A Multi-center Evaluation of the US Prevalence and Regional Variation in Macrolide-resistant Streptococcus pneumoniae from Blood or Respiratory Cultures Among Adult Patients

Vikas Gupta[1], Kalvin Yu[1], Steven P. Gelone[2]

[1]Becton, Dickinson and Company, Franklin Lakes, United States, USA; [2]Nabriva Therapeutics US, Inc., Fort Washington, PA, USA

Nabriva Therapeutics
Dublin, Ireland
www.nabriva.com

INTRODUCTION & PURPOSE

- *S. pneumoniae* is the most common etiology for community-acquired bacterial pneumonia (CABP).[1-2]
- Because of the significant healthcare burden associated with *S. pneumoniae*, the US Centers for Disease Control and Prevention (CDC) designated drug-resistant *S. pneumoniae* a pathogen of serious threat.[3]
- Macrolides have long been an important component of empiric CABP therapy; but increasing resistance has diminished effectiveness and prompted a change in the 2019 American Thoracic Society (ATS)/Infectious Diseases Society of America (IDSA) guidelines for CABP treatment.[2]
- Namely, although macrolide monotherapy is still considered an option for initial treatment of CABP in outpatients with no comorbid conditions, the ATS/IDSA 2019 update specifies that this therapy should only be used if local Pneumococcal resistance is <25%.[2]

OBJECTIVE

- We used microbiological laboratory data from a large US hospital database to determine the prevalence of macrolide-resistant *S. pneumoniae* in hospitalized and ambulatory patients throughout the US.

METHODS

Study Design

- This retrospective cohort study included microbiological results from adult patients with positive *S. pneumoniae* blood or respiratory cultures evaluated between October 2018 and September 2019 at 329 US facilities in the BD Insights Research Database (Becton, Dickinson and Company, Franklin Lakes, NJ, US).
- The primary objective was to determine the proportion of *S. pneumoniae* isolates resistant to macrolides in blood and respiratory cultures.
- The study dataset was approved as a limited, de-identified dataset for retrospective analysis and was exempted from patient consent by the New England Institutional Review Board (Wellesley, Massachusetts).

Susceptibility Testing

- Non-duplicate *S. pneumoniae* isolates, defined as first isolate of a species per 30-day period, were obtained from blood or respiratory cultures. Isolates from each source were considered separately.
- Assessment of macrolide-resistance was based on facility reports using commercial panels in local automated susceptibility testing platforms and application of locally defined laboratory breakpoints.
- Resistance to any member of the macrolide class (i.e. azithromycin, clarithromycin, or erythromycin) was considered macrolide resistant.

METHODS (continued)

Statistical Analysis

- Macrolide resistance rates were compared by use of the chi-square test with *P* values <0.05 indicating statistical significance. All analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC).

RESULTS

Nationwide *S. pneumoniae* Macrolide Resistance

- **Table 1** depicts the results of the nationwide macrolide resistance rates.
- A total of 3,626 *S. pneumoniae* isolates from blood (n=1,591; 43.9%) or respiratory (n=2,035; 56.1%) cultures were included.
- 22.8% of isolates where obtained from patients in the ambulatory setting, with the remaining 77.2% coming from inpatient settings.
- The overall rate of macrolide resistance in *S. pneumoniae* isolates was 39.5%
- The resistance rate in respiratory isolates (47.3%) was significantly higher than the rate in blood isolates (29.6%; $P < 0.0001$).
- Isolates obtained from ambulatory encounters had a significantly higher rate of macrolide resistance compared with isolates from inpatients (45.3% vs 37.8%; $P < 0.001$).

Table 1. Macrolide Resistance rates among *S. pneumoniae* across the USA

Setting	Number of Facilities	% Macrolide Resistant (n)		
		Blood Isolates	Respiratory Isolates	All Isolates
Total	329	29.6% (1,591)[a]	47.3% (2,035)[a]	39.5% (3,626)
Inpatient	313	28.2% (1,211)	45.2% (1,587)	37.8% (2,798)[b]
Ambulatory	231	33.9% (380)	54.9% (448)	45.3% (828)[b]

[a]Respiratory vs. blood (p<0.0001)
[b]Ambulatory vs. inpatient (p<0.001)

Geographic Differences in *S. pneumoniae* Macrolide Resistance

- Statistically significant differences ($P < 0.0001$) were observed in macrolide resistance in different US census regions (**Table 2**).
- Respiratory isolates from all US census regions revealed ≥25% macrolide resistance.
- The highest overall rate (i.e. combined respiratory and blood) of macrolide resistance was observed in the West North Central region (54.2%), followed by the South Atlantic (48.0%).

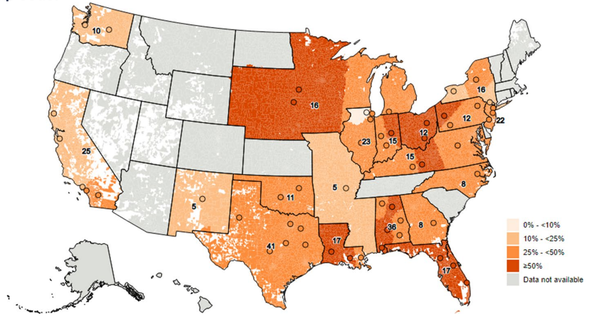
RESULTS (continued)

- Regions with overall *S. pneumoniae* macrolide resistance rates <25% were Mountain (13.9%), New England (18.2%), and Pacific (18.3%), driven primarily by the relatively low resistance rates in blood isolates, whereas respiratory isolates were ≥25%.
- Further delineation of the geographic distribution by zip codes (**Figure 1**) identified sub-regional and within-state differences in overall resistance rates. (e.g. California showed higher macrolide resistance in the southern part of the state.
  - Data therein represented 3,464 isolates collected from 314 facilities aggregated into geographic clusters of 5 or more hospitals from 2 or more integrated delivery networks. Shaded circles show the geographic centroid for each geographic cluster and numbers indicate the total number of included medical centers at the state level; facilities contributing <5 isolates were excluded.

Table 2. *S. pneumoniae* macrolide resistance rates by USA census region.

Census region (states)	Number of Facilities	% Macrolide Resistant (n)		
		Blood Isolates	Respiratory Isolates	All Isolates
West North Central: (IA, KS, MN, MO, ND, NE, SD)	12	52.1% (48)	55.0% (131)	54.2% (179)
South Atlantic: (DE, DC, FL, GA, MD, NC, SC, VA, WV)	40	30.3% (145)	60.8% (199)	48.0% (344)
East South Central: (AL, KY, MS, TN)	49	38.0% (229)	55.6% (252)	47.2% (481)
West South Central: (AR, LA, OK, TX)	71	35.6% (455)	48.5% (643)	43.2% (1098)
East North Central: (IL, IN, MI, OH, WI)	56	29.0% (217)	49.7% (320)	41.3% (537)
Middle Atlantic: (NJ, NY, PA)	50	28.3% (191)	39.8% (236)	34.7% (427)
Pacific: (AK, CA, OR, WA)	36	13.2% (257)	25.3% (190)	18.3% (447)
New England: (CT, MA, ME, NH, RI, VT)	5	4.0% (25)	25.0% (52)	18.2% (77)
Mountain: (AZ, CO, ID, MT, NM, NV, UT, WY)	10	4.2% (24)	33.3% (12)	13.9% (36)

Figure 1. Geographic distribution of *S. pneumoniae* macrolide resistance rates by zip code.



CONCLUSIONS

- *S. pneumoniae* blood and respiratory isolates from US facilities reveal a high burden of macrolide resistance with an overall 39.5% resistant rate.
- Macrolide resistance among *S. pneumoniae* obtained in the ambulatory setting was higher than those cultured in the inpatient setting.
- Macrolide resistance rates in respiratory *S. pneumoniae* across all census regions ranged from 25 – 60.8% and were higher than those observed in blood isolates.
- Given the ≥25% macrolide resistance threshold proposed by the ATS/IDSA CABP treatment guidelines, our data suggest alternative antibiotics, other than macrolide monotherapy, should be considered for empiric CABP therapy in the US.

REFERENCES

(1) Jain S, et al. N Engl J Med. 2015 Jul 30;373(5):415-27. (2) Metlay JP, et al. Am J Respir Crit Care Med 2019; 200:e45-67. (3) Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States, 2019. Available at www.cdc.gov/DrugResistance/Biggest-Threats.html. Accessed September 2020.

Disclosures

This work was supported by a grant from Nabriva Therapeutics US, Inc.. V.G. and K.C.Y. are employees of Becton, Dickinson & Company, which was contracted by Nabriva Therapeutics to conduct the study, and own stock in BD. S.P.G. is an employee of Nabriva and holds stock in Nabriva Therapeutics. These data have been published in OFID at https://academic.oup.com/ofid/advance-article/doi/10.1093/ofid/ofab063/6128791

Scan this QR code with your electronic device to receive a PDF file of the poster.

American Association of Nurse Practitioners Virtual National Conference, June 15th – Aug 31st, 2021