% vs. 0.7%; p=0.0231) were more common in the ICU, while *S. pneumoniae* (24.1% vs. 19.2%; p=0.0378), *P. aeruginosa* (10.2% vs. 6.9%; p=0.0393), and *M. pneumoniae* (8.0% vs. 2.5%; p<0.0001) were more common in the non-ICU setting.

Conclusions: The majority of microbiologically confirmed CABP admissions from a representative sample of US hospitals with a positive respiratory culture had a GP pathogen identified. Unlike previous reports, *S. aureus* was the most common pathogen identified overall and MRSA was the second most common. The selection of appropriate antibiotic therapy requires careful consideration of the most likely bacteriology based on admission to the ICU versus non-ICU setting.

*This abstract contains updated data.

INTRODUCTION

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

METHODS

- We analyzed first positive bacterial respiratory isolates for patients discharged with primary or secondary ICD10 codes for pneumonia and treated with empiric antibiotic therapy from 68 acute care hospitals in the BD Insights Research Database (Franklin Lakes, NJ, US) **(Table 1)**

Table 1. US Hospital Characteristics

	BD Facilities (*n*=68)	CMS* (*n*=4,656)
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%
Bed Size		
<100	12 (17.6%)	51.0%
100–300	27 (39.7%)	29.3%
>300	29 (42.6%)	19.7%

BD=Becton Dickinson.
*Center for Medicaid and Medicare Services (USA)

- Admissions were further classified as follows based on distribution of ICD10 codes **(Table 2)**: CABP A (lefamulin), CABP B (unspecified bacteria or included within spectrum of activity for lefamulin), CABP C (viral), CABP D (Gram-negative [GN] bacteria outside of spectrum of activity for lefamulin), and multiple categories. This analysis includes admissions classified as CABP A–B

Table 2. Pathogen Category Distribution by ICU vs. Non-ICU Status for CABP Admissions Treated With Empiric Antibiotic Therapy

Culture Type	ICU	Non-ICU	Total
Monomicrobial GP	378 (55.5%)	258 (46.1%)	636 (51.2%)
Monomicrobial GN	144 (21.1%)	170 (30.4%)	314 (25.3%)
Mixed GN and GP	50 (7.3%)	35 (6.3%)	85 (6.8%)
Polymicrobial GN	31 (4.6%)	21 (3.8%)	52 (4.2%)
Monomicrobial Other	16 (2.4%)	44 (7.9%)	60 (4.8%)
Polymicrobial GP	39 (5.7%)	10 (1.8%)	49 (3.9%)
3+ (GN, GP and Other)	23 (3.4%)	22 (3.9%)	45 (3.6%)
Total	**681 (54.9%)**	**560 (45.1%)**	**1,241***

CABP=community-acquired bacterial pneumonia; GN=Gram-negative; GP=Gram-positive; ICU=intensive care unit.
*ICU status unevaluable in 2 admissions.

- Gram-positive (GP), GN, and other respiratory bacterial pathogens in CABP A and CABP 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

METHODS (continued)

- 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*
- Healthcare-associated (HCA) episodes were defined as admitted from another acute care facility (eg, skilled nursing facility, long-term acute care hospital, rehabilitation hospital, hospice), admission in the prior 30 days, dialysis ICD10 code Z99.2 (dependence on renal dialysis), or cancer comorbidity as identified in the Agency for Healthcare Research and Quality Clinical Classifications Software (AHRQ CCS) comorbidity classification
- The Chi-square and Fisher's exact tests were used to test for significance

RESULTS

- A total of 1,243 CABP A and CABP B admissions without HCA risk factors had positive serology or respiratory cultures collected within 3 days of admission and were treated with empiric antibiotic therapy
- Of these admissions, 54.9% (681) were in the ICU
- Overall, 55.1%, 29.5%, 6.8% and 8.4% were positive for GP only, GN only, mixed GN/GP, or other bacterial pathogens, respectively. *Staphylococcus aureus* (41.9%), *S. pneumoniae* (21.4%), *Haemophilus influenzae* (10.1%), and *P. aeruginosa* (8.4%) were the most common bacterial pathogens, representing 81.8% of all episodes **(Tables 2 and 3)**

Table 3. Pathogen Distribution by ICU vs. Non-ICU Admission Status for CABP Admissions Treated With Empiric Antibiotic Therapy

Pathogen	ICU (*n*=681 Admissions)	Non-ICU (*n*=560 Admissions)	Total (*n*=1,241 Admissions*)	*P* value
MRSA	171 (25.1%)	99 (17.7%)	270 (21.8%)	0.0017
S. pneumoniae	131 (19.2%)	135 (24.1%)	266 (21.4%)	0.0378
MSSA	180 (26.4%)	69 (12.3%)	249 (20.1%)	<0.0001
H. influenzae	62 (9.1%)	63 (11.3%)	125 (10.1%)	0.2121
P. aeruginosa	47 (6.9%)	57 (10.2%)	104 (8.4%)	0.0393
M. pneumoniae	17 (2.5%)	45 (8.0%)	62 (5.0%)	<0.0001
L. pneumophila	19 (2.7%)	31 (5.5%)	50 (4.0%)	0.0163
K. pneumoniae	22 (3.2%)	19 (3.4%)	41 (3.3%)	0.8735
E. coli	16 (2.3%)	22 (3.9%)	38 (3.1%)	0.1119
M. catarrhalis	17 (2.5%)	18 (3.2%)	35 (2.8%)	0.4483
S. maltophilia	9 (1.3%)	18 (3.2%)	28 (2.2%)	0.0276
P. mirabilis	17 (2.5%)	10 (1.8%)	27 (2.2%)	0.3955
A. baumannii	17 (2.5%)	4 (0.7%)	21 (1.7%)	0.0231
S. marcescens	10 (1.5%)	8 (1.4%)	18 (1.5%)	1.0000
E. cloacae	8 (1.2%)	6 (1.1%)	14 (1.1%)	1.0000
E. aerogenes	4 (0.6%)	2 (0.4%)	6 (0.5%)	0.8776
K. oxytoca	2 (0.3%)	1 (0.2%)	3 (0.2%)	1.0000
M. morganii	3 (0.4%)	0	3 (0.2%)	0.1649

ICU=intensive care unit; MRSA=methicillin-resistant *Staphylococcus aureus*; MSSA=methicillin-susceptible *Staphylococcus aureus*.
*ICU status unknown in 2 admissions.

- Methicillin-resistant *Staphylococcus aureus* (MRSA) represented 52% of *S. aureus* episodes and 21.8% of all culture-positive episodes

RESULTS (continued)

- *S. aureus* (51.5% vs. 30.0%; p<0.0001), MRSA (25.1% vs. 17.7%; p=0.0017), and *Acinetobacter baumannii* (2.5% vs. 0.7%; p=0.0231) were more common in the ICU, while *S. pneumoniae* (24.1% vs. 19.2%; p=0.0378), *Pseudomonas aeruginosa* (10.2% vs. 6.9%; p=0.0393), and *M. pneumoniae* (8.0% vs. 2.5%; p<0.0001) were more common in the non-ICU setting
- Overall patient demographics were similar in admissions with pathogens covered by lefamulin versus pathogens not covered by lefamulin, except that admissions with pathogens covered by lefamulin were more likely to have been coded for fluid and electrolyte disorder and drug abuse **(Table 4)**

Table 4. Comorbidities in Admissions in Lefamulin Covered Pathogens vs. Non-Lefamulin Covered Pathogens

Comorbidity	Lefamulin Covered Pathogens, N (%)	Non-Lefamulin Covered Pathogens, N (%)	All Admissions, N (%)	*P* Value
Total Admissions	**979 (78.8%)**	**264 (21.2%)**	**1,243**	**–**
Hypertension	604 (61.7%)	174 (65.9%)	778 (62.6%)	0.2096
Fluid & electrolyte disorders	606 (61.9%)	143 (54.2%)	749 (60.3%)	0.0230
Chronic pulmonary disease	430 (43.9%)	131 (49.6%)	561 (45.1%)	0.0990
Deficiency anemias	277 (28.3%)	87 (33.0%)	364 (29.3%)	0.1402
Congestive heart failure	236 (24.1%)	75 (28.4%)	311 (25.0%)	0.1525
Weight loss	196 (20%)	61 (23.1%)	257 (20.7%)	0.2723
Obesity	201 (20.5%)	55 (20.8%)	256 (20.6%)	0.9139
Diabetes	154 (15.7%)	50 (18.9%)	204 (16.4%)	0.2121
Renal failure	158 (16.1%)	45 (17.0%)	203 (16.3%)	0.7236
Depression	150 (15.3%)	51 (19.3%)	201 (16.2%)	0.1183
Diabetes w/ chronic comp.	161 (16.4%)	35 (13.3%)	196 (15.8%)	0.2082
Hypothyroidism	151 (15.4%)	41 (15.5%)	192 (15.4%)	0.9661
Other neurological disorders	138 (14.1%)	43 (16.3%)	181 (14.6%)	0.3706
Coagulopathy	109 (11.1%)	22 (8.3%)	131 (10.5%)	0.1904
Peripheral vascular disease	89 (9.1%)	25 (9.5%)	114 (9.2%)	0.8499
Drug abuse	98 (10.0%)	12 (4.5%)	110 (8.8%)	0.0069
Alcohol abuse	84 (8.6%)	13 (4.9%)	97 (7.8%)	0.0524
Valvular disease	75 (7.7%)	15 (5.7%)	90 (7.2%)	0.2731
Paralysis	63 (6.4%)	21 (8.0%)	84 (6.8%)	0.3835
Psychoses	68 (6.9%)	16 (6.1%)	84 (6.8%)	0.6114
Liver disease	63 (6.4%)	18 (6.8%)	81 (6.5%)	0.8229
None	45 (4.6%)	8 (3.0%)	53 (4.3%)	0.2671
Pulmonary circulation disease	41 (4.2%)	9 (3.4%)	50 (4.0%)	0.5684
Rheumatoid arthritis	37 (3.8%)	10 (3.8%)	47 (3.8%)	0.9949
Chronic blood loss anemia	11 (1.1%)	3 (1.1%)	14 (1.1%)	0.9860
Peptic ulcer disease	8 (0.8%)	6 (2.3%)	14 (1.1%)	0.0567
AIDS	4 (0.4%)	–	4 (0.3%)	0.9662

CONCLUSIONS

- Based on a representative and contemporary sample from the US, the epidemiology of CABP may be changing in patients with a causative organism identified by serology, culture, or urinary antigen presenting to a hospital
- Gram-positive pathogens were the most common organisms identified, with *S. aureus* and *S. pneumoniae* identified as the most frequent regardless of ICU admission status
- The patient demographics comparing lefamulin eligible and non-lefamulin culture positive pathogens were similar with minor differences noted
- The selection of appropriate antibiotic therapy requires careful consideration of the most likely bacteriology based on admission to the ICU versus the non-ICU setting

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