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Major Article

Interhospital patient transfers between Ontario's academic and large community hospitals increase the risk of *Clostridium difficile* infection

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Interhospital patient transfers
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Background: The objective of this study is to determine the impact of interhospital patient transfers on the risk of *Clostridium difficile* infection (CDI).

Methods: The number of interhospital patient transfers and CDI cases for 11 academic and 40 large community hospitals (LCHs) were available from 2010-2015. These data were used to compute a CDI score for each sending facility as a measure of CDI pressure on the receiving facility. This CDI score was included as a variable in a multilevel mixed-effect Poisson regression model of CDI cases. Other covariates included year, CDI testing strategy, antimicrobial stewardship program (ASP), and criteria used for patient isolation. Hospital-specific random effects were estimated for the baseline rate of CDI (intercept) and ASP effect (slope).

Results: The CDI score ranged from 0-103, with a mean score ± SD of 20.4 ± 21.8. Every 10-point increase in the CDI score was associated with a 4.5% increase in the incidence of CDI in the receiving academic hospital (95% confidence interval [CI], 0.9-8.5) and 3.6% increase in the receiving LCHs (95% CI, 0.3-7). The random components of the model varied significantly, with a strong negative correlation of –0.85 (95% CI, –0.94 to –0.65).

Conclusions: Our results suggest interhospital patient transfers increase the risk of CDI. ASPs appear to reduce this risk; however, these ASP effects demonstrate significant heterogeneity across hospitals.

A previous study demonstrated an increased risk of *Clostridium difficile* infection (CDI) associated with interfacility patient transfers.[1] In this retrospective observational study from 2005-2011 using data from 480 hospitals in California, this impact was measured by incorporating measures of centrality, determined using network analysis, in the final model to estimate their effect on CDI cases. The study estimated for every increase of 1 in log (weighted indegree), there was a 3.3% (95% confidence interval [CI], 1.5-5.2) increase in CDI incidence, where weighted indegree is a measure of the total number of patients transferred between hospitals. The study did not attempt to determine the mechanism through which this increased risk was transferred, that is, they did not know whether the increased risk was caused by transferred patients who had CDI or by some other indirect mechanism.

In a subsequent study that measured the impact of interfacility patient transfers on the risk of CDI in long-term care facilities (LTCFs), the incidence rate ratio for the importation of cases of acute care CDI per doubling of the LTCF-associated CDI rate was 1.23 (95% CI, 1.14-1.33), conditional on both patient-level and regional-level covariates such as antibiotic use.[2] This study hypothesized that the increased incidence of CDI importation coupled with facility-level antibiotic use was responsible for 75% of the variation seen in the increased incidence rates of CDI among residents in LTCFs.

In Ontario, Canada's most populous province with >13 million residents, there are 12 academic and 45 large community hospitals (LCHs).[3] These hospitals account for >95% of all acute inpatient days among adults >18 years of age.[4] These hospitals are part of a provincial network of hospitals that are publicly funded and universally accessible under Canada's Medicare program. As a result, there are a significant number of interhospital patient transfers, sometimes affecting up to 3% of all inpatients.[5] Since 2008, there has been mandatory hospital reporting of hospital-associated CDI (HA-CDI) rates.[6] This study will explore the association between interhospital patient transfers and incidence rates of HA-CDI while taking into account hospital-level infection prevention and control (IPAC) practices and policies relevant to the control of CDI.

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METHODS

IPAC policies and practices survey

A survey was mailed to every academic hospital and LCH IPAC program manager. The survey was focused on IPAC practices and policies relevant to methicillin-resistant *Staphylococcus aureus*, vancomycin-resistant *Enterococcus*, extended-spectrum β-lactamase, and Carbapenem-resistant Enterobacteriaceae, along with CDI. The survey questionnaire consisted of 20 questions to be answered for each calendar year from 2010-2015 to determine both the current IPAC practices and policies and how these had changed over time. The survey was initially sent out in June 2016; nonresponders were resent the survey monthly for the following 6 months or until they responded. The survey questions and their range of responses relevant to CDI are available on request. In January 2017, the IPAC managers were contacted a second time to validate their responses.

Interhospital patient transfers

In Ontario, all nonemergent interhospital patient transfers require the sending hospital to register a medical transfer authorization number prior to transfer. All these registered numbers are stored in the Provincial Transfer Authorization Centre, a database maintained by the Ministry of Health and Long-Term Care (MOHLTC) and Ornge, the province's emergency medical transfer service.[5] The database was established in 2003. The database is not externally validated, meaning there is no validation done to ensure that patients were actually transferred after being registered for a medical transfer authorization number. The database identifies the sending and receiving facilities for each patient transfer. There are no patient-level data that are stored in the database.

CDI cases

The MOHLTC receives the number of HA-CDI cases (attributable to that hospital) and the number of patient days at risk for HA-CDI every month from every academic hospital and LCH in the province. These data are publicly available from Health Quality Ontario, an agency of the MOHLTC responsible for the public reporting of mandatory patient safety indicators.[6] Although the data submitted are not validated by the MOHLTC, the database has been shown to be consistent when compared against both the MOHLTC Public Health Laboratory CDI database and the Canadian Institute of Health Information administrative database.[7] The monthly data were summed for each calendar year to coincide with the IPAC survey response frequency.

CDI score

The CDI score was developed to account for *C difficile* disease pressure from the sending hospital, an established risk factor for HA-CDI.[8,9] *C difficile* disease pressure is defined as the number of HA-CDI cases present in the sending hospital in that calendar year. The CDI score represents a modification of the weighted indegree measure of connectivity used by Simmering et al.[1] It is a measure of connectivity that combines the total number of patients transferred into a hospital with the total number of HA-CDI cases from that sending hospital. The CDI score is a more efficient measure of connectivity compared with weighted indegree because in a regression analysis that must include separate variables for weighted indegree and HA-CDI disease pressure, along with an interaction term between the 2 variables, the CDI score can account for this in a single variable. Unlike measures of connectivity calculated from social network models, no special statistical analyses are required to calculate the CDI score, making it a much more accessible measure of connectivity.[10] The CDI score was calculated for every calendar year for each hospital. The steps involved in the calculation of the CDI score are represented in Table 1 for a hypothetical case.

Table 1
Calculation of the CDI score for a hypothetical case

Sending facility	Receiving hospital	Total (sender)	HA-CDI cases (sender)	% Total transfers (receiving)
	Patient transfers			
n	X	Y	Z	W
1	129	1,018	154	56.6
2	68	1,018	154	29.8
3	9	789	198	3.95
4	22	52	56	9.65
CDI score		$\Sigma^n [(X/Y) \times Z] \times W = 16.45$		

NOTE. In this example, a receiving facility accepts a total of 228 patients from 4 sending facilities, each of whom transfers out a variable number of patients (Y). The score is weighted by the transfers from each sending facility as a percentage of the total transfers into the receiving facility (W).
CDI, *Clostridium difficile* infection; *HA-CDI*, hospital-associated *C difficile* infection.

The linearity relationship between the CDI score and CDI cases was assessed using a scatterplot, and this was compared against the log-transformed CDI score. There was no significant difference in linear fit between the versions of CDI score and CDI cases; therefore, the native CDI score was included in the final model to simplify the interpretation of the regression output.

Study design and outcomes

A multilevel, mixed-effects Poisson distribution was used to model the mean number of HA-CDI cases for each hospital by calendar year. The predictor variables included in the baseline model were an indicator for calendar year (2010-2015), *C difficile* stool assay, criteria used for isolation, and presence of an antimicrobial stewardship program (ASP). The CDI score was added to the baseline model to determine if this improved goodness of fit. Goodness of fit was tested using the Akaike information criterion (AIC) and the likelihood ratio (LR) test. An AIC change of ≥2 units and a LR test statistic with a *P* value ≤.05 were used to identify improved model fit with the inclusion of the CDI score variable. Patient days at risk for each calendar year were included as the exposure to control for hospital size and permit the interpretation of the outcome as the incidence rate of HA-CDI. The model included a random component for the baseline incidence of HA-CDI (intercept) and the effect size for the ASP variable (slope) to detect heterogeneity between hospitals. The correlation between the random components was assessed with a Pearson correlation coefficient. STATA/MP 14.2 for Mac (64-bit Intel; Stata Corp, College Station, TX) was used for all statistical analyses. Because no personal health information was used in this study, research ethics board approval was not required.

RESULTS

IPAC survey

The response rate was 94.7% (54 out of 57 hospitals), with complete surveys from 51 of 54 hospitals. There were 11 academic hospitals and 43 LCHs that responded to the survey. There were a total of 315 annual observations, with 251 from LCHs and 64 from academic hospitals. The questions relating to the duration of CDI precautions and the type of CDI precautions were not included in the final model because of the lack of variability in responses from year to year; >90% of all time periods in both hospital types reported using additional precautions plus private rooms, and >92% of all time periods in both hospital types reported discontinuing precautions only after symptoms had