Differential yield of pathogens from stool testing of nosocomial versus community-acquired paediatric diarrhea

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OBJECTIVES: To evaluate the role of routine stool examination for all pathogens in paediatric nosocomial diarrhea (NAD) and community-acquired diarrhea (CAD) over a two-year period at Alberta Children's Hospital and current practices in other Canadian hospitals. A secondary objective was to characterize features that may predict NAD or CAD etiology.
STUDY DESIGN: Retrospective cohort study and telephone survey.
SETTING: Alberta Children's Hospital (retrospective review) and Canadian tertiary care paediatric centres (telephone survey).
METHODS: The health and microbiological records of all children with an admission or discharge diagnosis of diarrhea were reviewed using a standardized data collection form. In addition, a telephone survey of laboratories serving all paediatric hospitals in Canada was conducted using a standard questionnaire to obtain information about practices for screening for pathogens related to NAD.
RESULTS: Four hundred and thirty-four CAD episodes and 89 NAD episodes were identified. Overall, rotavirus and *Clostridium difficile* were the most commonly identified pathogens. Bacterial culture was positive in 10.6% CAD episodes tested, with *Escherichia coli* O157:H7 identified as the most common non-*C difficile* organism. In NAD, no bacteria were identified other than *C difficile* (toxin). Screening for ova and parasites had negligible yield. Viruses were more frequent in the winter months, while bacterial pathogens were more common in the summer and fall months. Over 50% of Canadian paediatric hospitals still routinely process NAD specimens similarly to CAD specimens.
CONCLUSIONS: There is a need for the re-evaluation of routine ova and parasite screening, and bacterial culture in nonoutbreak episodes of NAD in children.

Key Words: *Community-acquired infections; Diarrhea; Enteropathogens; Nosocomial infections*

Rendement différentiel des organismes pathogènes isolés à partir de spécimens de diarrhées pédiatriques nosocomiales et acquises dans la communauté

OBJECTIF : Évaluer le rôle de l'examen de selles de routine pour tous les organismes pathogènes en présence de diarrhées pédiatriques nosocomiales (DPN) et acquises dans la communauté (DPC) sur une période de deux ans, au

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Alberta Children's Hospital et pratique actuelle dans les hôpitaux canadiens. Un deuxième objectif était de dégager les caractéristiques permettant de déterminer l'étiologie des DPN ou des DPC.
MODÈLE DE L'ÉTUDE : Étude de cohorte rétrospective et enquête téléphonique.
CONTEXTE : *Alberta Children's Hospital* (examen rétrospectif) et centres pédiatriques de soins tertiaires (enquête téléphonique).
MÉTHODES : On a passé en revue à l'aide d'une formule de collecte de données standardisée les dossiers médicaux et les dossiers microbiologiques de tous les enfants ayant eu, au moment de leur admission ou de leur congé, un diagnostic de diarrhée. De plus, une enquête téléphonique auprès des laboratoires desservant tous les hôpitaux pédiatriques du Canada a été effectuée à l'aide d'un questionnaire standardisé afin de recueillir des renseignements sur les pratiques de dépistage des organismes pathogènes associés à la DPN.
RÉSULTATS : Quatre cent trente-quatre épisodes de DPN et 89 épisodes de DPC ont été recensés. Dans l'ensemble, le rotavirus et *Clostridium difficile* ont été les organismes pathogènes les plus fréquemment isolés. Les cultures bactériennes ont été positives dans 10,6 % des épisodes de DPC testés, *Escherichia coli* 0157:H7 ayant été identifié comme l'organisme non-*C. difficile* le plus courant. Dans la DPN, aucune bactérie n'a été identifiée à part *C. difficile* (toxine). Le dépistage des œufs et des parasites a donné un rendement négligeable. Les virus ont été plus fréquents au cours des mois d'hiver, alors que les organismes bactériens ont été plus courants pendant les mois d'été et d'automne. Plus de 50 % des hôpitaux pédiatriques canadiens procèdent encore de routine aux tests sur les spécimens de DPN et de DPC.
CONCLUSIONS : Il y a lieu de réévaluer le dépistage des œufs et des parasites de routine et les cultures bactériennes lors des épisodes non épidémiques de DPN chez les enfants.

Diarrheal diseases are a major cause of morbidity and hospitalization in North American children, and a leading cause of morbidity and mortality in children worldwide. It has been estimated that 16.5 million American children younger than five years of age have between 21 and 37 million episodes of diarrhea annually, and approximately 10.6% of hospitalizations in this age group are for diarrhea (1). Gastrointestinal infections account for 16.8% to 20% of hospital-acquired disease (2,3), and it was estimated that the mean cost per nosocomial infection was US$836 (1977 dollars) for diagnostic and therapeutic measures (4). Knowledge of etiological agents of infectious diarrhea at a particular institution may help to determine focused empirical therapy and to choose the appropriate stool tests, possibly reducing the cost of hospitalization without affecting patient care. Previous studies in other localities have documented significant site to site differences with respect to the types of pathogens causing paediatric infectious diarrhea (5-12), but have not clearly differentiated community-acquired diarrhea (CAD) from nosocomial diarrhea (NAD) (5-7,9,11). A wide range of viral, bacterial and parasitic causes of infectious diarrhea are now recognized. Because of the variety of organisms, it is difficult and expensive for clinical laboratories to do a complete etiological examination of diarrheal stool specimens. Some investigators, mostly studying adult populations, have recently questioned the appropriateness of performing a complete etiological examination on stool specimens for diarrheal diseases (13-18). The few published reports on stool testing in the paediatric population have either not differentiated CAD from NAD (19-21), or have excluded viral testing or screening for ova and parasites (17-21). Furthermore, it was unclear what the practice of screening diarrheal NAD stool specimens was among Canadian paediatric centres. In view of these considerations, we sought to characterize the infectious agents associated with both CAD and NAD at our paediatric institution and the characteristics of diarrhea due to different pathogens, and evaluate the appropriateness of screening for all pathogens in NAD in children.

PATIENTS AND METHODS

Patient profile: The Alberta Children's Hospital is a tertiary regional referral hospital in Calgary that is affiliated with the University of Calgary, Alberta. The hospital serves a population base of 1.2 million children, seeing children referred from southern Alberta, southeastern British Columbia, northern Montana and southwestern Saskatchewan. From April 1, 1993 to March 30, 1995, the health and microbiological records of all children with an admission or discharge diagnosis of diarrhea were reviewed. Using a standardized data collection form, the following information was abstracted from the patient records: age, sex, date of admission, frequency and duration of diarrhea, character of diarrhea, associated symptoms, whether specimens were obtained for different enteropathogens, results of such testing and the outcome of the patient. In addition, in July 1998, a telephone survey of laboratories serving all paediatric hospitals in Canada was conducted using a standard questionnaire to obtain information with regard to their practices for screening for pathogens related to NAD.

Definitions: Diarrhea was defined as stools unusually loose or frequent compared with the norm for each child, as perceived by the caregiver (22). A diarrheal episode was defined as occurrence of diarrhea in a child following more than one week of being well (22). NAD was defined as an occurrence of diarrhea in a child after 72 h of hospitalization, while all others were considered community acquired (23). A diarrheal episode was considered to be infectious if a pathogen was isolated from stool. Recent antibiotic use was defined as the use of antibiotics within one month of presentation. An episode was defined as having significant bacteremia if the bacteremia was treated with antibiotics.

Stool examination: Stool specimens were collected and transported in Enteric Plus (Dalynn Laboratory Products, Calgary, Alberta) media. The specimens were routinely inoculated onto a number of selective and differential media, including blood agar, MacConkey, Hektoen agar, Yersinia agar (CIN), MacConkey agar containing sorbitol, a campylobacter agar (CAMPY) and selenite broth (SEL-F). All plates and the SEL-F broth tube

were aerobically incubated at 37°C, except for the CAMPY plate, which was incubated in a microaerophilic atmosphere at 42°C. Enteric pathogenic isolates were screened off the primary plates using triple-sugar iron, urea, and motility/indole/lysine slants. Other routine biochemical tests, serotyping, and a VITEK (bio-Mérieux, St Louis, Missouri) Gram-negative identification card were used to identify each pathogenic stool isolate fully. *Clostridium difficile* was cultured on cefoxitin cycloserine fructose agar (CCFA). Stool was tested for *C difficile* toxin using an enzyme immunoassay (EIA) (Cambridge Biotech, Worcester, Massachusetts). Stool was tested for rotavirus and adenovirus by EIA (Cambridge Biotech). Electron microscopy (EM) for rotavirus was performed on a 50% stool suspension. Stool was cultured for adenovirus and enterovirus on cultures of LLC-monkey kidney cells (LLC-MK) and human carcinoma cells. Viral culture and EM were performed on request and if EIA testing was negative. All stool specimens for ova and parasites were collected and transported in sodium acetyl formalin. Preserved stools were then concentrated using a standard acetate-acetic acid-formalin fixative (24). Two slides were prepared: one slide, made from the washed stool, was stained permanently using a modified iron hematoxyline/Kinyoun stain (25), and another slide from the stool concentrate was examined unstained.

Statistical analysis: Differences in group proportions were compared by use of the ^{2} test or the Fisher's exact test. Differences in median were tested for significance using the Mann-Whitney U test. All statistical calculations were performed with Statistica version 5.0 (Statsoft Incorporated, Tulsa, Oklahoma). In all analyses, a two-tailed $P<0.05$ was considered statistically significant.

RESULTS

Epidemiology: During the study period, 12,305 patients were admitted to the hospital. Five hundred and twenty-three episodes of diarrhea were identified; 434 episodes occurred among 399 (3.2% of all discharges) patients with CAD (353 episodes/10,000 discharges/year) and 89 episodes of diarrhea in 81 patients (0.7% of discharges) with NAD (72 episodes/10,000 discharges/year). The median age of children with CAD at the onset of the diarrheal episode was 19.8 months (range 0.13 to 215.1 months), while for NAD episodes the median age was 19.0 months (range 0.17 to 209.9 months, P=1.00). Two hundred and forty-seven (56.9%) CAD episodes occurred in males versus 47 (52.8%) NAD episodes (P=0.48). Rotavirus EIA and bacterial cultures were performed on the majority of diarrheal episodes, while less than 30% were subjected to viral culture, EM, adenovirus antigen testing, and ova and parasite screen (Table 1). NAD episodes were subjected to adenovirus antigen and *C difficile* toxin testing more often than CAD.

Organisms identified: An infective agent was identified in 34.8% of all diarrheal episodes. Among patients with CAD, pathogens were identified in 143 (32.9%) episodes (116 episodes/10,000 discharges) versus 39 (43.8%) NAD episodes (31.7 episodes/10,000 discharges). Among patients who received specific diagnostic tests, pathogens were identified in 143 of 363 (39.4%) of CAD and 39 of 84 (46.4%) of NAD episodes. The majority of the diarrheal episodes in NAD were associated with a single pathogen; only one of 84 (1.2%) samples from NAD episodes tested was associated with two organisms (*C difficile* and *Blastocystis hominis*). Similarly, CAD episodes were also predominantly associated with a single pathogen. Multiple enteropathogens were identified in only six of 363 (1.7%) CAD episodes tested: *C difficile* and adenovirus in one, rotavirus and adenovirus in one, campylobacter and *B hominis* in one, *Escherichia coli* O157:H7 and *Enterobius vermicularis* in one, rotavirus and *B hominis* in one, and salmonella, aeromonas and rotavirus in one.

TABLE 1
Diarrheal episodes tested for specific organisms at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995

Type of test	Number of CAD episodes tested, n=434 (%)	Number of NAD episodes tested, n=89 (%)	P
Rotavirus EIA	248 (57.1)	63 (67.4)	0.07
Adenovirus EIA	66 (15.2)	22 (24.7)	0.03
Viral culture	64 (14.7)	15 (16.9)	0.61
Electron microscopy	64 (14.7)	15 (16.9)	0.61
Bacterial culture	274 (63.1)	57 (64.1)	0.87
Clostridium difficile toxin	119 (27.4)	54 (60.7)	<0.0001
Ova and parasite screen	128 (29.5)	22 (24.7)	0.36

CAD Community-acquired diarrhea; EIA Enzyme immunoassay; NAD Nosocomial diarrhea

Viruses were the organisms most commonly identified in the CAD and NAD specimens tested, accounting for one-third of each group. Bacteria were also frequent, but non-*C difficile* bacteria were never identified in any of 57 NAD diarrheal episodes tested. Rotavirus and *C difficile* were the most commonly identified pathogens in both CAD and NAD episodes (Table 2), accounting for one-fourth to one-third of all tested episodes. The majority of rotavirus infections occurred in the winter (P<0.0001), whereas *C difficile* toxin was identified mainly in the summer, fall and early winter (P<0.001). Screening for ova and parasites were positive in 11 CAD episodes, and the organisms identified were *B hominis* (n=4), *Giardia lamblia* (n=3), *Cryptosporidium* species (n=2), *Dientamoeba fragilis* (n=1) and *Enterobius vermicularis* (n=1). Whereas parasites were identified in 8.6% of CAD episodes tested, they were identified in only one NAD episode during which *B hominis* was found in association with campylobacter infection.

Specific testing by diarrheal episode: Rotavirus was detected primarily by EIA antigen screening in both CAD and NAD specimens (Table 2). The use of EM revealed rotavirus in a further 2% of cases. Viral culture was successful in isolating adenovirus in less than 10% of episodes tested, but was of greater value than adenovirus 40/41 antigen testing. Only one episode yielded enterovirus. Whereas in patients younger than five years of age one-third of CAD episodes tested for viruses were positive, virus-positive specimens dropped sharply in patients

TABLE 2
Organisms identified in diarrheal episodes at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995

	Type of test (number of positive episodes/number of episodes tested)				
Organism	**EIA**	**Culture**	**EM**	***Clostridium difficile* toxin**	**Total (brackets indicate?)**
Community-acquired diarrhea episodes					
Virus					79/266 (30.0)*
Rotavirus	72/248 (29.0)	N/A	2/64 (3.1)	N/A	73/258 (28.3)†
Adenovirus	1/66 (1.5)	5/64 (7.8)	N/A	N/A	6/111 (5.4)‡
Enterovirus	N/A	1/64 (1.6)	N/A	N/A	1/64 (1.6)
Bacteria					58/299 (19.4)§
C difficile	N/A	0/2 (0)	N/A	29/119 (24.4)	29/120 (24.2)
Other bacteria¶	N/A	29/274 (10.6)	N/A	N/A	29/274 (10.6)
Parasites	N/A	N/A	N/A	N/A	11/128 (8.6)
Nosocomial acquired diarrhea episodes					
Virus					22/67 (32.8)**
Rotavirus	19/60 (31.7)	N/A	1/15 (6.7)	N/A	20/67 (32.8) ††
Adenovirus	1/22 (4.5)	1/15 (6.7)	N/A	N/A	2/34 (5.9)‡‡
Bacteria					17/70 (24.3)
C difficile	N/A	N/A	N/A	17/54 (31.5)	17/54 (31.5)
Other bacteria	N/A	0/57 (0)	N/A	N/A	0/57 (0)
Parasites	N/A	N/A	N/A	N/A	1/22 (4.5)

**99 episodes tested for rotavirus, adenovirus and enterovirus – one episode positive for both rotavirus and adenovirus; †47 episodes tested by both enzyme immunoassay (EIA) and electron microscopy (EM) – one episode positive for rotavirus with both EIA and EM; ‡19 episodes tested by both EIA and culture; §94 episodes tested for* C difficile *toxin,* C difficile *by culture and routine bacterial culture; ¶Other bacteria:* Escherichia coli *(n=13, 3.0%), shigella (n=6, 1.4%), campylobacter (n=5, 1.2%), salmonella (n=4, 0.9%), staphylococcus (n=1, 0.2%), and aeromonas (n=1, 0.2%); **30 episodes tested for rotavirus and adenovirus; ††Eight episodes tested by both EIA and EM; ‡‡‡Three episodes tested by both EIA and culture. CAD Community-acquired diarrhea; N/A Not applicable; NAD Nosocomial acquired diarrhea*

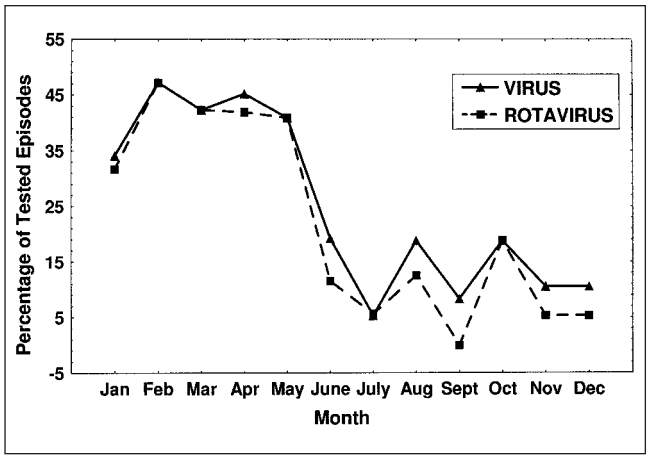

Figure 1) *Seasonal distribution of all viral-associated diarrhea at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995*

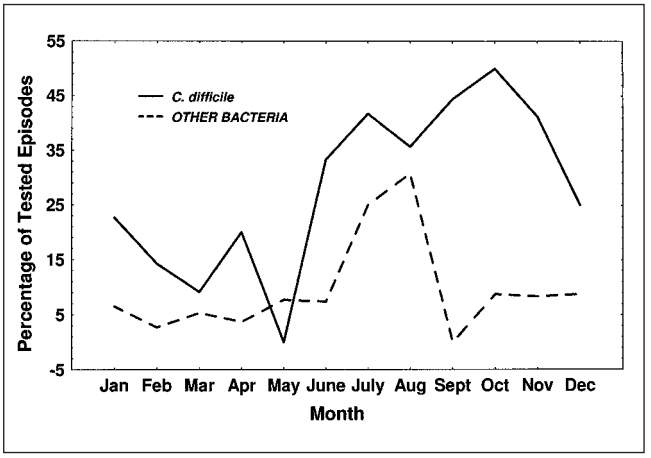

Figure 2) *Seasonal distribution of all bacterial-associated diarrhea at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995*

age five years and older (76 of 219 episodes in children younger than age five years versus three of 40 episodes in children aged five years and older, P<0.001). Infants younger than 12 months of age formed the majority (55.9%) of the NAD patient population (P<0.001). Virus-positive specimens, and rotavirus specifically, were highest in the winter months (P<0.0001) (Figure 1).

Testing for *C difficile* toxin produced positive results in one-fourth of CAD cases and one-third of NAD episodes (Table 2). Bacterial pathogens other than *C difficile* were positive in 10.6% of CAD specimens sent, with *E coli* O157:H7 identified as the most common non-*C difficile* organism. In NAD episodes, there were no positive bacterial cultures (P<0.001, NAD versus CAD). In contrast with viruses, bacteria were most commonly identified in patients age five years and older (27 of 212 episodes in children younger than five years versus 31 of 74 episodes in children five years and older, P<0.0001) presenting with CAD. *C difficile* was the only bacterial pathogen identified in NAD episodes and was not prevalent in any one age group (P=0.38). *C difficile* was identified most often in

TABLE 3
Clinical features of viral community-acquired diarrhea at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995

Clinical features	Viral diarrhea (%)*	Nonviral diarrhea (%)†	P
Vomiting	62/79 (78.5%)	15/284 (5.3)	0.04
Nausea	1/79 (1.3)	187/282 (66.3)	0.21
Fever	23/79 (29.1)	80/284 (28.2)	0.89
Malaise	39/79 (49.4)	130/284 (45.8)	0.61
Loss of appetite	34/79 (43.0)	139/284 (49.0)	0.37
Headache	0/79 (0)	8/284 (2.9)	0.21
MSK pain	0/79 (0)	5/284 (1.8)	0.59
Watery diarrhea	74/79 (93.7)	220/284 (77.5)	<0.001
Bloody diarrhea	5/79 (6.3)	63/284 (22.2)	<0.001
Mucousy diarrhea	6/79 (7.6)	46/284 (16.2)	0.07
Recent antibiotics	27/79 (34.2)	106/284 (37.3)	0.69
Day care	15/67 (22.4)	24/260 (9.2)	<0.01
Fast food	3/74 (4.1)	17/269 (6.3)	0.58
Other family‡	975 (12.0)	32/276 (11.6)	1.00
Animal exposure	7/65 (10.8)	29/238 (12.2)	0.83
Travel	3/77 (3.9)	3/274 (1.1)	0.12
Rash	12/76 (15.8)	47/273 (17.2)	0.86
Abdominal tenderness	4/77 (5.2)	39/279 (14.0)	0.05
Peritoneal signs	0/78 (0)	1/278 (0.4)	1.00

**Viral episodes were those in which a viral pathogen was isolated from a stool; †Non-viral episodes were those in which viral pathogens were not isolated from a stool; episodes in which no tests performed on stool samples were excluded; ‡Other family – other family members with diarrhea. MSK Musculoskeletal*

TABLE 4
Clinical features of bacterial community-acquired diarrhea at the Alberta Children's Hospital, Calgary, Alberta from April 1, 1993 to March 30, 1995

Clinical features	Bacterial diarrhea*	Non-bacterial diarrhea†	P
Vomiting	33/57 (42.1%)	216/304 (28.9%)	0.06
Nausea	7/58 (12.1)	9/305 (3.0)	<0.01
Fever	18/58 (31.0)	85/305 (27.9)	0.64
Malaise	36/58 (62.1)	133/305 (43.6)	0.01
Loss of appetite	40/58 (69.0)	133/305 (43.6)	<0.001
Headache	1/58 (1.7)	7/305 (2.3)	1.000
MSK pain	1/58 (1.7)	4/305 (1.3)	0.55
Watery diarrhea	37/58 (63.8)	257/305 (84.3)	<0.001
Bloody diarrhea	31/58 (53.4)	37/305 (12.1)	<0.0001
Mucousy diarrhea	14/58 (24.1)	38/305 (12.5)	0.03
Antibiotics	24/58 (41.4)	109/305 (35.7)	1.000
Day care	3/53 (5.7)	36/274 (13.1)	0.16
Fast food	7/54 (13.0)	13/289 (4.5)	0.02
Other family‡	12/55 (21.8)	29/296 (9.8)	0.02
Animal exposure	6/50 (12.0)	30/253 (11.9)	1.00
Travel	2/55 (3.6)	4/296 (1.4)	0.24
Rash	6/57 (10.5)	53/292 (18.2)	0.18
Abdominal tenderness	17/57 (29.8)	26/299 (8.7)	0.0001
Peritoneal signs	0/55 (0)	1/301 (0.3)	1.00

**Bacterial episodes were those in which a bacterial pathogen was isolated from stool; †Nonbacterial episodes were those in which bacterial pathogen was not isolated from stool; excludes episodes in which no tests were performed on stool sample; ‡Other family – other family members with diarrhea. MSK Musculoskeletal*

TABLE 5
Significant variables in logistic regression models of viral and bacterial community-acquired diarrhea (CAD)

	Viral CAD	Bacterial CAD*
Month at presentation (From January, as baseline, to December)		
Odds ratio	0.08	4.85
–95% CL	0.03	1.86
+95% CL	0.22	12.62
Increasing age at presentation		
Odds ratio	0.03	14.55
–95% CL	0.01	5.33
+95% CL	0.22	39.74

**Separate logistic regression models. CL Confidence limits*

specimens sent from June to December (P<0.001), while the other bacterial pathogens were isolated mainly in July and August (P<0.0001) (Figure 2).

Almost one-third of all CAD episodes underwent ova and parasite screening, with less than 10% of the specimens being positive (Table 2). Testing of NAD episodes had a negligible yield. CAD episodes occurring in children older than five years of age were just as likely to be positive for parasites as episodes in younger children (P=0.73). Although 12.5% of parasite-positive episodes occurred during the period June to August, there was no season in which parasites were more likely to be identified (P=0.47).

Clinical information: Viral CAD episodes were significantly associated with day care attendance, vomiting, watery diarrhea and abdominal tenderness (Table 3). CAD episodes in which bacterial pathogens were identified were linked with nausea, malaise, loss of appetite, blood or mucous in the stool, eating fast food recently, other family members with diarrhea and abdominal tenderness (Table 4). Antibiotic use was the only risk factor associated with bacterial NAD cases (11 of 17 bacterial episodes versus 25 of 70 nonbacterial episodes, P<0.02). Compared with episodes in which other bacteria were isolated, *C difficile*-associated diarrhea was more commonly associated with recent antibiotic use (63.0% versus 20.7%, P<0.001) and chemotherapy (32.8% versus 0%, P<0.001).

In a logistic regression model including vomiting, nausea, headache, watery versus bloody diarrhea, mucousy diarrhea, day care attendance, month of presentation and age at presen-

tation, only the latter two were associated with viral versus nonviral CAD (Table 5). In a separate logistic regression model for bacterial versus nonbacterial CAD vomiting, nausea, malaise, loss of appetite, watery versus bloody diarrhea, mucousy diarrhea, day care attendance, eating fast food recently, other family members with diarrhea, rash, abdominal tenderness, month at presentation and age at presentation were included. As with the model for viral CAD, only the month and older age at presentation were associated with bacterial versus nonbacterial CAD (Table 5).

Ten (66.7%) of the 15 laboratories that process stool specimens for paediatric hospitals across Canada (not including Alberta Children's Hospital) indicated that they still routinely receive requests for culture and sensitivity testing for bacteria other than *C difficile* in children with NAD. Eight (80%) of these 10 laboratories indicated that they still routinely perform such tests if requested, irrespective of duration of hospitalization. Five (38.5%) of 13 laboratories indicated that they have a policy, which was currently in practice, of only testing for *C difficile* toxin in such stool specimens. Two other hospitals were in the process of instituting this practice but did not have it in place at the time of the survey. Only one (6.67%) of the 15 laboratories routinely culture stool specimens for *C difficile* under any circumstances. Five (33.3%) of the 15 laboratories indicated that they still routinely receive requests for ova and parasite testing on NAD specimens. Three (60%) of these five routinely perform such tests if requested.

DISCUSSION

Recent studies, predominantly in adults, have questioned the value of routine screening of all stool specimens in nosocomial diarrhea (14,15,17,18,20,21). However, there has been very little information on this approach in paediatric nosocomial diarrhea. In previous studies conducted at our institution (20,21), we had noted that a single stool specimen was adequate for the identification of bacterial and parasitic pathogens in hospitalized children with diarrhea. Our current study indicates that testing for parasitic pathogens and bacteria other than *C difficile* is not necessary in children who have nosocomial diarrhea except in an outbreak setting. However, the telephone survey indicates that at least half of all paediatric centres surveyed still process stools from NAD patients for multiple pathogens.

The rate for infection associated NAD of 31.7/10,000 discharges reported in our study is much higher than the average of 11.3/10,000 discharges reported in the National Nosocomial Infections Surveillance (NNIS) for the years 1985 to 1991. This may reflect actual higher rates in our hospital, or may reflect more complete laboratory evaluations of patients with diarrhea or differences in patient populations in reporting hospitals. It has previously been noted that NNIS rates are likely an underestimate because most participating hospitals do not have diagnostic virology laboratories (26).

As previously noted by other investigators, rotavirus was the most common pathogen associated with infectious CAD and NAD at our institution (2,5,8-12,17,23,27-33). Enteric adenovirus, the second most common cause of viral-associated diarrhea in our study, has also been strongly implicated in paediatric diarrheal disease in the United States (2,9,11,28,32-35). Enterovirus was cultured from one of 64 (1.6%) CAD stool specimens sent, but was not identified in any of 15 NAD specimens. Enterovirus isolation rates of 2.0% to 3.2% have been previously reported (5,8,33), but these studies have not delineated CAD from NAD episodes. CAD was not separated from NAD episodes in other studies in which enteroviruses were identified in 7.4% to 25.1% of paediatric patients (10,36,37). Our low isolation rate may reflect regional differences in the role of these pathogens or differences in diagnostic measures. Our results confirmed results from earlier studies (4,23), in which the majority of rotavirus NAD cases were found in infants younger than 12 months old, and most common during the cold months (9,22,26,27,31,33,35,38-41).

The identified contribution of bacteria in this study of 19.4% for CAD and 23.3% for NAD is in the higher end of the documented rates of bacterial diarrheas in children of developed countries, which have ranged from 5.1% to 31% (6,8-10,12,21,27,33,36,42-44). Bacterial culture was positive in 10.6% CAD specimens, with *E coli* identified as the most common non-*C difficile* bacteria, present in 3% of CAD episodes. However, higher rates than ours have been reported for *E coli* (10% to 16.8%) (6,33,36,37,45), shigella (6% to 32.6%) (6,36,37,45,46), campylobacter (4.9% to 7.9%) (10,12), salmonella (4.1% to 11%) (8,9,10,18,34,36,37,46) and aeromonas (6.9%) (9). In only a few studies (37,45,46) was it clear that the population studies consisted only of CAD episodes. Two studies (45,46) took place in summer and fall, which biases their results in favour of bacterial isolation. The conclusions of the other studies may be explained if these episodes were cultured in the setting of an outbreak. The discrepancies could also be due to site to site differences because a study conducted by Church et al (21) at our institution revealed isolation rates for bacteria other than *C difficile* to be in the range of 0.2% to 2.3%, which are similar to the rates in our investigation. The identification of *C difficile* as the most common bacterial pathogen, although not unique (14,15,17,19), was notable in that it was the only bacterial organism identified in NAD, similar to the experience of Fan et al (18).

The association between *C difficile* diarrhea and antimicrobial exposure is well established (47-51). Although the role of *C difficile* as an etiological agent of diarrhea in the paediatric population is controversial, it cannot be excluded as a possible agent in children who have received previous antibiotic therapy and in whose stool other enteric pathogens have not been isolated (52). Previous authors have indicated that the incidence of community-acquired *C difficile* diarrhea is low, with less than one case/10,000 antibiotic prescriptions being reported from one large outpatient setting (48). Although we do not have similar comparisons with regards to rates per antibiotic usage, the high identification of *C difficile* in our NAD and CAD populations may reflect a high baseline rate of antibiotic usage, good detection techniques for *C difficile* or differences in our population in terms of food preparation and consumption. Similarly, patients with malignant disease receiving chemotherapy have been noted to be at risk for *C difficile* infection

because of the numerous courses of antibiotics that they receive and because cancer chemotherapy itself may predispose patients to gut colonization with *C difficile* (53-56). CAD episodes in which bacterial pathogens were isolated were predominantly in children older than five years of age. Caprioli et al (12) reported that stool specimens were positive for bacteria predominantly in children with a median age of 23 months, but failed to note how often stool specimens from older children were subjected to bacterial culture.

Our study confirms previous reports of low yield regarding bacterial stool culture (17,18) in children with NAD. A recent American study arrived at the same conclusions that bacterial cultures are not useful for nosocomial diarrhea (57). As in other published studies (14,15,17,19), positivity rates for *C difficile* toxin testing are higher than for other tests routinely performed on stool specimens. Screening for the presence of rotavirus antigen through EIA had relatively high yield for NAD episodes as well. Based on these findings, it would appear that testing for *C difficile* toxin and rotavirus antigen by the use of EIA are the only tests indicated in NAD episodes other than in the setting of an outbreak, where bacterial culture, and ova and parasite screening may be useful (58-60). Our study may be limited by the lack of universal use of EM at our institution, which may pick up Norwalk, toroviruses and other gastrointestinal viruses. These data need confirmation from other centres in Canada, in particular, the role of EM in routine management of nosocomial diarrhea needs clarification.

Ova and parasite examination in NAD may be indicated in the setting of compromised hosts where cryptosporidium may be implicated (61,62), or in inpatients who have multiple passes out of hospital and travel to local areas known to be endemic for parasites during these periods. There is controversy about the role of *B hominis* as a pathogen, and because it was identified only once along with rotavirus, its role as a cause of diarrhea in our study is dubious (63).

On univariate analysis, rotavirus was associated with day care attendance. This concurs with reported outbreaks of rotavirus-positive diarrhea in day cares (22,60). Vomiting, watery diarrhea and the absence of blood in the stool have been previously associated with rotavirus (4,8,23,35, 41,46,64). In studies conducted in both adults (13) and children (12,44), blood in stool, abdominal pain and nausea were identified as good clinical predictors of a positive bacterial culture. Despite significant associations found on univariate analysis, our logistic regression model concluded that only the age of the patient and the month at presentation were associated with the isolation of either bacterial or viral agents.

CONCLUSIONS

There is a need to re-evaluate the performance of complete etiological examinations on stool specimens in nonoutbreak cases of NAD in children, a practice still common in Canadian paediatric centres. Screening for *C difficile* toxin and rotaviruses will identify the majority of infectious pathogens in NAD, while a broader range of organisms needs to be sought in CAD. The use of clinical-epidemiological factors such as age of the patient, seasonality, antibiotic use and travel history may be useful in helping to focus the testing performed on stool specimens.

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