Poster #: 426

Trends in carbapenem non-susceptible (Carb-NS) Enterobacterales from hospitalized patients in the US from 2014-2020: A comparison between organisms with and without concerns for chromosomal AmpC beta-lactamase hyperproduction

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Introduction

- Carbapenem-resistant Enterobacterales (ENT) have been designated an "Urgent Threat" by the Centers for Disease Control and Prevention, underscoring the need for understanding epidemiological trends over time with these pathogens.[1]
- Hyperproduction of chromosomal AmpC beta-lactamases in conjunction with outer membrane porin down-regulation/loss is a key mechanism of carbapenem resistance in some ENT species.[2]
- The goal of our study was to evaluate trends in non-susceptibility to carbapenems (Carb-NS) in ENT over time in the US inpatient setting and to compare Carb-NS trends in ENT isolates with or without the potential for chromosomal AmpC beta-lactamase hyperproduction.

Methods

- We evaluated all adults with a positive ENT culture (first isolate of a species per 30-day period from blood, respiratory, urine, skin/wound, intra-abdominal, or other) between 2014 – 2020 in the inpatient setting of 314 US facilities in the BD Insights Research Database (Becton, Dickinson & Company, Franklin Lakes, NJ USA).
- Carb-NS was defined at the facility level as intermediate or resistant to imipenem, meropenem or doripenem or ertapenem based on facility interpretations of commercial panel readings.
- For this analysis, ENT were classified based on potential for hyperproduction of chromosomal AmpC beta-lactamase

Potential AmpC ENT	Non-AmpC ENT
Citrobacter freundii	*Escherichia coli*
Enterobacter cloacae	*Klebsiella pneumoniae*
Klebsiella aerogenes	*Proteus mirabilis*

  - Other ENT were excluded.
- Time series models were used to evaluate the monthly patterns of resistance trends as the proportion of Carb-NS ENT isolates per ENT isolates tested.
  - Models were adjusted by hospital characteristics (bed size, urban/rural status, US census region, and teaching status).

Results

- A total of 2,513,392 inpatient non-duplicate ENT isolates were evaluated across 20,033,197 admissions from 314 facilities.
  - 1.3% (n=31,628) were Carb-NS.
- Of the Carb-NS ENT isolates, 30.7% (9,717/31,628) were classified as potential AmpC ENT and 60.9% (19,277/31,628) were classified as non-AmpC ENT (Figure 1).
  - Together, these groups made up 91.7% of Carb-NS ENT.
- Trends over time (2014 – 2020) for Carb-NS ENT in US inpatients (Table 1 and Figure 2):
  - Decreasing trends were observed for overall % Carb-NS ($p < 0.001$) and % Carb-NS *K. pneumoniae* ($p < 0.0001$).
  - Increasing trends were observed for % Carb NS *P. mirabilis* and potential AmpC ENT ($p < 0.0001$ for both).

Figure 1. Trends in inpatient % Carb-NS ENT from 2014-2020.

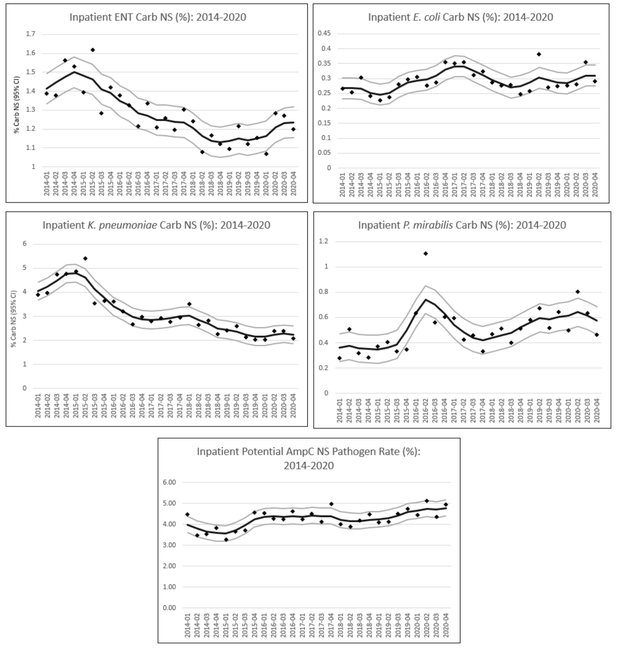


Table1. Model-estimated[a] Carb-NS rates and trends from 2014-2020 in US hospital inpatients.

ENT category	Number of Carb-NS ENT isolates	Number of ENT isolates tested	% Carb-NS (95% CI)	Relative rate change from 2014-2020 (95% CI)	P value
All evaluated ENT	31,628	2,513,392	1.26 (1.2, 1.33)	-0.57% (-0.88, -0.27)	<0.001
Non-AmpC					
E. coli	4,109	1,394,320	0.29 (0.27, 0.30)	0.14% (-0.23, 0.51)	0.348
K. pneumoniae	13,870	462,350	2.91 (2.55, 3.36)	-6.44% (-7.50, -5.41%)	<0.001
P. mirabilis	1,298	248,520	0.51 (0.44, 0.59)	0.79% (0.64, 0.93)	<0.001
Potential AmpC[b]	9,717	226,020	4.3 (4.2, 4.4)	0.71% (0.53, 1.10)	<0.001

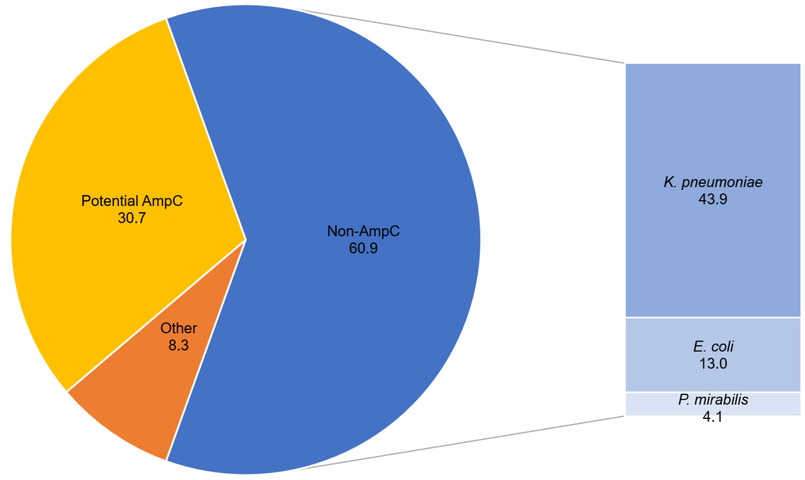
Green shading indicates significant decreases in Carb-NS over time; red shading indicates significant increases in Carb-NS over time

[a] Models were adjusted by hospital characteristics (bed size, urban/rural status, US census region, and teaching status)

[b] *C. freundii*, *E. cloacae*, *K. aerogenes*

Carb, carbapenem; CI, confidence interval; ENT, Enterobacterales

Figure 2. Distribution (%) of Carb-NS ENT isolates (n=31,628) from US inpatients (2014 – 2020). Percentages may not add to totals shown due to rounding.



Conclusions

- There was a significant decrease in overall inpatient % Carb-NS ENT and % Carb-NS *K. pneumoniae* from 2014-2020.
- However, increases in % Carb-NS were seen in *P. mirabilis* and significant increases in species with potential for hyperproduction of chromosomal ampC.
- Surveillance of Carb-NS ENT should include a broader set of pathogens beyond *K. pneumoniae* and *E. coli* to provide more comprehensive insights into resistance rates in inpatient ENT isolates.

Limitations

- Although we used an algorithm to remove colonizing bacteria from the analyses,[3] it is possible that some isolates were colonizers rather than causes of invasive infections.
- Ertapenem was included in the definition for carbapenem NS, which may have resulted in overestimates in rates of resistance of potential AmpC ENT.

Disclosures

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References

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2. Tamma P, et al. Clin Infect Dis 2019;69:1446–55.
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