

Temporal Trends in Antibiotic Use of New β -lactams for Gram-Negative Bacteria with Difficult-to-Treat Resistance in the Southeastern United States

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BACKGROUND

- Incidence of infections due to antimicrobial resistant organisms is estimated to be 2.8 million annually in the United States
- The most worrisome are Gram-negative bacteria (GNB) with difficult-to-treat resistance (DTR) defined as bacteria non-susceptible to penicillins, cephalosporins, carbapenems, and fluoroquinolones

- Multiple new, broad-spectrum, β -lactams have been developed to combat GNB with DTR

Figure 1. Timeline of New β -lactam Development



- The primary objective of this study was to examine the temporal trends in prevalence of GNB with DTR and the use of new β -lactams in the southeastern United States

METHODS

Study Design

- Multicenter, retrospective, cohort study
- 10 hospitals geographically spread within the Southeastern Research Group Endeavor (SERGE-45) between 2015-2020 [Table 1]

Data Collection

- Incidence of GNB with DTR: Enterobacterales, *Pseudomonas aeruginosa* (*P. aeruginosa*), *Acinetobacter* species
- Cumulative antibiotic use (AU) of new β -lactams: ceftolozane/tazobactam, ceftazidime/avibactam, cefiderocol, meropenem/vaborbactam, and imipenem/cilastatin/relebactam

Key Definitions

- GNB with DTR = nonsusceptible to all of the following: extended-spectrum cephalosporins (either ceftazidime or cefepime), carbapenems (either meropenem or imipenem/cilastatin), fluoroquinolones (either ciprofloxacin or levofloxacin), and piperacillin/tazobactam (if tested/reported)
- AU = days of therapy (DOT) per 1,000 patient days (PD) present

Statistical Analysis

- Temporal trends in prevalence of GNB with DTR and cumulative AU of new β -lactams: linear regression

RESULTS

Table 1. Hospital Characteristics

State	Bed Size	Automated System	EHR System
Alabama	200-500	MicroScan	Cerner
Florida	≥ 501	Vitek II	Allscripts
Georgia	≤ 200	MicroScan	CPRS
Georgia	201-500	Vitek II	Meditech
Georgia	≥ 501	Vitek II	Cerner
Mississippi	≥ 501	Vitek II	Epic
South Carolina	≥ 501	Vitek II	Cerner
South Carolina	201-500	Vitek II	Cerner
Texas	201-500	MicroScan	Cerner
West Virginia	≥ 501	Vitek II	Epic

Abbreviations: EHR, electronic health record

- Overall prevalence of GNB with DTR was 0.86% with numerical increase from 0.77% to 1.00% between 2015 and 2020 ($p=0.06$) [Figure 2]
- Cumulative AU of new β -lactams was 1.49 DOT per 1,000 patient-days present with numerical increase from 0.03 to 2.18 DOT per 1,000 patient-days present ($p=0.07$) [Figure 2]
- While the prevalence of DTR *P. aeruginosa* remained stable, there was a significant upward trend in prevalence of DTR *Acinetobacter* spp. (4.2% to 18.8%, $p<0.001$), and Enterobacterales (0.11% to 0.28%, $p=0.02$) [Figure 3]

CONCLUSIONS

- While overall prevalence of GNB with DTR and cumulative use of new β -lactams remain relatively low, the uptrend in prevalence of DTR isolates is concerning and may drive future increased use of new β -lactams
- Additional efforts to benchmark the use and appropriateness of new β -lactams are crucial to preserve their efficacy against GNB with DTR

REFERENCES

- CDC Antibiotic Resistance Threats in the United States, 2019.
- Kadri SS, et al. Clin Infect Dis 2018;67:1803.
- Ho S, et al. Curr Infect Dis Resp 2009;21:39.
- Zhanel GG, et al. Drugs 2018;78:65
- Taheri Y, et al. Front Pharmacol 2021;11:578823.

DISCLOSURES

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RESULTS

Figure 2. Prevalence of GNB with DTR and Cumulative AU of New β -lactams

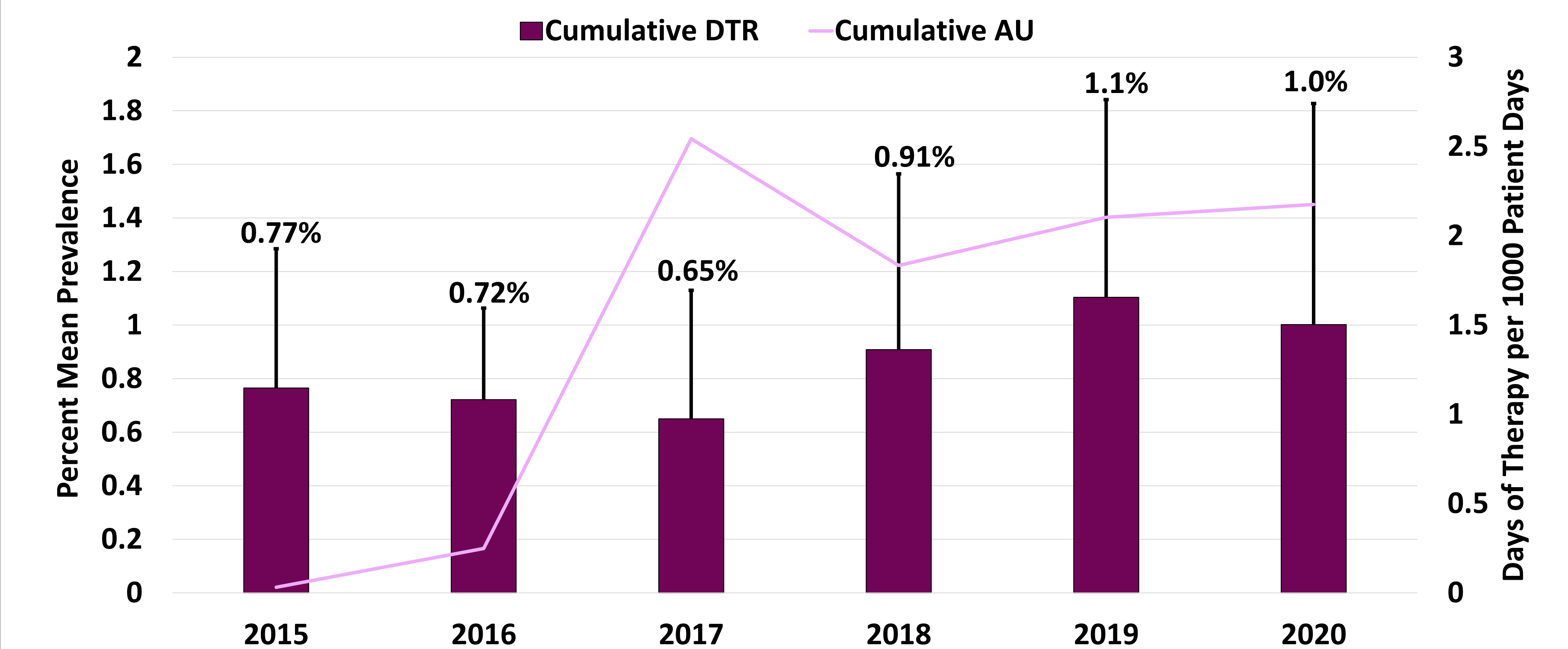


Figure 3. Prevalence of GNB with DTR: Enterobacterales, *P. aeruginosa*, and *Acinetobacter* spp.

