LETTER TO THE EDITORS

Clostridium difficile infection in intestinal transplant recipients

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Dear Editors,

Clostridium difficile infection (CDI) is a common complication among solid-organ transplant (SOT) recipients with an estimated incidence of 7–31% for lung recipients, 8–15% for heart, 3–19% for liver, 9% for intestinal, 4–16% for kidney, and 2–8% for pancreas–kidney recipients (1), and it is associated with increased mortality (2). There are limited data on CDI in intestinal transplant (ITx) recipients. This is a retrospective study that was conducted at Jackson Memorial Hospital, a 1558-licensed bed tertiary care teaching hospital. Our study was approved by the Institutional Review Board of University of Miami. The objectives of this study were to evaluate demographics, antibiotics and proton-pump inhibitors (PPI) usage, severity, treatments and outcomes of CDI in ITx recipients.

All adult and pediatric patients who underwent ITx (isolated and multivisceral) between January 2013 and December 2015 were evaluated. Only patients who developed CDI within one year post-transplant were considered. Diagnosis was made using glutamate dehydrogenase/toxin EIA and PCR in a two-step diagnostic algorithm that has been published (3). We evaluated whether there were differences in demographics, antibiotics and PPI usage within 90 days prior and after ITx, and one-year post-transplant survival between CDI-positive and CDI-negative patients. Continuous antibiotics or PPI for at least 4 days were considered as use. Quinolones, clindamycin, third- and fourth-generation cephalosporins, carbapenems, β-lactamase inhibitor combinations, aztreonam, and tigecycline were included. Time from transplant to CDI diagnosis was determined. CDI was community-acquired if diagnosed within 72 h of hospital admission. CDI was considered severe if WBC >15x10^3/μl, creatinine >1.5 × baseline or

Table 1. Demographics and severity, treatments and outcomes of *Clostridium difficile*

Pts	Age	Gender	ITx type	Antibx	PPI	Time from CDI to ITx	CDI onset	Severe CDI	Rx	Recurrences or relapse
1	3	Male	MV	CLI, CEF, MER	Yes	339	HA	No	MET (PO)	Recurrence
2	57	Female	MV	CEF, MER	Yes	130	CA	No	MET (PO)	No
3	3	Female	MV	CEF	Yes	175	CA	Yes*	MET (PO)	Relapse
4	46	Male	MV	LEV, MER	Yes	294	HA	No	MET (PO), VAN (PO)	No
5	48	Male	MV	LEV, CEF, MER, TIG	Yes	117	HA	No	MET (PO), VAN (PO)	No
6	1	Male	MV	PIP/TAZO	No	255	CA	Yes†	VAN (PO)	Relapse
7	36	Male	I	CEF	Yes	232	HA	No	MET (PO), VAN (PO)	No
8	1	Female	MV	PIP/TAZO, CEF	Yes	305	CA	Yes†	MET (PO)	No
9	40	Female	I	PIP/TAZO, CEF	Yes	77	CA	No	MET (IV), VAN (PO)	Recurrence
10	32	Male	MV	PIP/TAZO, CEF, MER	Yes	166	HA	Yes*	VAN (PO)	No

Pts, patients; ITx, intestinal transplant; Antibx, antibiotic, PPI, proton-pump inhibitor; CDI, *Clostridium difficile* infection; Rx, treatment; MV, multivisceral; CLI, clindamycin; CEF, cefepime; MER, meropenem; HA, hospital acquired; MET, metronidazole; PO, by mouth; CA, community acquired; LEV, levofloxacin; VAN, vancomycin; TIG, tigecycline; PIP/TAZO, piperacillin/tazobactam; I, isolated; IV, intravenous.

*creatinine >1.5 × baseline.

†WBC >15x10^3/μl.

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pseudomembranes. The CDI outcomes included were need for colectomy, death attributed to CDI, and recurrences (new-onset CDI within 12 weeks of previous CDI). If recurrence occurred within 4 weeks, it was considered relapse.

Fifty-one patients were included, 36 (71%) were multivisceral, 11 (22%) isolated, and 4 (8%) were modified multivisceral recipients. Ten (20%) ITx recipients developed CDI. No differences were found between CDI-positive and CDI-negative patients in age: 27 ± 22 vs. 29 ± 23 years; female gender: 4(40%) vs. 22(54%); antibiotic use: 10 (100%) vs. 39 (95%); antibiotic days: 32 ± 11 vs. 50 ± 41; ≥ 2 antibiotics: 7 (70%) vs. 27 (66%); PPI use: 9 (90%) vs. 40 (98%); and one-year post-transplant survival: 10 (100%) vs. 30 (73%), $P > 0.05$ in all, respectively. The median time from transplant to CDI was 204 days (77-339). CDI was community-acquired in five (50%) and severe in four (40%) patients, and four (40%) had recurrence or relapse (Table 1). None had colectomy or died from CDI.

The high incidence of CDI in our cohort could be explained by the frequent antibiotic and PPI usage among our patients. Antibiotic and PPI exposure are predisposing risk factors for CDI (4,5). Even though 40% of the cases were severe, our patients had good outcomes as none required colectomy or died from CDI. Contrary to liver transplant recipients (3), our cohort suggested that CDI can present late post-ITx and this can be explained by the high readmission rate seen in ITx recipients (6). There is a paucity of data regarding the impact of CDI on ITx recipients, and our study adds to the growing body of literature on CDI in SOT.

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