Correlation of High-Risk Antibiotic Use and Hospital-Associated *C. difficile* Infections: Data From 195 US Hospitals

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INTRODUCTION

- Antibiotics with known risk for *Clostridium difficile* infections (CDI) are widely used in hospitalized patients
- We evaluated hospital-level usage of high-risk antibiotics and associated CDI rates

METHODS

Data source

- We analyzed electronic microbiological and pharmacy data from July 1, 2016, through June 30, 2017, in the Becton Dickinson Insights Research Database (BD, Franklin Lakes, NJ).

Definition of high-risk antibiotics

- We defined 4 antibiotic classes as high-risk:
  - Cephalosporins (2nd/3rd/4th generation)
  - Fluoroquinolones
  - Carbapenems
  - Lincosamides
- Measured as days of therapy (DOT) per 1000 admissions, days at risk (DAR), and patient-days

Definition of CDI cases

- **CDI cases:** CDI cases were a positive stool *C. difficile* toxin or molecular assay result from a patient without a positive sample in the previous 8 weeks
- **Hospital-associated CDI cases (HA-CDI):** HA-CDIs included:
  - Specimens collected >3 calendar days after admission *or*
  - Specimens collected ≤3 calendar days from a patient with documented overnight stay in the same hospital in the prior 4 weeks

Statistical analysis

- We used Pearson r to assess the correlation
- We used Poisson regression model to estimate the relative risk of high-risk antibiotic use on HA-CDI, adjusting for community-onset/community-associate (COCA) CDI rate, hospital teaching status, and proton pomp inhibiter (PPI) use.

RESULTS

- Of the 195 study sites, 35% were teaching and 65% nonteaching; 37% large (>300 beds) and 62% small/medium (≤300 beds) size
- Overall median (interquartile range) of high-risk antibiotic use was 1190 (953, 1396) DOT per 1000 admissions; HA-CDI rate was 32 (22, 43) per 10,000 admissions
- The correlation between the 2 variables was 0.29 (*P*<0.0001; **Table 1, Figure 1**)
- Stratified by hospital teaching status and size, correlations ranged from 0.22–0.46 (all *P*<0.05; **Table 1**)
- Consistent patterns were observed when antibiotic use and HA-CDI rates were calculated using DAR (r=0.23, *P*=0.0015) or patient-days (r=0.25, *P*=0.0004; **Table 1**)
- Stratified by antibiotic class, HA-CDI rates were associated with use of cephalosporins (r=0.30, *P*<0.0001; **Figure 2**); associations with fluoroquinolones, carbapenems, or lincosamides were not significant due to overall less frequent use
- Although 46% (22/48) of hospitals in the top quartile of high-risk antibiotic use were in the top quartile of HA-CDI rates, only 10% (5/48) of hospitals in the lowest quartile of high-risk antibiotic use were in the top quartile of HA-CDI rates (**Table 2**)
- Adjusting for potential confounders, high-risk antibiotic use was associated with significant risk for HA-CDI
- Specifically, hospitals in the 2nd, 3rd, or 4th quartile of high-risk antibiotic use had 15%, 35%, and 32% increase in risk of HA-CDI compared with hospitals in the lowest quartile of antibiotic use (all *P*<0.001; **Table 3**)
- Higher PPI use was also associated with increased risk of HA-CDI (**Table 3**)
- COCA rate was significantly associated with HA-CDI (**Table 3**)

CONCLUSIONS

- Use of high-risk antibiotics, especially cephalosporins, is an independent driver of hospital-associated CDI
- The apparent association of PPI use with HA-CDI warrants further investigation
- Non–hospital-associated CDI prevalence at admission is predictive of HA-CDI rate
- Current results highlight the need for hospital antibiotic use surveillance and stewardship

Table 1. Correlation of Hospital High-Risk Antibiotic Use and HA-CDI Rates

Variable	# of hospitals	Antibiotic DOT/1000 admissions with CDI/10,000 admissions		Antibiotic DOT/1000 DAR with CDI/10,000 DAR		Antibiotic DOT/1000 patient-days with CDI/10,000 patient-days	
		r	*P*	r	*P*	r	*P*
Overall	195	0.29	<0.0001	0.23	0.0015	0.25	0.0004
Hospital teaching affiliation							
Teaching	68	0.46	<0.0001	0.35	0.0033	0.35	0.0037
Nonteaching	127	0.22	0.0147	0.22	0.0136	0.25	0.0038
Hospital size (# of beds)							
≤300	121	0.24	0.0093	0.26	0.0041	0.29	0.0014
>300	74	0.37	0.0011	0.20	0.0826	0.18	0.1238
Significant antibiotic class							
2nd, 3rd, 4th generation of cephalosporin	195	0.30	<0.0001	0.23	0.0011	0.25	0.0004

Table 2. Cross Table of HA-CDI Rate by High-Risk Antibiotic Use Quartile

CDI rate per 10,000 admissions	High-risk antibiotic use (days of therapy per 1000 admissions), # of hospitals (column %)				Total # of hospitals
	1st quartile (<953)	2nd quartile (953–1192)	3rd quartile (1193–1396)	4th quartile (>1396)	
1st quartile (≤22)	17 (35)	11 (22)	11 (23)	10 (21)	49
2nd quartile (23–32)	12 (25)	12 (24)	12 (25)	12 (25)	48
3rd quartile (33–43)	14 (29)	18 (36)	13 (27)	4 (8)	49
4th quartile (>43)	5 (10)	9 (18)	13 (27)	22 (46)	49
Total # of hospitals	48	50	49	48	195
Pooled CDI rate	27.70	31.40	36.30	39.80	

Table 3. Multivariable Poisson Model: Independent Predictors for HA-CDI

Variables	RR (95% CI)	*P*
High-risk antibiotic use (days of therapy per 1000 admissions)		
1st quartile (<953)	Reference	
2nd quartile (953–1192)	1.15 (1.07, 1.25)	0.0002
3rd quartile (1193–1396)	1.35 (1.25, 1.47)	<0.0001
4th quartile (>1396)	1.32 (1.22, 1.43)	<0.0001
Proton pump inhibitor use (days of therapy per 1000 admissions)		
1st quartile (<255)	Reference	
2nd quartile (255–330)	1.02 (0.95, 1.11)	0.5382
3rd quartile (331–372)	1.16 (1.07, 1.25)	0.0002
4th quartile (>372)	1.22 (1.13, 1.32)	<0.0001
COCA-CDI rate (number of cases per 10,000 admissions)		
1st quartile (<35)	Reference	
2nd quartile (35–55)	1.62 (1.49, 1.75)	<0.0001
3rd quartile (56–93)	1.77 (1.64, 1.92)	<0.0001
4th quartile (>93)	2.31 (2.14, 2.50)	<0.0001
Hospital teaching status		
Nonteaching	Reference	
Teaching	1.32 (1.26, 1.39)	<0.0001

Figure 1. Correlation of High-Risk Antibiotic Use and HA-CDI Rate

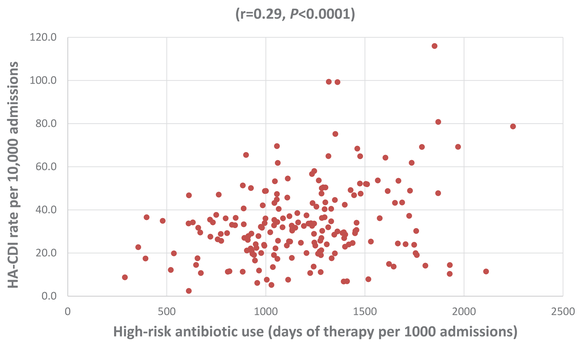
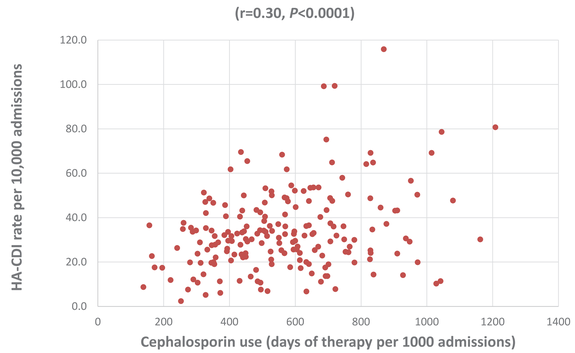


Figure 2. Correlation of Cephalosporin (2nd/3rd/4th Generation) Use and HA-CDI Rate



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