The Pediatric Microbiome in Patients with Ulcerative Colitis and Primary Sclerosing Cholangitis

Adult and pediatric patients with primary sclerosing cholangitis (PSC) often have associated ulcerative colitis (UC), and it has been hypothesized that gut microbiome changes may be the cause of this UC and PSC disease connection. Minimal data regarding such changes are present in the pediatric population, and the authors of this study attempted to describe diversification in both the bacterial and fungal microbiome in patients with UC and PSC compared to patients with UC alone.

This prospective study occurred at 2 pediatric hospitals in Italy in which patients with UC and PSC, patients with UC alone, and control patients all aged between 2 and 19 years old were recruited. Patients were diagnosed with PSC using standard physical examination and laboratory findings with the addition of characteristic findings on endoscopic retrograde cholangiopancreatography, magnetic resonance cholangiopancreatography, or liver biopsy. Patients with secondary sclerosing cholangitis were excluded. Patients were diagnosed with UC using Porto criteria and Montreal classification. Stool samples were collected from all patients, and these samples underwent both bacterial and fungal metagenomic analysis. Linear discriminant analysis effect sizes were used to determine taxa abundance.

A total of 26 patients with UC and PSC, 27 patients with UC alone, and 26 control patients were evaluated. Age, gender, body mass index, and endoscopic findings were not different between the two groups. Patients with UC and PSC were statistically more likely to be on azathioprine and ursodeoxycholic acid. As expected, patients with UC and PSC had significantly higher serum levels of alanine transaminase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT). Many microbiome differences between groups were noted.

Patients with UC and PSC and patients with UC alone had decreased bacterial alpha diversity (less bacterial diversity) and decreased beta diversity (less diversity between groups) compared to control patients. Bacterial analysis demonstrated increased Verrucomicrobia and Bacteroidetes in control patients while patients with UC alone had an increase in proteobacteria. Increased *Klebsiella*, *Haemophilus*, *Enterococcus*, and *Collinsella* were present in patients with UC alone while patients with UC and PSC had increased *Streptococcus.* Control patients had increased *Akkermansia*, *Bacteroides*, *Dialister*, *Parabacteroides*, and *Oscillospira* compared to both patients with UC and PSC and patients with UC alone.

Fungal analysis showed no real difference in either alpha or beta diversity. Statistically significant increases of Ascomycota were present in patients with UC and PSC and of Basidiomycota in control patients. Patients with UC and PSC had increased amounts of *Saccharomyces*, *Sporobolomyces*, *Tilletiopsis*, and *Debaryomyces.* Patients with UC alone had increased amounts of *Piptoporus*, *Candida*, and *Hypodontia.* Patients with UC and PSC and patients with UC alone had decreased amounts of *Meyerozyma* and *Malassezia.*

More positive bacterial correlations were noted compared to fungal correlations regarding serum AST, ALT, GGT, and body mass index. Some negative bacterial and fungal correlations were seen regarding Montreal scoring of ulcerative colitis. Linear discriminant function analysis demonstrated that patients with UC alone had a correlation with *Collinsella* and *Dorea* in fecal samples while patients with UC and PSC had a correlation with *Bacteroides* and *Saccharomyces* in fecal samples. Finally, patients with UC and PSC, patients with UC alone, and control patients appeared to have different bacterial metabolic profiles.

This study provides intriguing information about the microbiome of pediatric patients with UC and PSC compared to those pediatric patients with UC alone. Perhaps the results of this study can help in determining the risk of PSC occurring in pediatric patients with UC while also providing information about potential therapeutics in the

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setting of microbiome differences and changes in these patient populations.

Del Chierico F, Cardile S, Baldelli V, Alterio T, Reddel S, Bramuzzo M, Knafelz D, Lega S, Bracci F, Torre G, Maggiore G, Putignani L. Characterization of the Gut Microbiota and Mycobiota in Italian Pediatric Patients with Primary Sclerosing Cholangitis and Ulcerative Colitis. Inflamm Bowel Dis 2024; 30: 529-537.

The Association of Meals and Chronic Abdominal Pain in Children

Many children with chronic abdominal pain are diagnosed with functional dyspepsia or irritable bowel syndrome. Functional dyspepsia can be further characterized as postprandial distress syndrome (early satiety and postprandial fullness) and epigastric pain syndrome (epigastric pain before or after meals). Adult studies have found an association between postprandial distress syndrome and psychological disorders suggesting an alteration of the brain-gut axis.

The authors of this study performed a retrospective study of pediatric patients presenting with chronic abdominal pain for at least 8 weeks. All patients underwent a Rome IV criteria questionnaire, Sleep Disturbances Scale for Children (SDSC) to assess for sleep disorders, and a Behavior Assessment System for Children – Third Edition (BASC-3) to assess for emotional functioning. All included patients were followed for 2 years.

A total of 226 patients were evaluated in this study (mean age 13.9 ± 2.7 years; 72% female). At least one gastrointestinal (GI) symptom was reported in 87.6% of patients. There were significantly more females with abdominal pain associated with eating as well as increased nausea with eating compared to males, and adolescents (patients ≥ 13 years old) were significantly more likely to have nausea with eating compared to children (patients < 13 years old). Symptoms of increased abdominal pain with eating, increased nausea with eating, early satiety, and postprandial bloating were all related to one another significantly. BASC-3 indicators for anxiety and depression were statistically associated with increased nausea with eating, early satiety, and postprandial bloating in adolescent patients. SDSC scores demonstrated a significant correlation between a potential disorder in initiating and maintaining sleep in adolescents with increased nausea with eating as well as a significant correlation between excessive daytime somnolence and early satiety and postprandial bloating.

This study demonstrates that functional dyspepsia associated with postprandial distress correlates with potential anxiety and depression in adolescent patients. There appears to be some degree of correlation of such GI symptoms with disorders of sleep, and further research on improving sleep quality in pediatric patients with chronic abdominal pain is needed.

Benegal A, Friesen H, Schurman J, Colombo J, Friesen C. Meal Related Symptoms in Youth with Chronic Abdominal Pain: Relationship to Anxiety, Depression, and Sleep Dysfunction. J Pediatr Gastroenterol Nutr 2024; 78: 1091-1097.

Answers to this month's crossword puzzle:

1 I	N	2 F	L	3 A	M	4 M	A	5 T	I	6 O	N	■	7 V	■
B	■	A	■	N	■	E	■	E	■	O	■	8 H	A	S
9 S	10 A	T	■	11 G	A	L	L	S	T	O	N	E	S	■
■	H	■	■	I	■	T	■	T	■	■	■	M	■	■
12 W	I	13 L	S	O	N	S	■	14 S	I	15 G	M	O	I	16 D
H	■	A	■	D	■	■	■	■	■	A	■	■	■	E
17 I	18 S	P	■	19 Y	E	20 A	S	21 T	■	22 S	U	23 P	E	R
24 P	E	A	■	S	■	M	■	25 I	C	E	■	U	■	M
26 P	E	R	I	P	L	A	S	M	■	O	■	27 R	D	A
L	■	O	■	L	■	■	■	28 E	29 D	U	■	U	■	■
30 E	M	S	■	31 A	S	32 C	I	T	E	S	■	33 L	L	34 C
■	■	C	■	S	■	Y	■	A	■	■	■	E	■	A
35 A	G	O	N	I	S	T	■	36 B	R	37 U	N	N	38 E	R
I	■	P	■	A	■	O	■	L	■	N	■	39 C	A	T
40 R	A	Y	S	■	41 E	N	T	E	R	O	C	Y	T	E