

NOSOCOMIAL DIARRHEA IN CHILDREN: THE PGH EXPERIENCE

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ABSTRACT

In a prospective cohort study of nosocomial diarrhea in children admitted to the University of the Philippines-Philippine General Hospital's pediatric wards, a prevalence rate of 10% (42 cases out of 419 admissions) was gathered. A pathogen was isolated in 34 patients (81%), with Enterobacteriaceae as the main etiologic pathogens. The most common pathogen isolated was Escherichia coli in 15 cases (35.7%), followed by Klebsiella ozanae in 6 cases (14.3%), and Klebsiella pneumoniae in 4 cases (9.5%). The clinical features and associated conditions observed in patients who developed nosocomial diarrhea were: a) age - 1 year old or less, b) sex - male, c) presence of antimicrobials for a week or more, d) presence of a nasogastric tube, e) presence of enteral feeding, f) leukocytosis, and g) duration of hospital stay for a week or more. In patients whose nosocomial diarrhea were infectious in etiology, there was a significant ($p < 0.05$) chance of having a morbidity, compared to those patients in whom no pathogen was isolated from their stools.

INTRODUCTION

Community-acquired diarrhea in the pediatric population is one of the leading causes of morbidity and mortality in our country. Hence, the substantial information available; however, there is paucity of data regarding nosocomial or hospital-acquired diarrhea. Data from the National Nosocomial Infections Study of the United States indicate that the nosocomial diarrhea rate in that country from 1980-1984 was 1.3/10,000 discharges. This has been refuted by more recent studies^{1, 2, 4, 5, 6, 7} which indicate higher incidence.

Nosocomial diarrhea has almost always been assumed to be non-infectious in etiology. In many instances, when routine bacterial cultures specifically for Salmonella and Shigella are done, mostly they are negative. Recent studies, such as those by Hjelt in 1985, Lima and Guerrant in 1990, Zaidi, Farr, Yankauer and Paton in 1991, however, have identified Enterobacteriaceae as the main etiologic agents and the gastrointestinal tract as the likely reservoir of these pathogens.¹⁻⁸ If a more extensive search for an infectious etiology is done, and the evidence that it is more common is accepted, then concern arises as to its significance. Is it merely an unpleasant nuisance or is it some-

thing worse? The clinical significance of these organisms as nosocomial pathogens is further increased by their propensity to be resistant to antimicrobials, especially in a developing nation such as ours. The adequate information about nosocomial diarrhea could then enhance the development of appropriate preventive measures and the prioritization of our country's limited healthcare resources.

To date, no prospective studies have been done in the Philippines. It is hypothesized that nosocomial diarrhea is infectious in etiology.^{1, 2, 3, 4, 5, 6, 14, 15}

This study was therefore undertaken to determine the prevalence of nosocomial diarrhea in a large teaching hospital setting, and to determine the clinical features and outcome of such patients.

MATERIALS AND METHODS

This is a prospective cohort study of pediatric patients (> 1 month - 18 years old) admitted to the hospital from August 15 to November 15, 1993, with no history of diarrhea during the past 14 days prior to admission to the hospital, who developed diarrhea after at least 72 hours in the hospital, and whose diarrhea lasted at least 1 day.

The following patients were excluded: those patients with history of diarrhea during the past 14 days prior to admission, patients with severe malnutrition, patients who presented/developed melena, patients with malabsorption.

The parents of patients who fulfilled the above-mentioned criteria were asked to sign a written informed consent. The stools of patients who developed nosocomial diarrhea were collected and evaluated as follows: a) direct fecal smear for ova and parasites, b) Gram's stain for parasites, leukocytes, yeast cells, and hyphal elements, c) Rotazyme test for Rotavirus, and d) Modified Kinyoun's test for Cryptosporidium. The stools were also cultured on the following media: Salmonella-Shigella agar, Blood agar plate, MacConkey agar, Selenite F and Saboraud's dextrose agar. All examinations were performed by a single medical technologist in the Bacteriology Section of the hospital's Central Laboratory.

The clinical features and associated conditions of patients who developed nosocomial diarrhea were also studied, such as their age, sex, the presence of leukopenia/leukocytosis, immunosuppressive drugs,

nasogastric tube (NGT), enteral feeding, urinary catheter, laxatives, antibiotics, antacids/H₂ antagonists, and duration of hospital stay.

The effect of nosocomial diarrhea on morbidity (dehydration, administration of antibiotics, electrolyte imbalance, and extension of hospital stay) and mortality were also studied. These effects were analyzed using the Fischer's exact probability test.

RESULTS

There were 42 episodes of nosocomial diarrhea in 40 patients, among the 419 admissions during the study period, giving a prevalence rate of 10%. Table 1 shows the profile of these patients. The patients' age ranged from 1.5 months to 13 years old with a mean age of 12 months. The patients were predominantly male (57.1%). The hospital stay (from the date of admission to the time the patients developed diarrhea) ranged from 5-61 days, with a mean of 19.6 hospital days. Table 2 shows the underlying diagnoses of the patients at the time they developed nosocomial diarrhea. Almost all of the patients had multiple diagnoses. Fifty-percent of these diagnoses were infectious in etiology with majority of the patients with bronchopneumonia (73.8%).

A pathogen was isolated in 34 (81%) of the cases. These pathogens are shown in Table 3.

Table 1. Profile of Patients who Developed Nosocomial Diarrhea (n = 42)

	No.	%
1. Age		
Mean, months	12 (SD ± 3)	
Range: 1.5 months-13 years		
Distribution		
< 1 year	33	78.6
1-2 years	7	16.7
> 2 years	2	4.8
2. Sex		
Males	24	57.1
Females	18	42.9
3. Duration of hospital stay (from date of admission to occurrence of diarrhea)		
Mean, days	19.6 (SD ± 11)	
Range: 5-61 days		
Distribution		
> 3 days-6 days	5	11.9
1-2 weeks *	15	35.7
2-3 weeks	9	21.4
3-4 weeks	7	16.7
> 4 weeks	6	14.3

Enterobacteriaceae were the main pathogens isolated, with Escherichia coli as the most common pathogen (35.7%) isolated in the stools of the study subjects. Unfortunately, no serotyping was done due to the unavailability of reagents.

Table 2. Underlying Diagnoses of Patients with Nosocomial Diarrhea

Diagnosis	Number of Patients	%
Bronchopneumonia	31	73.8
Probable Sepsis	7	16.7
Congenital Heart Disease	7	16.7
Suppurative Meningitis	7	16.7
Hepatic Encephalopathy	4	9.5
Chronic Liver Disease		
a. Hepatitis	4	9.5
b. Biliary Atresia	3	7.1
Tuberculous Meningitis	2	4.8
Ruptured Retropharyngeal Abscess	1	2.4
Amebic Liver Disease	1	2.4
Chronic Idiopathic Thrombocytopenic Purpura	1	2.4
Congenital Hydrocephalus	1	2.4
Disseminated Koch's Infection	1	2.4
Hepatoblastoma	1	2.4
TORCHES	1	2.4
Nephrotic Syndrome	1	2.4
Complete Cleft and Palate, Bilateral	1	2.4
Bronchopulmonary Dysplasia	1	2.4

Table 3. Enteropathogens Isolated from Patients with Nosocomial Diarrhea

Enteropathogens	Number	%
Total	34/42	81.0
<u>Escherichia coli</u>	15	35.7
<u>Klebsiella ozanae</u>	6	14.3
<u>Klebsiella pneumoniae</u>	4	9.5
<u>Enterobacter cloacae</u>	3	7.0
<u>Enterobacter aerogenes</u>	2	4.8
<u>Aeromonas</u>	1	2.4
<u>Citrobacter diversus</u>	1	2.4
<u>Candida sp.</u>	1	2.4
<u>Rotavirus</u>	1	2.4
<u>Cryptosporidium</u>	1	2.4

Table 4. Associated Conditions in Patients with Nosocomial Diarrhea

Conditions	Number	%
Leukocytosis	25	59.5
Leukopenia	1	2.4
Presence of:		
Nasogastric tube	23	54.8
Enteral feeding	22	52.4
Urinary catheter	4	9.5
Drugs:		
Immunosuppressive drugs	4	9.5
Antacids	5	11.9
Antimicrobials		
Number		
0	2	4.8
1-2	12	28.6
> 2	28	66.7
Duration		
0	2	4.8
< 7 days	5	12.0
1-2 weeks	14	33.3
> 2 weeks	21	50.0

Table 4 lists the associated conditions present in the patients during inclusion to the study. Majority of patients had a nasogastric tube in place (54.8%); on enteral feedings (52.4%), receiving more than 2 antimicrobials (66.7%) and who were in the hospital for more than two weeks (52.4%). Almost sixty percent had leukocytosis.

Of the 34 patients in whom a pathogen was isolated, 3 required intravenous rehydration. Twenty-one responded to oral rehydration therapy. Three patients who were ready to be discharged required extended hospital stay, ranging from 2-5 days, average: 3 days. One patient required shifting of antibiotics to a third generation cephalosporin. No patient developed electrolyte imbalance. In the 2 patients who died, nosocomial diarrhea contributed to their demise. These patients developed acute tubular necrosis secondary to the hypovolemia and/or septic shock. (Table 5)

Table 5. Outcome of Patients with Nosocomial Diarrhea

Outcome	Number	%
A. Morbidity		
1. None	4	9.5
2. Dehydration	24	57.1
3. Extended hospital stay	3	7.1
4. Shifting of antibiotics		
B. Mortality	2	4.8

Using Fischer's Exact Probability test, patients who yielded a pathogen in their stools had an increased chance of morbidity and/or mortality compared to those in whom no pathogen could be isolated in their stools. (Table 6)

Table 6. Relationship of Outcome with Culture Results in Patients with Nosocomial Diarrhea

	Culture		Total
	Positive	Negative	
Presence of morbidity/mortality	30 (71.4%)	0 (0.0%)	30
Absence of morbidity/mortality	4 (9.5%)	8 (19.0%)	12
TOTAL	34	8	

p value at 0.000042

p < 0.05, Fischer's exact probability test

DISCUSSION

The study showed that nosocomial diarrhea is a fairly common occurrence in our hospital with a prevalence rate of 10%. In comparison to available data from foreign literature, these are the various rates of nosocomial diarrhea: Kelly (1983): 41%, Welliver (1984): 17%, Hjelt (1985): 7%, Guerrant (1990): 7.7%, Lima (1990): 5%, Zaidi (1991): 5.5%.^{1, 3, 4, 5, 6, 9, 10} Nosocomial diarrhea-associated deaths in 0.5% of cases, compared to Zaidi's study of 0.2%.

It also confirmed several reports of its infectious etiology (81% isolation rate in our study) with Enterobacteriaceae as the main pathogens isolated. This is in contrast to Zaidi's study in which the main pathogens isolated were Candida sp. and Entamoeba histolytica. This may be due to the difference in age group since Zaidi studied adult subjects, and theorized that his patients were exposed to multiple enteropathogens since childhood and have since developed immunity.^{1, 15, 16}

Clostridium difficile was not among the pathogens tested in this study. Aside from the major limitation of logistics, Tvede found that in 78% of the patients with diarrhea, the bacteria was isolated in patients during the initial 2 days of hospitalization indicating that most of the cases were community-acquired.^{9, 10, 11, 12, 13} Moreover, the pathogen was unusual in Zaidi's study, which was done in a tropical developing nation such as ours. Thus, Clostridium difficile was only ruled out by the absence of Gram-positive (+) bacilli in the Gram's stain of the stools collected.

Rotavirus was found in only one of the patients. This is much lower than what Guerrant and Hjelt has observed.^{3, 4, 6} That patient also yielded Cryptosporidium and Escherichia coli in her stool. During that time, the patient was clinically improving, and responded to oral rehydration therapy; thus, current therapy as of that time was continued.

Notable factors associated with the occurrence of nosocomial diarrhea included the presence of a nasogastric tube which serve as entry points and reservoir of organisms entering the gastrointestinal tract.

Although acid secretion of the stomach serves as an initial barrier for enteropathogenic organisms, the prolonged use of antibiotics which could have altered the normal gastrointestinal flora and the reduced immunocompetence have probably predisposed these patients to the development of bacterial overgrowth which could have overwhelmed even the acid gastric barrier. It was also noted that infants were more often at risk to the development of nosocomial diarrhea mainly because of immunologic handicaps as well as other dietary factors contributing to the causation of nosocomial diarrhea. These children are dependent on their caretakers for food as their usual source of nutrition is milk formulas which in the hospital setting may not be hygienically prepared. In relation to this, the use of enteral feeding by bolus or drip, may have also contributed inasmuch as the formulas used are good media for the growth of microorganisms under hospital conditions of hot and humid temperature and the practice of letting the formula stand for several hours. In summation, the presence of multiple pathogens in the hospital environment to which the patients were exposed to were risks to be contended with each day that the patient stayed in the hospital.^{14, 15, 17}

It is noteworthy that 26 (61.9%) patients who developed nosocomial diarrhea had leukocytosis. Zaidi noted leukopenia in 2 patients who subsequently died. However, again, the difference in the age groups studied is an important factor to be considered. The underlying illness may also have contributed to the leukocytosis which have been observed in our patients. At this point, no definite conclusion can be reached as further investigation is needed to demonstrate that leukocytosis is a significant factor in nosocomial diarrhea and its implications in morbidity and mortality.

Few studies have analyzed the resulting morbidity and mortality due to nosocomial diarrhea. Zaidi found that severe complications, such as dehydration, hematochezia, abdominal distension, and candidemia developed in 7% of the patients. These complications occurred only in patients in whom a pathogen was isolated.¹ This was likewise noted in our study in 81% of the cases. Death related to nosocomial diarrhea was found in the 2 patients who died. Zaidi found nosocomial diarrhea to be directly attributed to the patient's demise in only 4 of the 21 patients who died. Lima reported that nosocomial diarrhea was an important risk factor for acquiring other nosocomial infections, especially urinary and pulmonary infections.^{1, 5}

CONCLUSIONS

Nosocomial diarrhea occurs at a prevalence rate of 10%, in our institution, during the study period (August 15-November 15, 1993). Nosocomial diarrhea is infectious in etiology, with Enterobacteriaceae as the

main pathogens isolated. The clinical features and associated conditions observed in patients who develop nosocomial diarrhea are the following: a) age - 1 year old or younger, b) sex - male, c) presence of antimicrobials for a week or more, d) duration of stay in the hospital for a week or more, e) presence of a nasogastric tube, f) presence of enteral feedings, and g) presence of leukocytosis.

In patients whose nosocomial diarrhea are likely to be infectious in etiology, a higher chance of having a morbidity has been observed.

RECOMMENDATIONS

1. A prospective case-control study, done on a 12-month period must be done to get a clear picture of the incidence rate to note seasonal variation, and to be able to identify significant risk factors.
2. Testing for Clostridium difficile (by culture and/or cytotoxin detection) and serotyping of Escherichia coli must be done to further elaborate their presence in nosocomial diarrhea in our country.

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