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Microbiology and Outcomes Among Patients Hospitalised With Suspected Community-Acquired Bacterial Pneumonia (CABP): A Multi-Centre Retrospective Cohort Study

Marya D. Zilberberg,[1] Ying P. Tabak,[2] Elizabeth Alexander,[3] Vikas Gupta,[2] Kalvin C. Yu,[2] Patrick J. Scoble,[3] Andrew F. Shorr[4]

[1]EviMed Research Group, LLC, Goshen, MA, USA; [2]Becton, Dickinson and Company, Franklin Lakes, NJ, USA; [3]Nabriva Therapeutics US, Inc., King of Prussia, PA, USA; [4]Medstar Washington Hospital Center, Washington, DC, USA

Nabriva Therapeutics
Vienna, Austria
and King of Prussia, PA, USA
www.nabriva.com

INTRODUCTION & PURPOSE

- Community-acquired pneumonia affects >1.5 million patients each year in the United States and is associated with significant morbidity and mortality[1]
- Current guidelines recommend blood culture sampling only in select cases among patients with suspected community-acquired bacterial pneumonia (CABP)[2]
- We hypothesised that 1) the type of culture source (eg, respiratory, blood, or both) that led to pathogen identification would correlate with outcomes and 2) select pathogens in CABP would be associated with worse clinical outcomes

METHODS

Study Design

- This was a retrospective cohort study of data from 104 US acute care hospitals from October 2015 through December 2017

Data Source

- BD Insights Research Database (Becton, Dickinson and Company, Franklin Lakes, NJ, USA), including microbiological results, general laboratory results, pharmacy orders, and administrative data

Patients

- Adult patients (aged ≥18 years) hospitalised for suspected CABP
- Suspected CABP was identified by any of the following International Classification of Diseases, Tenth Revision (ICD-10) code algorithms plus evidence of antimicrobial treatment for >48 hours AND positive bacterial results from respiratory and/or blood culture, urine antigen test, or blood serology test during admission period
  - In addition to a bacterial pathogen–positive respiratory and/or blood culture result, urine antigen tests were used to identify *Streptococcus pneumoniae* and *Legionella pneumophila*; blood serologies were used to identify *Mycoplasma pneumoniae*
  - Primary ICD-10 diagnosis code for pneumonia
  - Primary ICD-10 diagnosis code for sepsis AND a secondary diagnosis code for pneumonia
  - Primary ICD-10 diagnosis code for acute respiratory failure AND a secondary diagnosis code for pneumonia
- Suspected CABP was considered healthcare-associated pneumonia (HCAP) when ≥1 of the following risk factors was present: an admission from a skilled nursing/long-term care facility, previous hospital discharge within 90 days, dialysis, or a cancer diagnosis[3]

Outcomes Evaluated

- Distribution of bacterial pathogens across culture source
- In-hospital death
- Length of stay (LOS)
- Total hospital stay cost as calculated by each institution (eg, cost accounting system)

Statistical Analysis

- Patient characteristics and outcomes between the groups based on the source of positive bacterial culture/serology (eg, blood, respiratory, or both) were evaluated in a univariate analysis

METHODS (continued)

- Mixed models to estimate the association of culture source and bacterial pathogen with mortality, LOS, and costs were evaluated, adjusting for
  - Demographics (eg, age and sex)
  - Comorbidities (Agency for Healthcare Research and Quality [AHRQ] Comorbidity Software [Elixhauser Comorbidity Index])[4]
  - HCAP risk factor presence
  - Intensive care unit (ICU) admission status within 3 days of admission
  - Acute Laboratory Risk of Mortality Score (ALaRMS), a published clinical severity score incorporating demographics and 24 laboratory test results on admission[5]
  - Infectious Diseases Society of America (IDSA) guidelines[2] concordance/discordance with empiric treatment status defined as
    - Guideline concordance in the non-ICU during the admission period: antimicrobial order(s) for at least either a respiratory fluoroquinolone (R-FQ) or β-lactam + macrolide or R-FQ
    - Guideline concordance in the ICU during the admission period: antimicrobial order(s) for at least a β-lactam + macrolide or FQ
    - Episodes not meeting the above were considered guideline discordant
  - Bacterial pathogens were grouped into the categories evaluated in the model based on univariate results on mortality

RESULTS

- Among 6457 patients with a bacterial pathogen–positive culture/serology result, 55.6% were respiratory positive, 33.9% were blood positive, and 10.5% were both respiratory/blood positive (**Table 1**)
- Blood cultures were the only means for pathogen identification in nearly 34% of patients
- Patients who were bacterial pathogen positive for both respiratory/blood cultures were younger but sicker (ICU admission, 64.5% vs 46.3% and 41.1%, respectively; *P*<0.0001) than those with either respiratory- or blood-positive cultures
- Among pathogens, *Staphylococcus aureus* accounted for 26.7% overall, Gram-negative bacteria accounted for a combined 30.7%, and *S. pneumoniae* accounted for 14.6%
- In-hospital mortality rates were 9.1%, 10.4%, and 17.5% for patients with only bacterial pathogen–positive respiratory cultures, only bacterial pathogen–positive blood cultures, or with both types of cultures yielding a bacterial pathogen, respectively
- Adjusted mortality was highest (OR=1.57 [95% CI, 1.20-2.06; *P*=0.001]) among patients with both types of cultures positive for a bacterial pathogen compared to those with only a positive respiratory culture (**Table 2**)
- The methicillin-resistant *S. aureus*–positive (MRSA+) monomicrobial infections had a 96% (OR, 1.96; 95% CI, 1.35–2.84; *P*=0.0004) higher mortality risk than the reference group (*S. pneumoniae*)
- MRSA+ monomicrobial infection was also associated with 3.1 days of excess LOS and $7464 excess total cost per case compared to the reference group (*S. pneumoniae*), both *P*<0.0001 (**Figures 1** and **2**)

Strengths and Limitations

- The strength of this study is that it was a regionally distributed large multi-centre evaluation in the US and thus generalizable to a broader population
- To avoid limitations associated with solely relying on claims data, this analysis incorporated other clinical data elements (eg, culture/serology results, measures of clinical severity of illness) and pharmacy orders to define the cases
- Because respiratory culture quality can hinder the definitive verification of the causative pathogen for suspected CABP, we referenced "suspected" CABP in this study
- This was a retrospective cohort analysis that did not include chart review and chest radiograph evaluation for suspected CABP

RESULTS (continued)

Table 1. Patient Characteristics by Culture Source

Variable	Overall N=6457 n	Overall %	Respiratory Positive n=3591 (55.6%) n	Respiratory Positive %	Blood Positive n=2190 (33.9%) n	Blood Positive %	Respiratory/ Blood Positive n=676 (10.5%) n	Respiratory/ Blood Positive %	*P* Value
Age, y									
≤60	2090	32.4	1218	33.9	619	28.3	253	37.4	<0.0001
61–70	1597	24.7	897	25.0	497	22.7	203	30.0	
71–80	1471	22.8	832	23.2	503	23.0	136	20.1	
>80	1299	20.1	644	17.9	571	26.1	84	12.4	
Sex									
Male	3447	53.4	1878	52.3	1192	54.4	377	55.8	0.1218
Female	3010	46.6	1713	47.7	998	45.6	299	44.2	
HCA admission									
Yes	3020	46.8	1687	47.0	1021	46.6	312	46.2	0.9115
No	3437	53.2	1904	53.0	1169	53.4	364	53.9	
ICU admission									
Yes	2997	46.4	1662	46.3	899	41.1	436	64.5	<0.0001
No	3460	53.6	1929	53.7	1291	59.0	240	35.5	
ALaRMS (clinical severity score)[5]									
1st quartile	1163	18.0	822	22.9	266	12.2	75	11.1	<0.0001
2nd quartile	1288	20.0	795	22.1	396	18.1	97	14.4	
3rd quartile	1603	24.8	808	22.5	638	29.1	157	23.2	
4th quartile	2403	37.2	1166	32.5	890	40.6	347	51.3	
AHRQ Comorbidity Index[4]									
Mean (SD)	4.8 (2.3)		4.6 (2.4)		5.0 (2.3)		5.2 (2.2)		<0.0001
Median (IQR)	5 (3–6)		5 (3–6)		5 (3–7)		5 (4–7)		
IDSA 2003 Empiric Therapy Guideline[2]									
Discordant	3548	55.0	1821	50.7	1301	59.4	426	63.0	<0.0001
Concordant	2909	45.1	1770	49.3	889	40.6	250	37.0	
Pathogen category									
S. pneumoniae	942	14.6	506	14.1	351	16.0	85	12.6	<0.0001
Any Gram-negative (the top 5 are below)	1982	30.7	1307	36.4	635	29.0	40	5.9	
Pseudomonas aeruginosa	528	8.2	460	12.8	56	2.6	12	1.8	
Escherichia coli	331	5.1	108	3.0	210	9.6	13	1.9	
Haemophilus influenzae	255	4.0	185	5.2	66	3.0	4	0.6	
Klebsiella pneumoniae	220	3.4	125	3.5	90	4.1	5	0.7	
Legionella pneumophila	147	2.3	147	4.1					
Atypical*	197	3.1	197	5.5					
MRSA monomicrobial	696	10.8	418	11.6	221	10.1	57	8.4	
MRSA polymicrobial	219	3.4	122	3.4	22	1.0	75	11.1	
MSSA monomicrobial	633	9.8	348	9.7	242	11.1	43	6.4	
MSSA polymicrobial	178	2.8	102	2.8	18	0.8	58	8.6	
Other Gram-positive	536	8.3	77	2.1	450	20.6	9	1.3	
Other polymicrobial	1074	16.6	514	14.3	251	11.5	309	45.7	

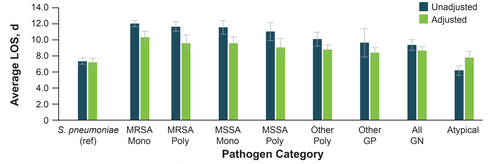
AHRQ=Agency for Healthcare Research and Quality; ALaRMS=Acute Laboratory Risk of Mortality Score; HCA=healthcare-associated; ICU=intensive care unit; IDSA=Infectious Diseases Society of America; IQR=interquartile range; MRSA=methicillin-resistant *S. aureus*; MSSA=methicillin-susceptible *S. aureus*; SD=standard deviation. **L. pneumophila, Chlamydophila pneumoniae,* or *M. pneumoniae.*

Table 2. Multivariable Mixed Model for Mortality

Variable	OR	95% CI LL	95% CI UL	*P* Value
Age, y				
61–70	1.54	1.15	2.07	0.0041
71–80	1.51	1.14	1.99	0.0041
>80	1.97	1.44	2.69	<0.0001
≥60	Reference			
Sex				
Male	1.18	0.99	1.40	0.0709
Female	Reference			
ICU admission status				
ICU	5.01	3.73	6.73	<0.0001
Non-ICU	Reference			
HCA admission status				
HCA	1.44	1.14	1.82	0.0020
Non-HCA	Reference			
ALaRMS (clinical severity score)[5]				
2nd quartile	2.45	1.34	4.48	0.0035
3rd quartile	3.74	2.03	6.89	<0.0001
4th quartile	7.02	3.73	13.21	<0.0001
1st quartile	Reference			
Culture source				
Respiratory only	Reference			
Blood only	1.06	0.84	1.33	0.6216
Respiratory and blood	1.57	1.20	2.06	0.0011
Pathogen				
S. pneumoniae	Reference			
Any Gram-negative	1.21	0.91	1.62	0.1932
Atypical*	1.22	0.64	2.33	0.5486
MRSA monomicrobial	1.96	1.35	2.84	0.0004
MRSA polymicrobial	1.07	0.67	1.71	0.7866
MSSA monomicrobial	1.31	0.94	1.84	0.1094
MSSA polymicrobial	0.97	0.56	1.68	0.9071
Other Gram-positive	1.39	0.91	2.14	0.1294
Other polymicrobial	1.31	0.92	1.88	0.1381
AHRQ Comorbidity Index[4]	1.06	1.01	1.11	0.0182
IDSA 2003 Empiric Therapy Guideline[2]				
Discordant	0.99	0.82	1.18	0.8780
Concordant	Reference			

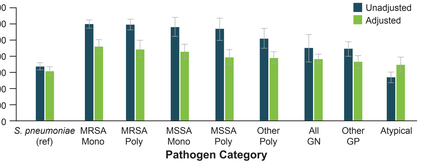
AHRQ=Agency for Healthcare Research and Quality; ALaRMS=Acute Laboratory Risk of Mortality Score; CI=confidence interval; HCA=healthcare-associated; ICU=intensive care unit; IDSA=Infectious Diseases Society of America; LL=lower limit; MRSA=methicillin-resistant *S. aureus*; MSSA=methicillin-susceptible *S. aureus*; OR=odds ratio; UL=upper limit. **L. pneumophila, C. pneumoniae, M. pneumoniae.*

Figure 1. Unadjusted and Adjusted LOS by Pathogen Category



GN=Gram-negative; GP=Gram-positive; LOS=length of stay; Mono=monomicrobial; MRSA=methicillin-resistant *S. aureus*; MSSA=methicillin-susceptible *S. aureus*; Poly=polymicrobial. Error bars represent 95% confidence intervals.

Figure 2. Unadjusted and Adjusted Total Cost per Case by Pathogen Category



GN=Gram-negative; GP=Gram-positive; Mono=monomicrobial; MRSA=methicillin-resistant *S. aureus*; MSSA=methicillin-susceptible *S. aureus*; Poly=polymicrobial. Error bars represent 95% confidence intervals.

CONCLUSIONS

- Patients with bacterial pathogen–positive cultures in both respiratory/blood sources had worse outcomes than those with respiratory bacterial pathogen–positive culture alone
- Despite guidelines suggesting a low yield for blood cultures in CABP, we found that blood cultures were crucial for identifying clinical important pathogens such as *S. aureus* in patients who present to the hospital with pneumonia. Concomitantly, correct pathogen identification is a necessary step in the process of insuring a patient gets appropriate antibiotic therapy
- Among patients with suspected CABP who have an identified organism, *S. aureus* and *S. pneumoniae* remain the most common bacterial pathogens
- After controlling for illness severity, comorbidities, and other confounders, MRSA is associated with the highest risk for mortality, longer LOS, and higher cost

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