Healthcare-Associated Urinary Tract Infection (HA-UTI): A Risk Factor for *Clostridioides difficile* Infection (CDI)? Results of a Real-World Data Analysis

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IDWeek 2020
October 21-25, 2020

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Poster No.
794

Background

It is estimated that 223,900 cases of CDI occur annually in hospitalized patients resulting in 12,800 deaths and $1 billion in attributable costs.[1] Antimicrobial use is the major risk factor for CDI[2,3]. Antimicrobials used to treat UTI have been identified as a factor in both recurrent CDI[4] and in community-acquired CDI.[5] This real-world data (RWD) analysis seeks to explore the relationship between HA-UTI and Hospital-Onset CDI (HO-CDI).

Methods

An electronic infection surveillance system (EISS – MedMined, Becton Dickinson and Company Digital Health, Birmingham, AL) was the source of de-identified real-world data from 290 hospitals. Algorithmically-derived measures of healthcare-associated infections (ADM-HAIs), and records of all-cause antimicrobial orders, for all inpatient admissions for the period 10/1/18–9/30/19 were analyzed. All patients who presented with a urine ADM-HAI – suggestive of HA-UTI – and no other HAI (Urine+ patients), were observed for subsequent HO-CDI. Similarly, HO-CDI was algorithmically-derived and those patients were represented as CDI+. Urine+ patients were compared to patients with no HAI of any type, other than CDI (ADM-HAI Free patients), and relative risk (RR) was estimated. The analysis was repeated for the subgroup of patients who received an antimicrobial order for any reason.

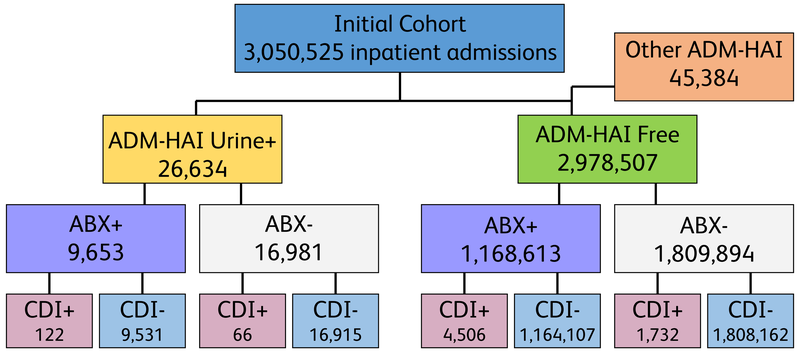
Results

3,050,525 inpatient admissions were analyzed. 26,634 were identified as Urine+ patients. 188 of those patients subsequently presented with HO-CDI. 2,978,507 were identified as HAI-free patients. 6,238 of those patients ultimately presented with HO-CDI. The incidence of HO-CDI was significantly higher in Urine+ patients compared to HAI-free patients (RR=3.37, 95 % CI[2.92, 3.89], $p < 0.0001$). When the analysis was repeated to examine only patients who received antimicrobial orders for any reason, Urine+ patients continued to be at higher risk of subsequent HO-CDI compared to HAI-free patients (RR=3.28, 95 % CI[2.74,3.92], $p < 0.0001$).

Discussion

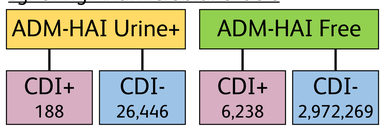
The overall incidence of HO-CDI in the entire cohort was 2.23 cases per 1,000 admissions. This is consistent with the rates of HO-CDI and health care facility-associated CDI, 2.09 and 2.24 cases per 1,000 admissions, respectively, as were observed in a global meta-analysis of 229 publications.[6]

The risk of HO-CDI following a likely HA-UTI remained elevated even among patients receiving antimicrobials for reasons other than to treat an HAI. This may be due to different or incremental antimicrobial use in HA-UTI patients or to those patients having a longer length of stay (LOS), thus increasing odds of HO-CDI. HA-UTI has been found to increase LOS by 4 to 10 days.[7,8]



Legend
Other ADM-HAI: ADM-HAI other than urine (e.g. blood, respiratory, wound, etc.), or a combination thereof
ABX+ or ABX-: Antimicrobial order for any reason was placed (+), or no antimicrobials were ordered (-)
CDI+ or CDI-: CDI subsequent to ADM-HAI (+), or no CDI (-)

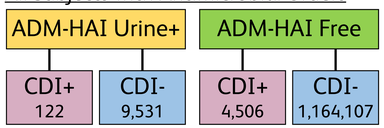
HA-UTI and HAI-Free Cohort
Ignoring Antimicrobial Orders



0.71 % 0.21 %

Relative Risk: 3.37 ($p < 0.0001$)

ABX+ Cohort
All Subjects with Antimicrobial Orders



1.26 % 0.39 %

Relative Risk: 3.28 ($p < 0.0001$)

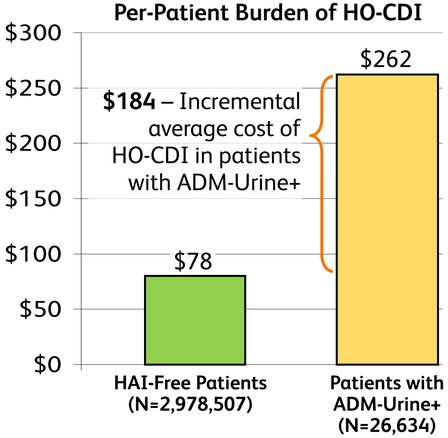
	Total Cohort	Analysis Cohort (HA-UTI and HAI-Free)
HO-CDI	6,809	6,426
Admissions	3,050,525	3,005,141
Incidence (per 1000 admissions)	**2.23**	**2.14**

Cost of HO-CDI: $37,083[9,10]

Average Cost of HO-CDI in HAI-Free patients= **$78 per admission**

Average Cost of HO-CDI in ADM-Urine+ patients = **$262 per admission**

Per-Patient Burden of HO-CDI



A large meta-analysis determined the attributable cost per case of HO-CDI to be $34,157[9] ($37,083 in 2020 dollars[10]). That translates to a per-admission burden of HO-CDI in HAI-Free patients of $78. Based on these observations, HA-UTI patients with a 3.3 RR of HO-CDI would bear an HO-CDI burden of $262. The $184 per-patient incremental burden of HO-CDI in ADM-HA-UTI patients may provide additional incentive for the prevention of HA-UTI.

Limitations

The terms of the EISS data use agreements blinded the researchers to the identity of the subject hospitals. To that end, efforts to evaluate any ancillary clinical interventions by a given hospital, or patient characteristics beyond the RWD collected electronically by the EISS, were not possible. Factors that may have influenced these findings, and were not considered in the analysis, include, but are not limited to, the following:

- Patient age, acuity, co-morbidity level, length of stay, and prior history/ colonization of CDI
- Attention to specific units or hospital service
- Dose, duration and specific antimicrobial classes ordered
- Whether the antimicrobials ordered were actually administered
- Specific CDI strains and/or specific UTI pathogens

Conclusions

The presence of a urine ADM-HAI, suggestive of HA-UTI, was associated with an increased risk of subsequent HO-CDI. This association held when only patients with antimicrobial orders were considered. These observations mirror findings from other published studies, however, other factors may have contributed to increased or decreased risk for both HA-UTI and HO-CDI.

References

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BD-21204