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Epidemiology and Predictors of Multidrug-Resistant Community-Acquired and Health Care-Associated Pneumonia

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There are limited U.S. data describing the risk factors for multidrug-resistant organism (MDRO) isolation in community-acquired pneumonia (CAP) and health care-associated pneumonia (HCAP). However, concern for the presence of these pathogens drives the prescribing of empiric broad-spectrum antibiotics for CAP and HCAP. A retrospective study of all adults hospitalized with community-onset pneumonia (CAP and HCAP) at a large U.S. medical center from January 2010 to December 2011 was conducted. The objective was to ascertain the rate of pneumonia caused by MDROs and to evaluate whether HCAP is a risk factor for MDRO pneumonia. Univariate and propensity score-adjusted multivariate analyses were performed. A total of 521 patients (50.5% CAP and 49.5% HCAP) were included. The most common etiologies of pneumonia were primary viral and *Streptococcus pneumoniae*. MDROs were isolated in 20 (3.8%) patients overall, and MDROs occurred in 5.9% and 1.9% of HCAP and CAP patients, respectively. The presence of an MDRO was not associated with HCAP classification (odds ratio [OR] = 1.95; 95% confidence interval [95% CI], 0.66 to 5.80; $P = 0.23$) or with most of its individual components (hemodialysis, home infusion, home wound care, and ≥48-h hospitalization in the last 90 days). Independent predictors of MDRO included the following: *Pseudomonas aeruginosa* colonization/infection in the previous year (OR = 7.43; 95% CI, 2.24 to 24.61; $P < 0.001$), antimicrobial use in the previous 90 days (OR = 2.90; 95% CI, 1.13 to 7.45; $P = 0.027$), admission from a nursing home (OR = 4.19; 95% CI, 1.55 to 11.31; $P = 0.005$), and duration of hospitalization in the previous 90 or 180 days ($P = 0.013$ and $P = 0.002$, respectively). MDROs were uncommon in HCAP and CAP. HCAP did not predict MDRO isolation. Local etiology of community onset pneumonia and specific MDRO risk factors should be integrated into therapeutic decisions to prevent empirical overprescribing of antibiotics for methicillin-resistant *Staphylococcus aureus* (MRSA) and *P. aeruginosa*.

Pneumonia is the leading infectious cause of mortality in the United States with 53,667 attributed deaths in 2011 (1). The etiology of pneumonia varies depending on the patient population being observed. Traditionally, pneumonia has been divided into community-onset pneumonia, which is most commonly due to *Streptococcus pneumoniae*, atypical bacteria, and respiratory viruses, and hospital-acquired pneumonia (HAP), which more frequently involves resistant pathogens such as *Pseudomonas aeruginosa* and methicillin-resistant *Staphylococcus aureus* (MRSA) (2, 3).

Due to the increase in complicated and chronically ill patients treated in the outpatient setting, the 2005 American Thoracic Society (ATS)/Infectious Disease Society of America (IDSA) guidelines introduced the health care-associated pneumonia (HCAP) classification as a way to identify patients from the community who may be at risk for infection with antimicrobial-resistant pathogens (3). This recommendation greatly expanded the number of patients treated with broad-spectrum antimicrobial agents. For example, over 30% of 58,118 community-onset pneumonia patients in 128 Veterans Affairs (VA) hospitals received empirical treatment with vancomycin (4). The HCAP classification has been controversial, because its ability to predict multidrug-resistant organisms (MDROs) has not been consistently replicated, and the frequency of MDROs in patients with HCAP has varied significantly (5, 6). A recent systematic review and meta-analysis of 24 studies worldwide demonstrated this and found that the prevalence of MRSA and *P. aeruginosa* in HCAP varied from 0.7% to 30% and 0.7% to 23%, respectively (7). In addition, viruses are a frequent primary cause of community-onset pneumonia and are often not described in these studies (8–10).

Due to the varying rates of MDRO isolation and overall lack of U.S. data, determining the regional etiology of community-onset pneumonia (CAP and HCAP) is essential for optimizing patient outcomes while minimizing unnecessary broad-spectrum antimicrobial use. The ATS/IDSA guidelines state that one "recognize the variability of bacteriology from one hospital to another, specific sites within the hospital, and from one time period to another, and use this information to alter the selection of an appropriate antibiotic treatment regimen" (3). More data are required from U.S. centers characterizing the etiology of CAP and HCAP. The aim of this study was to characterize the etiology, MDRO risk factors, and clinical outcomes for patients with CAP and HCAP at a large U.S. academic medical center.

MATERIALS AND METHODS

This was a retrospective observational cohort study of all consecutive patients admitted with CAP or HCAP to The Nebraska Medical Center (a 627-bed academic medical center in Omaha, NE, USA) between 1 January

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2010 and 31 December 2011. This protocol was approved by the University of Nebraska Medical Center Institutional Review Board.

Study population. Patients that were ≥19 years of age (the age of majority in Nebraska) were assessed for study inclusion. Patients were identified by primary International Statistical Classification of Diseases and Related Health Problems revision 9 (ICD-9) codes for pneumonia (480.0 to 483.99 and 485 to 487) and had to meet the study definition for pneumonia at hospital admission for study inclusion. Patients were excluded if they had active thoracic malignancy or cystic fibrosis or were transferred from another hospital.

Definitions. Pneumonia was defined as a new/progressive radiographic infiltrate at presentation plus two or more of the following: temperature of >38°C or <36°C, white blood cell count [WBC] of >12,000 or <4,000 cells/mm^3, or new/worsening respiratory symptoms (e.g., cough, shortness of breath). Patients were classified as having HCAP if they met the following criteria from the 2005 IDSA/ATS guidelines: hospitalization for at least 48 h in the preceding 90 days, residence in a nursing home or extended-care facility, home infusion therapy, home wound care, or chronic dialysis (3). Study-defined MDROs included MRSA, *Pseudomonas aeruginosa*, extended-spectrum beta-lactamase (ESBL)-producing *Enterobacteriaceae*, carbapenem-intermediate or -resistant *Enterobacteriaceae* (CIRE), *Acinetobacter* spp., and *Stenotrophomonas maltophilia*. A positive history for MDRO infection/colonization included any patients with a positive clinical or screening culture for the MDRO of interest in the previous 12 months. Immunocompromised status was defined as any patient with at least one of the following factors: AIDS (CD4 T cell count of <200 cells/mm^3 or AIDS-defining illness), active malignancy receiving chemotherapy, history of solid-organ transplantation on immunosuppressive agents, immunosuppressive therapy (including 10 mg prednisone/day for at least 30 days or equivalent), or other underlying immune deficiency. Patients were considered to have aspiration risk if they had at least one of the following: cerebrovascular disease, mechanical obstruction of esophageal function (e.g., stricture, carcinoma), impaired consciousness (drug overdose, alcohol, etc.), or a history of vomiting or witnessed aspiration. The severity of pneumonia was assessed using the CURB-65 score (CURB-65 is an acronym for the risk factors *c*onfusion, blood *u*rea nitrogen, *r*espiratory rate, *b*lood pressure, and age 65 or older) (11).

Microbiologic evaluation. Respiratory cultures (e.g., sputum sample, bronchoalveolar lavage sample), blood cultures, urine antigens (*Streptococcus pneumoniae*, *Legionella*), respiratory virus panels (xTAG; Luminex, Austin, TX, USA), and rapid influenza virus antigen tests (Alera, Waltham, MA, USA) were assessed as available. Two authors (A.E.G. and T.C.V.S.) independently assessed all positive respiratory cultures, blood cultures, urine antigens, and respiratory viral assays in order to determine the causative pathogen(s). During the study period, institutional guidelines with recommendations for obtaining respiratory and blood cultures were available on the institutional antimicrobial stewardship website; these guidelines were consistent with IDSA recommendations (3, 4).

Predictors of MDRO. Data collected to identify predictors of MDRO included the following: demographic information, components of the HCAP classification, duration of previous hospitalization, comorbid conditions, immunocompromised status, aspiration risk, and previous exposure to antimicrobials.

Endpoints. The primary endpoint was the isolation of an MDRO. Risk factors for MDRO were evaluated as outlined below. Thirty-day mortality was the secondary endpoint.

Statistical analysis. Dichotomous variables were compared using the χ^2 or Fisher's exact test as appropriate. Continuous variables were compared using the Mann-Whitney U test. Predictors of MDRO were initially identified by univariate regression. Due to the low rate of MDRO infections, we elected to not use the conventional multivariate analysis due to the potential for overfitting; hence, we built a propensity score that included variables that were significantly associated with MDRO infections in the univariate analysis (i.e., age, comorbid conditions, and CURB-65 score). Thereafter, we created a multivariable logistic regression model that included the propensity score in addition to the covariates of interest to control for potential confounders. All tests were two-tailed tests with a significance level of <0.05. Statistical analyses were performed using SPSS (version 20.0; Chicago, IL, USA).

RESULTS

A total of 521 patients (50.5% CAP and 49.5% HCAP) were included in the study with characteristics summarized in Table 1. The median age of the cohort was 65 years, and 55% were female.

Pneumonia etiology. Microbiologic tests obtained for patients in the cohort included the following: blood cultures (88.7%), respiratory culture (42.6%), *S. pneumoniae* urine antigen (18%), *Legionella* urine antigen (15.7%), respiratory virus panel (15%), and influenza virus rapid antigen (16.3%). Bacterial investigations occurred in the same proportion among patients with HCAP and CAP. Patients with CAP more frequently had positive respiratory viral panels (19%) and influenza virus rapid antigen tests (19%) obtained than HCAP patients did (11% and 13%, respectively). The etiology of pneumonia was determined in 19% of the cohort and is listed in Table 2. The most common identified etiology was primary viral pneumonia followed by *S. pneumoniae*. At least one MDRO was isolated in 20 (3.8%) patients in the overall cohort with MDRO occurring in 15/258 (5.9%) HCAP patients and 5/263 (1.9%) CAP patients. MRSA was isolated in 11/521 patients (2.1%), and *P. aeruginosa* was isolated in 9/521 patients (1.7%). No ESBL-producing *Enterobacteriaceae* or CIRE were isolated.

Predictors of MDRO. Predictors of MDRO by univariate analysis are found in Table 1. Statistically significant associations with MDRO included the following: CURB-65 scores of >1 and >2, intensive care unit admission, history of cerebrovascular accident, congestive heart failure, blood urea nitrogen level of >19 mg/dl, presence of HCAP, admission from a nursing home, number of days hospitalized in the previous 180 days, antibiotic use in the previous 90 days, and history of colonization or infection with *P. aeruginosa* or any MDRO. *P. aeruginosa* colonization/infection within the previous 12 months was noted in 4.0% (21/521) of the population and was significantly associated with *P. aeruginosa* pneumonia (23.8% with previous colonization versus 0.8% without previous colonization; $P < 0.001$). MRSA pneumonia occurred in 7.1% and 1.8% of patients with and without a history of MRSA colonization/infection within the previous 12 months, respectively ($P = 0.11$). While the classic HCAP definition of hospitalization for >48 h in the previous 90 days was not associated with MDRO isolation, the total number of days hospitalized in the last 90 or 180 days was associated with MDRO isolation.

In the propensity score-adjusted multivariate logistic regression analysis, duration of previous hospitalization in the last 90 or 180 days, *P. aeruginosa* colonization/infection in the previous year, antimicrobial use in the last 90 days, and admission from a nursing home were all predictors of MDRO (Table 3). HCAP classification was not an independent predictor of MDRO (adjusted odds ratio [AOR] = 1.95; 95% CI, 0.66 to 5.80; $P = 0.23$).

Outcomes. Patients with MDRO isolation had a longer median length of stay compared to patients with no MDRO isolated (9 days versus 4 days, respectively; $P < 0.001$) and higher median CURB-65 scores (2 versus 1, respectively; $P = 0.005$). The overall cohort mortality at 30 days was 3.1% (16/521) with 5.8% and 0.4% of patients with HCAP and CAP experiencing mortality at 30 days, respectively ($P = < 0.001$). The propensity score-adjusted multi-

TABLE 1 Baseline characteristics of patients with community-acquired pneumonia

Characteristic[a]	No. of CAP patients (%) unless otherwise specified			
	All patients ($n = 521$)	Patients with MDRO pneumonia ($n = 20$)	Patients with no MDRO isolated ($n = 501$)	*P* value[b]
Age, yr [median (IQR)]	65 (52, 79)	73 (62, 82)	65 (52, 78)	0.059
Female	289 (55.5)	9 (45)	280 (55.9)	0.337
CURB-65 score				
Median (IQR)	1 (0, 2)	2 (1, 3)	1 (0, 2)	0.005
Score of >1	217 (41.7)	15 (75)	202 (40.3)	0.002
Score of >2	85 (16.3)	7 (35)	78 (15.6)	0.021
ICU admission	40 (7.7)	4 (20)	36 (7.2)	0.035
Ventilator required	43 (8.3)	3 (15)	40 (8)	0.264
Comorbidities				
CVA history	68 (13.1)	6 (30)	62 (12.4)	0.022
CHF	86 (16.5)	7 (35)	79 (15.8)	0.023
COPD	144 (27.6)	6 (30)	138 (27.5)	0.81
Liver disease	30 (5.8)	1 (5)	29 (5.8)	0.877
BUN level of >19 mg/dl	206 (39.5)	15 (75)	191 (38.1)	0.001
Diabetes	148 (28.4)	9 (45)	139 (27.7)	0.093
Immunocompromised	59 (11.3)	1(5)	58 (11.6)	0.363
Aspiration risk	107 (20.5)	7 (35)	100 (20)	0.103
CAP	263 (50.5)	5 (25)	258 (51.5)	0.02
HCAP	258 (49.5)	15 (75)	243 (48.5)	0.02
Admission from a nursing home	127 (24.4)	13 (65)	114 (22.8)	<0.001
Hospitalization for 48 h in the last 90 days	167 (32.1)	9 (45)	158 (31.5)	0.206
Home infusion therapy	4 (0.8)	0	4 (0.8)	0.688
Home wound care	21 (4)	2 (10)	19 (3.8)	0.166
Hemodialysis clinic	28 (5.4)	1 (5)	27 (5.4)	0.94
No. of days hospitalized in the last 90 days [median (IQR)]	0 (0, 3)	0 (0, 10)	0 (0, 3)	0.092
No. of days hospitalized in the last 180 days [median (IQR)]	0 (0, 7)	6 (0, 22)	0 (0, 6)	0.03
Antibiotic use in the last 90 days	166 (31.9)	12 (60)	154 (30.7)	0.006
History of colonization with:				
Any MDRO	57 (10.9)	7 (35)	50 (10)	<0.001
MRSA	28 (5.4)	3 (15)	25 (5)	0.052
Pseudomonas	21 (4)	5 (25)	16 (3.2)	<0.001
CRE	2 (0.4)	0	2 (0.4)	0.777
ESBL-producing bacteria	2 (0.4)	0	2 (0.4)	0.777
VRE	14 (2.7)	1 (5)	13 (2.6)	0.514

[a] IQR, interquartile range; ICU, intensive care unit; CVA, cerebrovascular accident; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; BUN, blood urea nitrogen; CAP, community-acquired pneumonia; HCAP, health care-associated pneumonia; MDRO, multidrug-resistant organism; MRSA, methicillin-resistant *Staphylococcus aureus*; CRE, carbapenem-resistant *Enterobacteriaceae*; ESBL, extended-spectrum beta-lactamase; VRE, vancomycin-resistant *Enterococcus*.
[b] *P* values reported for comparisons between patients with MDRO pneumonia versus patients with no MDRO isolated.

variate logistic regression analysis showed an association between HCAP and mortality (AOR = 11.60; 95% CI, 1.48 to 90.75; $P = 0.02$). The mortality rate at 30 days was 10% in patients with an MDRO isolated versus 2.8% for those with no MDRO isolated ($P = 0.122$). Furthermore, in the propensity score-adjusted multivariate logistic regression analysis with adjustments for age, CURB-65 score, and comorbidities, the presence of MDRO was not associated with an increased mortality (AOR, 1.80; 95% CI, 0.34 to 9.61; $P = 0.49$). There was no difference in mortality at 30 days between patients with an identified pneumonia etiology compared to those without an identified etiology (4% versus 3%, respectively; $P = 0.48$).

DISCUSSION

In this 2-year observational cohort study of 521 patients with CAP and HCAP, there was a 3.8% prevalence of MDRO. This low prevalence of MDRO community-onset pneumonia contrasts with previous studies in the United States (12–14). Kollef et al. evaluated the etiology of pneumonia in a large database of hospitalized patients from 59 U.S. centers and found a high rate of MDRO

TABLE 2 Identified etiology of pneumonia

Etiology of pneumonia[a]	No. of patients (%)[b]		
	All patients ($n = 99$)	HCAP patients ($n = 46$)	CAP patients ($n = 53$)
Gram-positive bacteria	48 (48)	21 (46)	27 (51)
Streptococcus pneumoniae	24 (24)	5 (12)	19 (36)
Staphylococcus aureus	17 (17)	11 (24)	6 (11)
MRSA	11 (11)	8 (17)	3 (5.7)
MSSA	6 (6)	3 (6.5)	3 (5.7)
Streptococcus spp. other than pneumococcus	5 (5)	3 (6.5)	2 (3.8)
Other	2 (2)	2 (4.3)	0
Gram-negative bacteria	33 (33)	21 (46)	12 (23)
Enterobacteriaceae	13 (13)	8 (17)	5 (9.4)
Pseudomonas aeruginosa	9 (9)	7 (15.2)	2 (3.8)
Haemophilus influenzae	5 (5)	1 (2.2)	4 (7.5)
Moraxella catarrhalis	4 (4)	3 (6.5)	1 (1.9)
Other	2 (2)	2 (4.3)	0
Atypical	2 (2)	0	2 (3.8)
Polybacterial culture	9 (9)	6 (13)	3 (5.7)
Virus	32 (32)	13 (28)	19 (36)
Rhinovirus	12 (12)	3 (6.5)	9 (17)
Influenza virus	9 (9)	3 (6.5)	6 (11.3)
Influenza A virus	6 (6)	2 (4.3)	4 (7.5)
Influenza B virus	3 (3)	1 (2.2)	2 (3.8)
Parainfluenza virus	5 (5)	2 (4.3)	3 (5.7)
Metapneumovirus	4 (4)	2 (4.3)	2 (3.8)
RSV	2 (2)	2 (4.3)	0
Adenovirus	1 (1)	1 (2.2)	0
Primary viral pneumonia	26 (26.3)	11 (24)	15 (28)
Mixed bacterial/viral pneumonia	6 (6)	1 (2.2)	5 (9.4)

[a] MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*; RSV, respiratory syncytial virus.
[b] The percentages may equal >100%, given some patients had polybacterial or mixed bacterial/viral pneumonia. HCAP, health care-associated pneumonia; CAP, community-acquired pneumonia.

HCAP (26.5% with MRSA, 25.3% with *P. aeruginosa*) (12). However, only culture-positive patients were included, viral etiologies of pneumonia were not evaluated, and patients were not assessed for study inclusion by their clinical, laboratory, and radiological presentation; these limitations likely contributed to an overestimation of the MDRO prevalence. Two subsequent retrospective studies, each conducted at the same U.S. institution, found a similarly high rate of MDRO, including MRSA and *P. aeruginosa* in patients with culture-positive HCAP (13, 14). In contrast, a prospective study of all patients admitted to a United Kingdom medical center with community-onset pneumonia over a 4.5-year period found a low rate of MDRO in HCAP with 2.2% of patients having MRSA and 2.2% having *P. aeruginosa* (15). Similarly, Aliberti et al. conducted a prospective study of consecutive hospitalized patients with community-onset pneumonia at a single center in Italy and found an overall MDRO rate of 3.3% (16).

There are multiple potential reasons for the different MDRO isolation rates. One explanation may be the method of analysis. The previously mentioned United States-based studies included only patients with a bacterial pathogen isolated (12–14). These studies do not reflect the true spectrum of CAP and HCAP, since prospective studies have defined a specific microbiologic etiology only in 16% to 63.8% of CAP patients and 21% to 67.5% of those with HCAP (15–19). Moreover, pathogens such as *S. aureus* and *P. aeruginosa* may be more easily grown from sputum specimens compared to *S. pneumoniae* (2). This may result in overdetection of MDRO pathogens relative to more typical respiratory pathogens. Similarly, it is less likely that patients with community-onset pneumonia and an unrevealing respiratory tract culture have pneumonia due to an MDRO; thus, there is clinical value to a negative culture when deciding whether broad-spectrum antibiotics are warranted.

Furthermore, the variability of MDRO prevalence may be based on geographic location and patient population. The National Healthcare Safety Network reports that there is "great variation in the degree of spread of antimicrobial-resistant infections" (20). As an example, 29% of *Klebsiella pneumoniae* from 14 New York City hospitals harbored the carbapenemase KPC (21). In contrast, no CIRE or ESBL-producing Gram-negative bacilli were found in our study, and only 10 patients have had KPC-positive Gram-negative bacilli at our institution over the last 4 years (unpublished data). Based upon our 2011 institutional antibiogram, third-generation cephalosporin resistance and carbapenem resistance was identified in only 4.9% and 0.3% of institutional cultures yielding *Enterobacteriaceae*. Our microbiologic findings in community-onset pneumonia are more consistent with studies conducted outside the United States and may be more relatable to areas with low rates of MDRO isolation (15–17, 22, 23). These findings strongly suggest that treatment choices should be guided by local microbial epidemiology.

Multiple independent risk factors for MDRO were identified in our study. A novel finding was the association between the duration of previous hospitalization in the last 90 or 180 days and the isolation of MDRO. Previous studies have found hospitalization for >48 h in the last 90 days to be a predictor of MDRO isolation, but to our knowledge, none have attempted to quantitate the risk based on previous durations of stay (16, 19, 24). The 48-h cutoff used in the HCAP definition was likely based upon the traditional definition of a nosocomial infection (3). However, the risk of acquiring an MDRO is likely increased with increased duration of prior hospitalization, previous antimicrobial exposure, and the rate of MDRO in the local environment. Epidemiologic studies of MRSA and ESBL Gram-negative colonization support this by demonstrating that colonization is associated with a prolonged hospital stay (25, 26).

The 2005 ATS/IDSA guidelines did not specifically include patients with a known colonization or previous infection with an MDRO in the HCAP definition. However, we found that patients with a clinical culture positive for *P. aeruginosa* in the previous 12 months was independently associated with MDRO isolation in patients with pneumonia. Furthermore, a history of *P. aeruginosa* in the previous 12 months was associated with *P. aeruginosa* pneumonia. Previous MRSA colonization/infection in the previous 12 months did not reach statistical significance for predicting MRSA pneumonia ($P = 0.11$). Shindo et al. recently found that a previous MRSA history in the last 90 days was associated with MRSA pneumonia (19). These findings suggest that previous colonization/infection with MDRO pathogens should be included in empirical antimicrobial decisions.

While the HCAP classification was not independently associated with MDRO in our propensity score-based multivariate

TABLE 3 Predictors of multidrug-resistant organisms[a]

Risk factor	No. of patients (%)		Statistical measure[b]	
	Patients with MDRO pneumonia ($n = 20$)	Patients with pneumonia but no MDRO isolated ($n = 501$)	Univariate analysis	Multivariate analysis
Presence of HCAP	15 (75)	243 (49)	3.37 (1.35–8.41) 0.009	1.95 (0.66–5.80) 0.226
Hospitalization for 48 h in the last 90 days	9 (45)	158 (32)	1.78 (0.72–4.37) 0.211	1.23 (0.47–3.19) 0.678
Home infusion therapy home	0 (0)	4 (0.8)	0 (0) 0.999	0 (0) 0.999
Hemodialysis	1 (5)	27 (5.4)	0.92 (0.12–7.16) 0.940	0.627 (0.08–5.06) 0.661
Admission from a nursing home	13 (65)	114 (22.8)	6.31 (2.46–16.18) 0.027	4.19 (1.55–11.31) 0.005
Home wound care	2 (10)	19 (3.8)	2.82 (0.61–13.03) 0.185	3.78 (0.78–18.38) 0.100
Previous MRSA colonization/infection	3 (15)	25 (5)	3.36 (0.92–12.23) 0.066	3.57 (0.95–13.43) 0.06
Previous *Pseudomonas* colonization/infection	5 (25)	16 (3.2)	10.10 (3.27–31.22) 0.001	7.43 (2.24–24.61) 0.001
History of antibiotic use in previous 90 days	12 (60)	154 (30.8)	3.19 (1.14–8.90) 0.027	2.90 (1.13–7.45) 0.027
Immunocompromised	1 (5)	58 (11.6)	0.40 (0.05–3.06) 0.379	0.51 (0.07–3.98) 0.523
No. days hospitalized in the last 90 days [median (IQR)]	0 (0, 10)	0 (0, 3)	1.06 (1.02–1.10) 0.002	1.06 (1.01–1.10) 0.013
No. days hospitalized in the last 180 days [median (IQR)]	6 (0, 22)	0 (0, 6)	1.05 (1.02–1.07) 0.001	1.04 (1.02–1.07) 0.002

[a] MDRO, multidrug-resistant organism; IQR, interquartile range; MRSA, methicillin-resistant *Staphylococcus aureus*.
[b] For each analysis (univariate or multivariate) and each risk factor, the first line shows the odds ratio, the second line shows the 95% confidence interval in parentheses, and the third line shows the *P* value.

analysis, one component of the definition, admission from a nursing home, was. Many previous studies have attempted to validate the utility of the HCAP definition for identification of risk factors for MDRO isolation with mixed results (7, 19). A recent meta-analysis of 24 studies suggested that the HCAP classification poorly discriminated between patients at a high or low risk for MDRO (7). Importantly, the authors suggest that utilizing the current HCAP classification will yield unnecessary MDRO therapy in areas with a low prevalence of MDRO and undertreatment in areas with high rates of MDRO. A new definition that incorporates MDRO epidemiology in the patient population of interest and patient-specific risk factors is needed. Reflexive prescribing of combinations of broad-spectrum antibiotics directed at MDROs for all patients meeting the current definition of HCAP is inappropriate and results in increased costs of care and increased risk of drug side effects

and toxicity and contributes to selective pressure favoring the emergence of antibiotic resistance.

Primary viral pneumonia was identified in 5% of the overall cohort (5.7% of patients with CAP, 4.3% of patients with HCAP) and was the most commonly identified pneumonia etiology. Consistent with our findings, previous studies have shown that primary viral infections are a common cause of CAP (8, 10). Although primary viral HCAP has not typically been a focus of investigation, a recent study suggests patients admitted with nursing home-acquired pneumonia are at a high risk for primary viral pneumonia (9). The recognition of viruses as primary causes of CAP and HCAP may increase over time with the increased utilization of more-sensitive molecular assays (27). The identification of a primary viral pneumonia has implications for antimicrobial stewardship, given that patients with primary viral pneumonia could potentially have antibacterial treatment withheld and antiviral therapy initiated (e.g., influenza).

Mortality at 30 days occurred infrequently in our cohort, which is consistent with the low median CURB-65 score of 1. Only 16.3% of the cohort had a CURB-65 score of >2, a cutoff that would be associated with an anticipated mortality of greater than 3% (11). Previous studies have suggested an increased mortality rate with HCAP compared to CAP in univariate analysis (12, 15, 17, 23). In our study, the high mortality with HCAP was likely due to more comorbidities and higher admission disease severity. Chalmers et al. found that HCAP was not independently associated with mortality after adjustments for differences in baseline severity of illness, comorbidities, and particularly withholding aggressive therapy, which was frequent in the HCAP group (15).

Our study has some limitations. It is a retrospective study and is subject to misclassification bias. While this study was conducted at a single center in the United States and the epidemiologic findings may not apply elsewhere, they are useful in defining the "variability of bacteriology from one hospital to another" and accounting for local resistance patterns as suggested in the ATS/IDSA guidelines (3). Identified independent predictors for MDRO were based on a limited number of patients given the infrequency of isolating MDRO pathogens in our patient population. Respiratory cultures were obtained in 43% of patients, and a specific etiology of pneumonia was identified in only 19% of our cohort, so other potential etiologies of pneumonia may not have been identified.

Our study makes substantial contribution to the existing body of epidemiologic data on pneumonia in the United States and suggests that MDROs may be infrequent causes of community-onset pneumonia at some centers. Based upon our findings and those of others, it is unlikely that all patients with HCAP require empirical treatment for MRSA and *P. aeruginosa* as originally suggested (3, 12). More data are needed to better describe the etiology of community-onset pneumonia in the United States, specifically prospective, multicenter studies which include characterization of primary viral pneumonia and culture-negative pneumonia. In conclusion, MDRO prevalence in the local patient population and specific MDRO risk factors should be considered when selecting empirical therapy for community-onset pneumonia.

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