



# Risk factors for small bowel bacterial overgrowth and diagnostic yield of duodenal aspirates in children with intestinal failure: a retrospective review

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## Abstract

**Background:** Children with intestinal failure (IF) are at risk for small bowel bacterial overgrowth (SBBO) because of anatomical and other factors. We sought to identify risk factors for SBBO confirmed by quantitative duodenal culture.

**Methods:** A single-center retrospective record review of children who had undergone endoscopic evaluation for SBBO (defined as bacterial growth in duodenal fluid of  $>10^5$  colony-forming unit per mL) was performed.

**Results:** We reviewed 57 children with median (25th–75th percentile) age 5.0 (2.0–9.2) years. Diagnoses included motility disorders (28%), necrotizing enterocolitis (16%), atresias (16%), gastroschisis (14%), and Hirschsprung disease (10.5%). Forty patients (70%) had confirmed SBBO. Univariate analysis showed no significant differences between patients with and without SBBO for the following variables: age, sex, diagnosis, presence of ileocecal valve, and antacid use. Patients receiving parenteral nutrition (PN) were more likely to have SBBO (70% vs 35%,  $P = .02$ ). Multiple logistic regression analysis confirmed that PN administration was independently associated with SBBO (adjusted odds ratio, 5.1; adjusted 95% confidence interval, 1.4–18.3;  $P = .01$ ). SBBO was not related to subsequent risk of catheter-related bloodstream infection (CRBSI).

**Conclusion:** SBBO is strongly and independently associated with PN use. Larger prospective cohorts and more systematic sampling techniques are needed to better determine the relationship between SBBO and gastrointestinal function.

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Intestinal failure (IF) is a consequence of intrinsic intestinal enteropathies, massive small bowel resection resulting from disease processes such as necrotizing enterocolitis (NEC), congenital anomalies, or dysmotility syndromes. Medical management of children with IF is challenging because of the various associated medical and surgical complications. Small bowel bacterial overgrowth (SBBO) and catheter-related bloodstream infections (CRBSIs) are 2 of the most common complications with a direct impact on morbidity and mortality [1,2].

A component of intestinal adaptation after gastrointestinal resection is bowel dilatation. Small bowel bacterial overgrowth is thought to be a direct result of intestinal dilation and subsequent stasis, which, in turn, promotes excess bacterial proliferation and inflammation [3]. In children with SBBO, enteral nutrition tolerance is often limited because of symptoms associated with intestinal malabsorption, which renders them dependent on parenteral nutrition (PN). The administration of PN requires a central venous catheter and, hence, increases the risk for CRBSI in these children.

There are some data to suggest that children with IF have increased intestinal permeability, and it has been hypothesized that SBBO can be a potential source of bacteria contributing to CRBSI [2,4,5]. Bacterial translocation has been noted in animal models, but data supporting its occurrence in humans are limited [6-8]. In addition, the medical literature describing the clinical and microbiological features of SBBO in children is limited. In a cohort of children with IF, we therefore sought to determine possible predictors of SBBO confirmed by quantitative duodenal cultures and to study the relationship between SBBO and CRBSI.

## 1. Methods

After obtaining institutional review board approval (M08-04-0163), we conducted a retrospective medical record review of children with IF who were followed at the Center for Advanced Intestinal Rehabilitation (CAIR) at Children's Hospital Boston between April 2006 and November 2010. The CAIR program is composed of a group of gastroenterologists, general and transplant surgeons, nurses, dietitians, pharmacists, and social workers dedicated to the care of patients with IF. All patients who underwent upper endoscopy for refractory gastrointestinal symptoms (ie, abdominal bloating, emesis, and diarrhea or increased stoma output) were included. All patients had endoscopically obtained duodenal aspirates sent for quantitative aerobic and anaerobic cultures. All cultures were prepared and analyzed according to the microbiology guidelines of the Children's Hospital Boston Microbiology Laboratory [9]. Growth of  $10^5$  colony-forming unit per mL or more of any bacterial or fungal species was defined as a positive result for SBBO. Aspirates without any growth or less than  $10^5$  colony-forming unit per mL were considered negative for SBBO.

## 1.1. Statistical analysis

Associations between possible risk factors and occurrence of SBBO were assessed by Fisher's Exact test for binary proportions and the Mann-Whitney  $U$  test for medians. Multiple logistic regression was applied to identify independent predictors of SBBO, adjusting for covariate imbalances, with the likelihood ratio test used to assess significance [10]. A subgroup analysis was performed to examine the association between SBBO and CRBSI using Fisher's Exact test for the  $2 \times 2$  table. Statistical analysis was performed using the SPSS statistical package (version 19.0; SPSS Inc/IBM, Chicago, IL). Two-tailed  $P < .05$  was considered statistically significant.

## 2. Results

Fifty-seven patients were identified who underwent upper endoscopy and duodenal aspirate and culture during the study period. The underlying IF diagnoses included 16 patients (28%) with primary motility disorders, 9 (16%) with NEC, 9 (16%) with intestinal atresias, 8 (14%) with complicated gastroschisis, 6 (10.5%) with Hirschsprung's disease, 3 (5%) with cloacal exstrophy, and 6 (10.5%) with other conditions requiring surgical resection. The median age of the children was 5.0 years (25-75% range, 2.0-9.2 years), and 27 (47%) were male. Thirty-four patients (60%) were receiving either full or partial PN at the time of upper endoscopy. The remaining patients received all of their nutrition through the oral route and/or via an enteral feeding tube.

Forty patients (70%) were found to have SBBO, and 17 (30%) were not. Table 1 lists details of the spectrum of bacterial species found on duodenal aspirate cultures. The most common gram-positive organisms included *Streptococcus viridans* and *Enterococcus* species. Gram-negative organisms most often found included *Escherichia coli* and *Klebsiella pneumoniae*. *Candida* was found in 2 aspirates in association with other bacterial organisms.

Table 2 summarizes factors tested by univariate and multivariable analyses. Univariate analysis did not show significant differences between patients with and without SBBO for the following variables: age, sex, and whether the primary diagnosis was a primary motility disorder. Therapeutic and anatomical differences such as the presence of an ileocecal valve, surgical management with a lengthening procedure, treatment with gastric acid-blocking medicines, and ethanol lock therapy for prevention of CRBSI were also not significantly associated with the presence of SBBO. In addition, liver function (as assessed by hepatic transaminase level and bilirubin) and nutritional status (serum albumin) were not found to be associated with SBBO.

Patients receiving PN were significantly more likely to have SBBO (70% vs 35%,  $P = .02$ ). The length of time that PN was administered before endoscopy was not significantly

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