Poster # P0387

Correlation of High-risk Antibiotic Use and Hospital-associated *C. difficile* Infections: Data from 195 US Hospitals

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Background and Objective

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

Materials and Methods

Data source

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

Definition of high risk antibiotics

- We defined four antibiotic classes as high-risk:
  - Cephalosporins (2nd/3rd/4th-generation)
  - Fluoroquinolones
  - Carbapenems
  - Lincosamides

  Measured as days of therapy (DOT) per 1,000 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 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 antibiotics use on HA-CDI, adjusting for percent of admissions age 65 or older.

Results

- Of the 195 study sites, 35% were teaching and 65% nonteaching; 37% large (beds >300) and 62% small/medium (beds≤300) size.
- The overall median (interquartile range) of high-risk antibiotic use was 1,190 (953, 1,396) DOT per 1,000 admissions and HA-CDI rates was 32 (22, 43) per 10,000 admissions.
- The correlation between the two variables was 0.29 (P<0.0001) (Table 1 and Figure 1).
- Stratified by hospital teaching status and size, correlations ranged from 0.22 to 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) while associations with fluoroquinolones, carbapenems or lincosamides were not significant due to overall less frequent use.
- While 46% (22/48) hospitals in the top quartile of high-risk antibiotic use were in the top quartile of HA-CDI rates, only 10% (5/48) hospitals in the lowest quartile of high-risk antibiotic use were in the top quartile of HA-CDI rates (Table 2).
- Adjusting for proportion of patients age 65 or older, high risk antibiotics use was associated with significant risk for HA-CDI.
- Specifically, hospitals in the 2nd, 3rd, or 4th quartile of high risk antibiotics use had 12%, 15%, and 28% increase in risk of HA-CDI compared to hospitals in the lowest quartile of antibiotics use, controlling for the percent of admissions age 65 or older all P<0.01 (Table 3).
- Hospitals in the top quartile of proportion of patients with age 65 or older had 45% increase in risk for HA-CDI independently compared to hospitals in the lowest quartile (1st quartile) of admissions of older patients (Table 3).

Conclusions

- **Use of high risk-antibiotics, especially cephalosporins is an independent driver of hospital-associated HA-CDI.**
- **Highest proportion of patients with age 65 or older is independently associated with high HA-CDI rates.**
- **Future consideration of other potential confounders (e.g. CDI test type and use intensity, non-hospital-associated CDI prevalence) could further strengthen the observed correlation. Meanwhile, current results highlight the need for hospital antibiotic use surveillance and stewardship.**

Tables

Table 1. Correlation of hospital high risk antibiotics use and HA-CDI rates

Variable	# of hospitals	Abx DOT/1,000 admissions with CDI/10,000 admissions		Abx DOT/1,000 DAR with CDI/10,000 DAR		Abx DOT/1,000 patient days with CDI/10,000 patient days	
		r	P	r	P	r	P
Overall	195	0.29	<.0001	0.23	0.0015	0.25	0.0004
Hospital teaching affiliation							
Teaching	68	0.46	<.0001	0.35	0.0033	0.35	0.0037
Non-teaching	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	<.0001	0.23	0.0011	0.25	0.0004

Table 2. Cross table of HA-CDI rate by high risk antibiotics use quartile

CDI rate per 10,000 admissions	High risk antibiotics use [days of therapy per 1,000 admissions], # of hospitals (column %)				Total # of hospitals
	1st quartile (<953)	2nd quartile (953 to 1,192)	3rd quartile (1,193 to 1,396)	4th quartile (>1,396)	
1st quartile (≤22)	17 (35)	11 (22)	11 (23)	10 (21)	49
2nd quartile (23 to 32)	12 (25)	12 (24)	12 (25)	12 (25)	48
3rd quartile (33 to 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	

Note: 46% (n=22) hospitals in the top quartile of high risk antibiotics use (>1,396 DOT per 1,000 admissions) were in the highest CDI quartile (>43 CDI per 10, 000 admissions). In contrast, only 10% (n=5) in the lowest antibiotics use quartile was in the highest CDI quartile.

Table 3. Multivariable Poisson model: independent predictors for HA-CDI

Variable	Relative Risk (95% CI)	P-value
Hospital level high risk antibiotics use (days of therapy per 1,000 admissions)		
1st quartile (<953)	Reference	
2nd quartile (953 - 1,192)	1.12 (1.04, 1.20)	0.0029
3rd quartile (1,193 - 1,396)	1.15 (1.07, 1.24)	0.0002
4th quartile (>1,396)	1.28 (1.19, 1.38)	<.0001
Hospital level percent of admissions with age 65 years or older		
1st quartile (<34%)	Reference	
2nd quartile (34% - 39%)	0.96 (0.89, 1.03)	0.2227
3rd quartile (40% - 44%)	1.03 (0.96, 1.11)	0.3631
4th quartile (>44%)	1.45 (1.35, 1.55)	<.0001

Figures

Figure 1. Correlation of high risk antibiotics use and HA-CDI rate

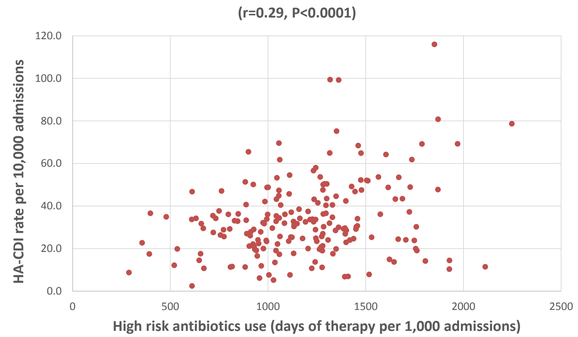
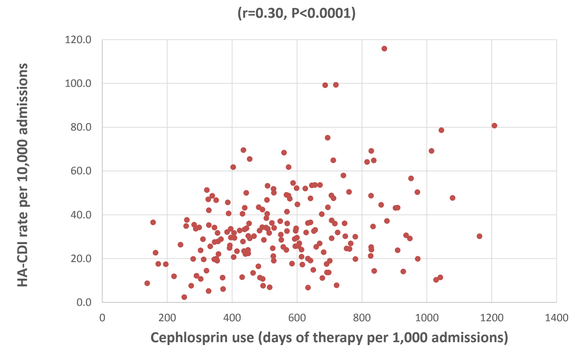


Figure 2. Correlation of cephalosporin (2nd/3rd/4th generation) use and HA-CDI rate



Reference:

McDonald LC et al. Clinical Practice Guidelines for *Clostridium difficile* Infection in Adults and Children: 2017 Update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *CID* 2018.

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