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State of the Science Review

Clostridium difficile infection in pregnant and postpartum women in 2 hospitals and a review of literature

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Background: Healthcare-associated *Clostridium difficile* infection (CDI) in pregnant/postpartum women is underreported, especially outside of North America. We report a cluster of cases in 2 neighboring secondary care hospitals in South-East England. The objective of this study was to identify the epidemiology and risk factors for infection.
Methods: An investigation into a cluster of cases of confirmed CDI in pregnant/postpartum women was performed over a 12-month period, from June 2016 to June 2017.
Results: Eleven cases, in 10 patients, were identified, including 1 patient who had a relapse. Eight of 10 patients developed symptoms after hospital discharge. All patients had received broad-spectrum antibiotics prior to CDI onset. Environmental vectors, such as labor room mattresses, that were found difficult to effectively decontaminate after heavy contamination with blood, feces, and other body fluids may have been possible reservoirs. An infection control care bundle was successful in preventing further cases.
Conclusions: Antibiotic use and exposure to the organism in a contaminated labor room environment are likely risk factors for healthcare-associated CDI in postpartum women. Active surveillance is necessary to prevent these infections, as these cases often present after hospital discharge.

BACKGROUND

Pregnant and postpartum women have traditionally been considered "low-risk" patients for acquiring *Clostridium difficile*-associated disease, as this cohort of women are young and otherwise usually healthy. However, these women are increasingly recognized as being susceptible to this infection. Reports from North America[1-3] suggest a rate of *C. difficile* infection (CDI) in peripartum women of 0.07–0.7/1,000 deliveries and as high as 7.5/1,000 deliveries at times of healthcare-related outbreaks.[4] A more recent retrospective cohort study by Ruiter et al[2] on women admitted for delivery, using the Healthcare Cost and Utilization Project Nationwide Inpatient Sample from the United States, reported a CDI rate of 0.3/1,000 deliveries per year. Deficiencies in immune regulation during pregnancy, exposure to *C. difficile* spores from infants, and antibiotic use have been proposed as possible risk factors. Exposure to *C. difficile* spores in the healthcare environment as an additional risk factor has been explored further in only 1 study.[5]

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In the last decade, an increasing prevalence of CDI was reported globally due to increasing antibiotic use, poor infection control programs in hospitals, and the prevalence in high proportion of the hypervirulent strain of *C. difficile*, which was endemic in healthcare settings. In 2005, the Morbidity and Mortality Weekly Report reported 33 cases of CDI in women, of which 10 were peripartum—a population thought to be at low risk. Garey et al[5] subsequently reported a cluster of 4 cases in a single unit among peripartum women, 2 of whom were reported to be infected with the epidemic strain. A retrospective review by Venugopal et al[3] at a single center identified 8 of 12 cases of CDI among antenatal and postpartum women to be healthcare associated.

However, the rate of CDI in maternity patients outside of North America is largely unknown. In England, this may be because most of these patients present after discharge from the hospital, and current mandatory surveillance systems do not capture information regarding recent obstetric history. The rate of infection in 15–44-year-old female patients reported by Public Health England is 6.7/100,000 population,[6] with 711 cases reported in England in 2016/2017.

Of the 11 retrospective reviews and surveillance and outbreak studies reported in pregnant/postpartum women so far,[1-5,7-12] only 4 studies[3-5,12] have been related to healthcare-associated CDI, and only 2 of these 11 studies[3,5] undertook molecular analysis of isolates.

In this study, we report a cluster of cases of CDI identified between June 2016 and June 2017 in postpartum women in 2 hospitals in South-East England. We report on risk factors and molecular typing results of *C. difficile* in postpartum women along with a literature review of peripartum CDI.

CASE DEFINITION

A case was defined as any pregnant or postpartum (up to 6 weeks after delivery) woman who developed diarrhea or other signs and symptoms suggestive of CDI *and* who tested positive for CDI by a 2-step testing algorithm using *C. difficile* glutamate dehydrogenase (GDH) and toxin tests *or* who had presence of pseudomembranous colitis on colonoscopy or biopsy. A patient was classified as a new case (to include a relapse or a reinfection) if 28 days had passed since their current positive and last *C. difficile* positive test, and they had become symptomatic again after resolution of symptoms.

MATERIALS AND METHODS

Setting

Cases were identified in 2 hospitals: Frimley Park (Hospital A) and Royal Berkshire National Health Service (NHS) Foundation Trust (Hospital B)—both secondary care hospitals with approximately 800 beds each. These hospitals serve a population of approximately 1.1 million in the Surrey, Hampshire, and Berkshire counties of South-East England. The catchment areas, staff supporting the maternity services, and the environment in which these services are provided (both antenatal and postnatal) are entirely separate for the 2 hospital sites.

Risk factor analysis and infection control measures

After identification of the first 3 cases in both hospital sites, an incident team was convened that included the Infection Prevention and Control (IPC) teams, the obstetric teams from both hospitals, the respective IPC Clinical Commissioning Group (responsible for IPC in the community), and leads and representatives from Public Health England.

Antepartum, delivery, postpartum, and laboratory records of all cases were reviewed to obtain patient demographics and medical histories, including comorbidities, pregnancy complications, antibiotic use, time of onset of CDI, severity, and outcome (Table 1). Severe CDI was defined as cases with a white blood cell count >$15x10^9$/L, or an acute rising serum creatinine (i.e., >50% increase above baseline), or a temperature of >38.5°C, or evidence of severe colitis (abdominal or radiologic signs).[6]

A detailed investigation to identify potential reservoirs of infection and infection control practices, including hand hygiene compliance; compliance with use of personal protective equipment; compliance with cleaning and decontamination standard operating protocols (SOPs) of equipment and patient environment; staffing ratios and skill mix within wards; compliance with prompt isolation of suspected cases admitted to hospital/collecting stool sample for CDI diagnosis; and commencement of appropriate treatment was undertaken. All antibiotics prescribed, both in the community and in the hospital, anytime during pregnancy or in the postpartum period to the time of a positive *C. difficile* test, were recorded.

Testing for *C. difficile* infection, molecular typing, and environmental sampling

All fecal samples that met the criteria for a *C. difficile* test[13] from hospitalized patients as well as community patients in the Surrey, Hampshire and Berkshire counties of South-East England were tested using a 2-stage testing algorithm as recommended by the Department of Health.[13] Tests included a GDH test (Proflo *C. difficile* GDH, Pro-lab diagnostics for tests from Hospital A and C. DIFF CHEK 60, Tech Lab Inc. at Hospital B) as the first step and, if positive, a *C. difficile* toxin test (Proflo *C. difficile* Toxin A/B, Pro-lab diagnostics at Hospital A and C. DIFFICILE TOX A/B II, Tech Lab Inc. at Hospital B) as a second step.

Stool samples from 7 of the 10 patients were available for further testing (3/10 were unavailable for further typing, as these samples were either insufficient or not saved). Available samples were sent to the *C. difficile* Ribotyping Network laboratory in Southampton, United Kingdom, for ribotyping. Isolates with related ribotypes were further tested at the central reference laboratory in Colindale, United Kingdom, using multilocus variable number of tandem repeats analysis (MVLA).

Environmental sampling was conducted in Hospital A, at the time when the last 2 cases identified in this cluster were recognized, to determine the degree of contamination of the environment with fecal flora. The investigating team sampled environmental areas in Hospital A because Hospital B did not have an on-site microbiology laboratory to process environmental samples. Environmental vectors that were expected to be at high risk of contamination during delivery from the fecal flora of mother or baby and those who were in prolonged or close contact with pregnant women were selected for environmental sampling. Areas sampled included the labor room mattresses, labor room beds and their removable parts at the foot end of the beds, ultrasound machines in the labor ward (including transvaginal probes), birthing pools, equipment trolleys, and baby cots in the labor rooms. Cellulose sponges (MWE Polywipe premoistened sponge in peel pouch) pre-moistened with phosphate buffer (Medical Wire & Equipment Co.)[13,14] were used to sample the environment. The sponges were inoculated into brain-heart infusion broth, which was subcultured on Oxoid *C. difficile* selective chromogenic plates, blood agar, and fastidious anaerobic plates after 3 and 7 days incubation. The plates were read at 24 and 48 hours after incubation. Colonies growing on the plates were identified using matrix-assisted laser desorption/ionization, time of flight.

Table 1
Patient characteristics and ribotyping results of the 10 cases

Case no. (hospital site)	Age (years)	Gravida/Parity (including current delivery)	CDI onset: weeks postpartum	Type of delivery	Pregnancy complications (excluding infections)	Comorbidities	Prior antibiotic use (indication)	Ribotyping result
1 (B)	31	G1P1	3	SVD with forceps & episiotomy	Nil	Nil	AMX (UTI antepartum) AUG (episiotomy wound infection)	ND
2 (B) Relapse	31	G1P1	7	SVD with forceps & episiotomy	Nil	Nil	AMX (UTI antepartum) AUG (episiotomy wound infection)	ND
3 (B)	29	G2P2	3	SVD	Nil	Nil	PTZ, CLI, AMX, AUG (postpartum sepsis)	ND
4 (B)	26	G1P1	6	Elective LSCS	Nil	Nil	AUG (LSCS prophylaxis), CLOX & MTZ (wound infection), AUG (UTI)	ND
5 (A)	34	G1P1	4	SVD with 3A tear	Nil	Osteoporosis (previous eating disorder)	CLI &MTZ (wound infection)	O15
6 (A)	26	G1P1	5	Emergency LSCS	Pre-eclampsia	Nil	CLX (UTI antepartum), CXM &MTZ (LSCS prophylaxis), CLX (UTI postpartum)	SPORADIC
7 (B)	33	G1P1	5	SVD with episiotomy	Nil	Nil	AMX (UTI antepartum), MTZ & AUG (wound infection), AUG (wound infection)	OO5
8 (B)	37	G1P1	1	Emergency LSCS	Gestational diabetes	Nil	AMX (UTI antepartum), AUG(LSCS prophylaxis), CLI &PTZ (postpartum sepsis)	OO5
9(A)	35	G1P1	3	SVD with 3A tear	Nil	Sickle cell trait	AUG & MTZ (wound infection)	OO5
10 (A)	37	G1P1	6	SVD with Forceps & Episiotomy	Nil	Nil	CLOX & MTZ (wound infection), AUG (postpartum UTI)	O14
11 (A)	27	G1P1	4	SVD	Nil	Recurrent UTI (previous SPC)	Nitrofurantoin (antepartum UTI), trimethoprim (antepartum UTI), AUG &MTZ (endometritis)	O14

AMX, amoxicillin; *AUG*, coamoxiclavulinic acid; *CLI*, clindamycin; *CLOX*, flucloxacillin; *CLX*, cephalexin; *LSCS*, lower segment Caesarean section; *MTZ*, metronidazole; *ND*, not done; *PTZ*, piperacillin-tazobactam; *SPC*, supra pubic catheter; *SVD*, spontaneous vaginal delivery; *UTI*, urinary tract infection.

Table 2
Infection control measures instituted after outbreak recognition

Environmental decontamination	Instituted use of chlorine-based disinfection in labor wards
	Deep clean of all the inpatient areas of the maternity service
	Special attention to decontamination of maternity beds and mattresses between patients
	Management of birthing pool deliveries with education and training in cleaning and maintenance
	Enhanced decontamination of equipment such as trans-vaginal ultrasound scan probes
Antibiotic use	Planned review of antibiotic guidelines for maternity, with potential reduction of polymicrobial and broad-spectrum antibiotic use
	Education and training of maternity prescribers in reviewing antibiotic prescriptions regularly
Hand hygiene and Personal protective equipment	Emphasis on hand washing with soap and water before and after any contact with patient/patient environment
	Appropriate use of gloves and aprons was reiterated
Early recognition, diagnosis and treatment	All general practitioners in the region/maternity staff were notified of the cluster, with reminders to recognize and test for the infection
	Isolation of any cases presenting to hospital with symptoms indicative of infectious diarrhea
	Prompt treatment on confirmation of CDI diagnosis

CDI, *Clostridium difficile* infection.

Infection control measures instituted are listed in Table 2. These included enhanced decontamination of the environment with the introduction of chlorine-based disinfectant with a compatible detergent (in place of detergent alone that was being used in 1 of the hospitals, since the maternity unit was thought to be at low risk for CDI); special attention to decontamination of mattresses; review of antibiotic guidelines; emphasis on hand washing and appropriate use of personal protective equipment; early diagnosis/isolation; and appropriate management of suspected and confirmed cases. Additional measures included increasing the awareness of maternity staff through periodic ward visits, establishing trust infection prevention and control committees and obstetric clinical governance committees, and reminding local and regional general practitioners to recognize and test for CDI in this cohort of patients where necessary.

RESULTS

Between June 2016 and June 2017, 5 cases (in 5 patients) of CDI were identified at Hospital A, and 6 cases (in 5 patients) were identified at Hospital B. The timeline of cases detected in the 2 hospitals is shown in Figure 1.

Patient characteristics are described in Table 1. The rate of CDI in pregnant and postpartum women (based on our case definition) at Hospitals A and B, over a 3-year period, increased from 0 to 0.55 and from 0.41 to 0.93 per 1,000 deliveries, respectively. This was thought to be a significant increase in the incidence of CDI because the rate of infection had more than doubled compared to the previous 3 years before the onset of this cluster—with 7 patients with CDI in both hospitals in the 3 years before the onset of this increased incidence to 10 new patients within a 12-month period in the 2 hospitals. All 10 patients had delivered in either of the 2 hospitals. Eight of 10 patients had a community onset of

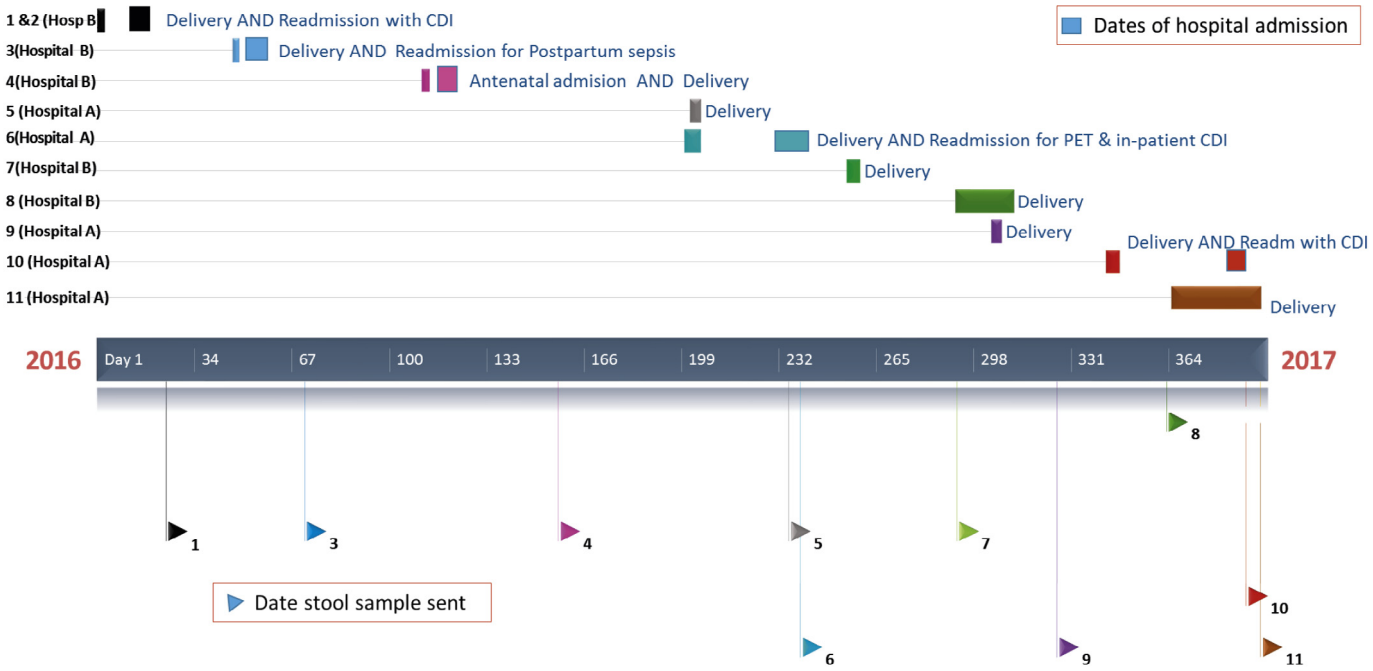

Fig 1. Timeline of the 11 cases of CDI (in 10 patients).

infection; 1 patient developed symptoms of CDI in the same admission as the admission for delivery; and 1 patient developed symptoms on a second admission to the hospital after her delivery (due to a pregnancy-related complication). Two patients required hospital admission for management of CDI.

All cases presented between 1 and 6 weeks after discharge from the hospital (mean, 29 days after hospital discharge). The mean length of pregnancy-related hospital stay for our cases prior to CDI diagnosis was 5 days (range, 1–18 days). The patients were between 26 and 37 years old (mean age, 32 years).

Pregnancy history included Gravida 1, Parity 1 in 9 patients, and 1 patient who was Gravida 2, Parity 2. No significant pregnancy-related complications were reported, other than gestational diabetes in 1 case and pre-eclampsia in a second case. Osteoporosis, sickle cell trait, and recurrent urinary tract infections (UTIs) were the only reported comorbidities in 3 cases. Three patients delivered by lower segment Caesarean section, 4 by spontaneous vaginal delivery (2 of whom had a third-degree tear), and 3 by spontaneous vaginal delivery with an episiotomy.

A detailed investigation into potential risk factors for an increase in the incidence of CDI at the 2 units revealed good compliance with hand hygiene/use of personal protective equipment and with hospital protocols on prompt diagnosis, isolation, and treatment of suspected cases. The staffing ratios and skill mix within the obstetric units were satisfactory. Environmental cleanliness inspections during our investigation revealed that the labor room mattresses were being inadequately decontaminated in Hospital A. The mattress and bed were complex, and all areas that were potential reservoirs of pathogens had not been accessed for cleaning by staff either because they had inadequate training or because staff often had limited time because of high turnover of patients in these wards. Other potential sources were transvaginal ultrasound probes and birthing pools (which had an SOP for decontamination that was being followed by staff members using this equipment).

All patients received antibiotic treatment in the antepartum or postpartum period on 1–3 occasions for indications other than CDI. The mean time from delivery to last antibiotic prescription was 14.5 days. The most commonly used antibiotic was coamoxiclav (11 of 35 episodes, 31%), followed by metronidazole, amoxicillin, and clindamycin. The most common indication for antibiotic prescription was UTI (9 of 21 indications, 43%), followed by wound infection (29%).

Antibiotic usage data from the 2 hospitals were reviewed. An overall increase was observed in the defined daily doses of antibiotics (including an increase in the use of coamoxiclav and metronidazole) used since 2012, in each of the 2 obstetric units. This was unrelated to the number of deliveries in the hospitals. Antibiotic prescribing guidelines were unchanged over 2 years, and root cause analysis concluded that all antibiotic prescribing was consistent with local guidelines.

All patients had mild to moderate CDI based on severity classification, according to Public Health England guidance.[15] One patient who had a relapse of CDI and another patient who re-presented to the hospital 3 weeks after delivery with diarrhea, which was confirmed as CDI, were the only 2 patients who required hospital admission for the management of CDI. No patients developed a complication of CDI or died as a result of this infection.

Ribotyping of the *C. difficile* isolates was performed on 7 of the 10 patients, from whom samples were retained (Table 1). Three of the 7 isolates were ribotype 005 (1 in Hospital A and 2 in Hospital B), and 2 patients from Hospital A who delivered 3 weeks apart had ribotype 014. The ribotypes of the remaining 2 cases were ribotype 015 and a sporadic ribotype. Further typing by MVLA of the 3 ribotype 005 isolates revealed that these were not closely related (summed tandem repeat difference >10). The samples from the 2 patients with ribotype 014 were insufficient for further typing with MVLA. In the South-East England region, the most common ribotypes, reported by Public Health England, from samples submitted by hospitals (criteria for submission: outbreak/high incidence

of CDI or increased severity/mortality/recurrence associated with CDI)[16] are reported to be sporadic ribotypes, followed by ribotypes 015, 005, 002, and 014.

Environmental sampling of the labor ward showed heavy contamination with enteric flora-type organisms, including Group B beta-hemolytic *Streptococcus* and *C. perfringens*, which were isolated from nearly half of all areas sampled, most (66%) of which were from labor room mattresses. *C. difficile* was not isolated from any of the samples.

Review of literature on pregnancy and peripartum *C. difficile*-associated diarrhea

A search of literature from all languages on Medline PubMed, EMBASE, and CINAHL from 1946 to January 2018 was performed. We identified 11 retrospective studies[3-5,7-12] and 8 case reports[8,17-23] on CDI in peripartum/pregnant/postpartum women (Table 3). All studies were from the United States, with the exception of our current study and 3 case reports.

Two large epidemiologic studies[1,2] looking at trends of CDI in this group of women showed an increasing rate of infection in the United States, from 0.07/1,000 deliveries in 2003 to 0.3/1,000 deliveries in 2013. They identified the following risk factors: women older than 35 years, presence of inflammatory bowel disease, and treatment with antibiotics for infections. Rouphael et al[7] reported on a passive surveillance of severe CDI in pregnancy/postpartum of 10 patients in 2005–2006; 2 of these 10 patients were reported to have died.

The cluster of cases reported in this study had the lowest rate of Caesarean section (30%) of all case series and epidemiologic studies reported. Between 90% and 100% of cases had prior antibiotic exposure in all studies reported so far (including this report). One case report[20] identified carriage of the epidemic strain by the infant as a risk factor. Where it was reported, 16 of 76 (21%; range, 9%–50%) cases in this literature review had at least 1 episode of relapse (10% in this report).

Four studies[3-5,12] reported healthcare-associated CDI in pregnant/postpartum women. Molecular typing of isolates was performed in only 2 reports[3,5]; in both, molecular typing revealed distinct strains of *C. difficile*, similar to findings in our study.

DISCUSSION

Our study suggests that CDI in peripartum women may be an underreported problem outside of North America. These populations of women are young and therefore considered low risk for this infection. As far as we could ascertain, apart from 1 case report of toxic megacolon in a pregnant woman with no apparent risk factors for CDI, there have been no reports from the United Kingdom or Europe.[19]

All our patients had antibiotics prescribed at a mean time of 14.5 days after delivery. Also, in our cohort of cases, the mean duration from the time of last antibiotic exposure to the development of CDI was 14 days. Therefore, our case definition of a 6-week period would be expected to identify most cases. Hesgens et al[24] reported that there may be a 7–10-fold increased risk of CDI during the first month after antibiotic exposure, and this effect can last up to 3 months. In our hospitals, no additional cases of CDI in this group of women were reported if a wider definition of up to 3 months after delivery/last antibiotic exposure was used.

In our cohort, the mean age of women with CDI was 32 years. A previous case-control study[4] did not show a significant difference in age between cases and controls (30 years vs. 29 years). In their case-control study, Unger et al[4] reported that Caesarean section, previous hospitalization during pregnancy, and significant underlying illness were statistically significant ($P < .001$) differences between the 2 groups. In our cohort, however, only 1 patient (10%) had a history of hospitalization prior to delivery (Figure 1), compared to 55% reported by Unger et al. Significant underlying illnesses were present in 30% of our patients, which is similar to the 25% reported by Unger et al. None of our patients had infants or young children (<2 years of age) in their home environments, a greater proportion of whom are known to be asymptomatic carriers of *C. difficile*.[25]

Exposure to antibiotics and exposure to the organism are the 2 most important risk factors for CDI.[26] Healthy adults who are exposed to the spores may remain asymptomatic and are likely to develop symptoms when antibiotic exposure compromises gut microbiota and promotes the propagation of *C. difficile.* Moreover, the down-regulation of Th1 response associated with immune regulation during pregnancy[5] may further predispose pregnant/postpartum women to developing this infection.

Overall antibiotic use increased in both the hospitals over the years preceding the incident. However, the delivery rates remained nearly the same over this time. All patients in our study had been exposed to 1 or more courses of antibiotics before becoming symptomatic. This is likely to have predisposed them to developing CDI infection after exposure to the bacterium, which may have been acquired in the hospital or in the community.

The potential risk factors identified in our investigation, with ongoing active surveillance to capture any others, were evidence of increased antibiotic use and inadequate decontamination of labor room mattresses, both macroscopically and based on environmental sampling results. After institution and reinforcement of infection control interventions (Table 2), the incidence of CDI dropped dramatically, from 0.55 and 0.93 cases per 1,000 deliveries in the 2 hospitals, respectively, to 0 cases for more than 9 months, to the time of writing this report.

Given the increased incidence of infection in this specific cohort of related patients—all cases having occurred within a close interval of time and all patients having been exposed to a known risk factor (antibiotic use)—along with our findings of inadequate decontamination of the labor room environment and, importantly, the absence of additional cases after the institution of infection control interventions in the hospitals, it is likely that an environmental vector within healthcare, coupled with increased use of antibiotics in a physiologically immunosuppressed population, is the most plausible explanation for the CDI cluster in our cohort of pregnant/postpartum women.

Typing results in our study revealed that the cases were not closely related at a molecular level. In this region, the most prevent types of ribotypes were isolated ribotypes. This was similar to the findings of 2 other studies,[3,5] which also reported that *C. difficile* isolates were not identical at a molecular level. Gross contamination of the labor room environment with blood, body fluids, and feces can be expected when women are going through labor. This is unlike any other area of the hospital. One study[27] reported on the recognition of asymptomatic carriers and patients exposed to *C. difficile* as important factors in the epidemiology of CDI. Ye et al[28] reported a *C. difficile* carriage rate of 3.7% in pregnant women. Environmental contamination from multiple sources (i.e., contamination of labor room environment by women asymptomatically colonized with *C. difficile,* which is likely to be with ribotypes that are most prevalent locally*)* may explain unrelated *C. difficile* strains in healthcare-associated CDI outbreaks.

There are several potential reservoirs of infection within this environment. Therefore, meticulous attention to environmental cleaning and decontamination of equipment in these areas is

Table 3
Literature review of peripartum *C. difficile*-associated diarrhea

N	Time period of study	Type of study	Healthcare-associated CDI	CDI rate reported	Ceasarian section	Prior antibiotics use	Other risk factors identified	Relapse	Severe disease/ death	Typing results	Reference
2757	1999-2013 (U.S.A)	Retrospective cohort study of delivery admissions	—	0.3/1000 deliveries per year (2013)	—	—	>35 years age; multiple pregnancy; Crohn's; ulcerative colitis; other infections	—	Mortality rate 8/1000 (0.8%)	—	Ruiter et al[2]
1706	1998-2006 (U.S.A)	Retrospective trend analysis of CDI in hospital discharges of peripartum women	—	0.07/1000 delivery related discharges (2006)	1138/1706 (67%)	—	—	—	—	—	Kuntz et al[1]
10 (6 Antepartum, 4 Postpartum)	2005-2006 (U.S.A)	Passive surveillance of severe cases	—	—	—	9/10	—	2/10	5 toxic megacolon; 7 ICU admissions; 2 deaths	—	Rouphael et al[7]
10	2004-2005 (U.S.A)	Voluntary reporting to PDPH	—	—	—	9/10	—	5/10	—	—	MMWR[8]
22 (11 Antepartum; 11 postpartum)	1997-2011 (U.S.A)	Retrospective chart review of CDI in women between 15 and 40 years	—	—	10/11 (91%) Postpartum cases	11/11 Postpartum cases	—	2/22 Postpartum cases	1 case requiring ICU admission	—	Neshatian et al[9]
5	2000-2009 (U.S.A)	Retrospective view of hospital database for cases	—	—	—	—	—	—	—	—	Malhotra et al[10]
3	1985-1995 (U.S.A)	Review of hospital records of women on the obstetrics and gynecologic services in 1 hospital		—	2/3	2/3	—	—	—	—	James et al[11]
4 (1 Antepartum, 3 Postpartum)	2007-2008 (U.S.A)	Review of data from microbiology lab data in 1 hospital	3/4	—	2/4	4/4	—	1/4	No	2/4 hypervirulent strain (*tcdC* gene deletion/ presence of binary toxin)	Garey et al[5]
12 (5 Antepartum; 7 Postpartum)	2003-2007 (U.S.A)	Retrospective review (data from microbiology lab data) in 1 hospital	8/12	0.7 /1000 admissions	8/12	11/12	—	2/12	1 severe case; no deaths	7 of 12 typed by REA—only two identical types	Venugopal et al[3]
20	2006-2007 (U.S.A)	Case-control study of an outbreak in 1 hospital	20/20	7.5/1000 deliveries	14/20	19/20	Combination antibiotic treatment	-	1 case requiring colectomy; no deaths	—	Unger et al[4]
3 (3 Postpartum)	1985 (U.S.A)	Outbreak report from a single center	3/3	—	3/3	3/3	—	—	—	—	Arsura et al[12]
10 (10 postpartum)	2016- 2017 (U.K)	Retrospective review of cases from 2 hospitals with increased incidence of CDI	10/10	0.6 & 0.9 per 1000 deliveries	3/10	10/10	—	1/10	Nil	3 Ribotype 005; 2 Ribotype 014; 1 Ribotype 015; 1 sporadic	Meda et al (Current report)

(*continued on next page*)

Table 3
Continued

N CASE REPORTS	Time period of study	Type of study	Healthcare-associated CDI	CDI rate reported	Caesarean section	Antibiotic use prior (6 months) to CDI	Other risk factors identified	Relapse	Severe disease/death	Typing results	Reference
1 (Antepartum)	2017 (U.S.A)	Case report	—	—	—	Yes	—	Yes; Required fecal microbiota transplant	—	—	Saeedi et al[17]
1 (Antepartum)	2010 (India)	Case report	—	—	—	Yes	—	No	—	—	Mridula et al[18]
1 (Antepartum)	2010 (Italy)	Case report	—	—	—	No	—	No	Toxic megacolon	—	Candiotto et al[19]
1 (Postpartum)	2008 (U.S.A)	Case report	—	—	—	Yes	Infant carried same epidemic strain	Yes	No	REA BI/ PFGE NAP1	Hecker et al[20]
1 (Postpartum)	2007 (U.S.A)	Case report	—	—	Yes	Yes	—	No	Toxic megacolon	—	Ghai et al[21]
1 (Antenatal)	2005 (U.S.A)	Case report	—	—	—	Yes	—	No	Toxic megacolon/ death	—	MMWR[8]
1 (Postpartum)	1999 (Lebanon)	Case report	—	—	No	Yes	—	Yes	—	—	Alef et al[22]
1 (Postpartum)	1985 (U.S.A)	Case report	—	—	Yes	Yes	—	No	No	—	McNeeley et al[23]

CDI, *Clostridium difficile* infection; *ICU*, intensive care unit; *MMWR*, Morbidity and Mortality Weekly Report; *PDPH*, Philadelphia Department of Public Health; *PFGE*, pulsed-field gel electrophoresis; *REA*, restriction endonuclease analysis.

essential to prevent healthcare-associated infections. Although environmental sampling failed to detect *C. difficile* in the maternity inpatient areas, this was possibly due to recognized difficulties in growing this organism in vitro.[29,30] The presence of other enteric bacteria found in the labor wards is suggestive of contamination of the environment with gut and pelvic flora of women at the time of delivery. Our investigations also revealed that the type of mattresses and beds used in labor wards are extremely complex in terms of cleaning after contamination. The beds and mattresses in Hospital A were replaced just a few weeks prior to the onset of this incident. The requirement to put laboring women in the lithotomy position meant that these mattresses and beds had multiple detachable and moveable parts and joints, some of which were inaccessible to effective decontamination, and staff members may not have been fully familiar with decontamination SOPs for these new mattresses. The same type of mattresses and beds were used in both hospitals. Considering the rapid turnover of patients in busy maternity units, it can be expected that, unless dedicated staff time is made available for effective decontamination, removal of pathogens after heavy contamination of these mattresses may be compromised.

No patients in our cohort developed severe CDI or complications of CDI or died as a result of CDI. All cases were managed with oral metronidazole and/or oral vancomycin using standard antibiotic regimes.[9]

After implementation of the targeted infection control measures (Table 2), the incidence of infection at both hospitals dropped rapidly, and no additional cases of *C. difficile* infection in this population have been identified in either of the 2 hospitals with active surveillance in place for over 9 months, at the time of writing this report. Therefore, irrespective of a precise reservoir of the pathogen within healthcare, our study reinforces the importance of recognizing the potential for exposure to the organism in the hospital environment and prudent antibiotic use in this cohort of patients who are immunosuppressed and likely to be exposed to antibiotic treatment. It also shows the necessity of looking to hospital links for community-onset CDI cases, while reviewing the epidemiology of CDI in pregnant and postpartum women. With current surveillance systems in the United Kingdom, these links currently may remain largely undetected.

Our study had several limitations. We were not able to obtain a complete social history of the patients, which may have predisposed them to *C. difficile* acquisition outside of healthcare (e.g., occupation as a carer for elderly people or exposure to pets). We did not compare our cases with controls to determine if any significant differences existed between the 2 groups. Because of the low baseline incidence of this infection during non-outbreak periods, large multicenter, case-control studies would be useful to answer questions related to risk factors of acquisition of *C. difficile* in this population. Further research and development of more sensitive methods of environmental isolation of *C. difficile* would also help in understanding the epidemiology of healthcare-associated CDI.

CONCLUSIONS

The epidemiology of CDI in pregnant and postpartum patients is underreported outside of North America. The maternity environment is unique owing to the degree of contamination expected at the time of delivery, and meticulous attention to disinfection is required to prevent healthcare-associated infections. Use of broad-spectrum antibiotics likely predisposes these women to CDI. Molecular typing alone may not be useful in identifying healthcare-associated case clusters.

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SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.ajic.2018.06.001.

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