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RESEARCH ARTICLE

Prevalence of gastrointestinal symptoms among autistic individuals, with and without co-occurring intellectual disability

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Abstract

Gastrointestinal symptoms (GI) are very common among individuals on the autism spectrum. Prior research reports mixed findings regarding whether individuals with autism and co-occurring intellectual disability (ID) have elevated risk of gastrointestinal symptoms relative to individuals with autism alone. GI symptoms can be challenging to assess in individuals with autism spectrum disorder (ASD) and/or ID given challenges with language, communication, and interoception. Prior research has tended to only include individuals with documented presence or absence of GI symptoms or conditions, that is, to exclude observations in which there is uncertainty regarding presence of GI symptoms. Therefore, none of the prior autism studies reported the association between ID and the certainty regarding presence or absence of GI symptoms. The objective of this study was to examine differences in parental certainty and odds of reporting gastrointestinal signs and symptoms among children on the autism spectrum, with and without intellectual disability. Participants were 308 children (36% ID) with a clinical diagnosis of autism spectrum disorder (6–17 years). Parents endorsed whether their child had experienced or displayed a range of signs or symptoms related to GI problems in the past 3 months. Parents of autistic children with ID were less certain about the presence of more subjective symptoms, including abdominal pain, nausea, and bloating. Conversely, certainty regarding more objective signs (e.g., constipation, diarrhea, spitting up, etc.) was not significantly different. More accurate measures for GI signs/symptoms are needed for this population.

Lay Summary

The goal of this study was to see if children with both autism and intellectual disability (ID) are more likely to have GI symptoms/signs or uncertainty regarding these symptoms/signs, compared to children with just autism. Parents were given a list of GI symptoms and signs and asked whether their child had those in the last 3 months (yes, no, or unsure). Parents of autistic children with ID were less certain about the subjective symptoms, meaning we need better tools to test for GI symptoms in this population. Parents of autistic children with ID had similar rates of certainty about objective symptoms as autistic parents of children without ID.

KEYWORDS
autism, comorbidities, gastrointestinal, intellectual disability, measurement

INTRODUCTION

Gastrointestinal symptoms (GI) are very common among individuals on the autism spectrum. The presence of GI symptoms is both impairing and associated with co-occurring conditions, such as sleep disorders, self-injurious and aggressive behaviors, nutritional problems, and other behavioral and medical problems (Bauman, 2010; Buie et al., 2010; Calliope Holingue, Newill, Lee, Pasricha, & Daniele Fallin, 2018). How often GI symptoms occur among autistic children is unclear, however. Prevalence estimates are highly variable due to the heterogeneity of autism spectrum disorder (ASD) and the challenges with accurate and reliable measurement of GI symptoms (Buie et al., 2010; Calliope Holingue et al., 2018). For instance, the prevalence estimate of having one or more GI symptoms ranges from 4.2% to 96.8% across studies of ASD, with a median of 46.8% (Calliope Holingue et al., 2018). This trend holds for individual symptoms as well. For example, the median prevalence estimate for constipation is 22%, with a range of 4.3%–45.5% (Calliope Holingue et al., 2018). The most common GI symptoms in autistic individuals seem to be constipation, diarrhea, and abdominal pain (Buie et al., 2010; Calliope Holingue et al., 2018; McElhanon, McCracken, Karpen, & Sharp, 2014).

GI symptoms can be challenging to assess in children on the spectrum, given language and communication impairments and atypical interoception (Buie et al., 2010; DuBois, Ameis, Lai, Casanova, & Desarkar, 2016; Calliope Holingue, Poku, Pfeiffer, Murray, & Fallin, 2021). However, these measurement challenges may be compounded among autistic children with co-occurring ID. Among autistic children with unrecognized and unresolved GI symptoms, behaviors and conditions such as irritability, aggressive behavior, anxiety, and sleep disruptions may indicate GI distress (Buie et al., 2010; Horvath, Papadimitriou, Rabsztyn, Drachenberg, & Tildon, 1999; Nikolov et al., 2009). It is conceivable that among autistic children with co-occurring ID, the higher prevalence of these behavioral and medical problems could indicate unmanaged GI symptoms.

Roughly 1 in 3 autistic children have ID (Maenner et al., 2021). Autistic individuals with co-occurring ID may be more likely to experience GI symptoms for several reasons. First, having co-occurring ID may raise the likelihood of other co-occurring conditions, which in turn may be associated with an increased risk of GI symptoms. For example, ASD with co-occurring ID is associated with epilepsy (Amiet et al., 2008). While the literature is scarce, Turk et al. (2009) found that having ASD and epilepsy was associated with greater incontinence compared to having ASD alone (Turk et al., 2009). Taking medications for co-occurring conditions such as epilepsy may further contribute to GI symptoms. For example, antiepileptic drugs can cause heartburn, nausea, constipation, vomiting, diarrhea, and dysphagia (Jahromi et al., 2011). The presence of ID also significantly raises the likelihood of psychotropic medication use among children on the autism spectrum (Rosenberg et al., 2010), which can also lead to GI symptoms. For example, mood stabilizers can cause dyspepsia, diarrhea, constipation, and abdominal pain (Alao & Dewan, 2001). Psychotropic medication use, particularly polypharmacy, is widespread in autistic individuals (Feroe et al., 2021). Autistic individuals with co-occurring intellectual disability are even more likely to be exposed to psychotropic medication use (Rosenberg et al., 2010), in part because these medications are often used to manage "problematic behaviors" which are common in individuals with intellectual disability and can include self-injurious behaviors, aggressive behaviors, disruptive behaviors, PICA (eating of non-foods), as well as other behaviors that can affect learning, social relationships, communication, and can cause harm to oneself or others (Di Sarro et al., 2023; Hassiotis et al., 2009; Matson & Rivet, 2008; Matson, Sipes, Fodstad, & Fitzgerald, 2011; O'Brien & Pearson, 2004; Tsakanikos, Costello, Holt, Sturmey, & Bouras, 2007). Therefore, if individuals with co-occurring ID are more likely to be taking psychotropic medications, it is reasonable to expect a greater risk of corresponding side effects such as GI symptoms among autistic children with ID. Third and finally, ASD with co-occurring ID may also increase the degree of core autism features, including restrictive/repetitive behaviors and sensory aversions (Matson & Shoemaker, 2009). These, in turn, may contribute to restrictive diets, inadequate fiber and fluid intake, and nutritional deficiencies, which may cause or exacerbate GI problems (Sharp et al., 2018; Yap et al., 2021).

The epidemiology of GI symptoms among autistic individuals with ID is quite mixed. Nikolov et al. (2009) found that among children with pervasive developmental disorders, those with GI problems did not differ in terms of adaptive functioning or autism characteristics compared to those individuals without GI problems. However, they did show higher severity of irritability, anxiety, and social withdrawal (Nikolov et al., 2009). Similarly, in a sample of children on the spectrum, those with GI problems did not differ in frequency of co-occurring ID, though they were more likely to have cerebral palsy and seizure-like activity (Maenner et al., 2012). In a separate study (Restrepo et al., 2020), although GI problems among preschoolers on the spectrum were associated with self-injurious behaviors, restricted stereotyped behaviors, aggressive behaviors, sleep problems, and attention problems, there were no significant associations between GI problems and developmental or adaptive measures.

Previous research has shown a positive association between the presence of ID and GI symptoms or conditions in the ASD population. Using Medicare claims, Gilmore et al. (2021) found that older autistic adults with ID had higher odds of GI conditions than older autistic

adults without ID (Gilmore, Harris, Longo, & Hand, 2021). Penzol et al. (2019) found that in a sample of individuals aged 1–53 years, who were admitted to a hospital-based comprehensive ASD medical program, functional GI disorders were significantly more common among individuals with co-occurring ID (Penzol et al., 2019). A Medicaid claims study found that GI disorders were not significantly more common among middle-aged and older autistic adults with co-occurring ID (57.8% vs. 43.0%, 95% CI 1.57 [0.8, 3.2]) (Bishop-Fitzpatrick & Rubenstein, 2019), although the confidence interval and relatively small sample size ($n = 64$ vs. $n = 79$) suggest this may be due to inadequate statistical power. Together, these data suggest that autistic individuals with co-occurring ID may be more likely to have GI conditions.

Yet, some literature suggests a negative association between GI symptoms and ID among autistic individuals. Mannion and Leader (2013) found that, among children and adolescents on the spectrum, parent reports of GI symptoms varied by ID level in the child. Specifically, abdominal pain, constipation, diarrhea, and bloating were most frequently reported in children without ID, followed by those with moderate, mild, and severe ID, respectively. Nausea was also most frequently reported for those without ID, followed by those with mild, moderate, and severe ID. Though the sample sizes across these ID groups were relatively small, the findings show greater parental report of GI symptoms among autistic children without co-occurring ID (Mannion & Leader, 2013). However, this could be due to parental under-detection of GI symptoms in individuals with co-occurring ID.

The studies above vary in size, some with considerably larger sample sizes compared to this study (Gilmore et al., 2021; Penzol et al., 2019), and others with similar (Maenner et al., 2012) or smaller (Bishop-Fitzpatrick & Rubenstein, 2019; Mannion & Leader, 2013) samples. Notably, however, studies have historically restricted analytic data to include only individuals with documented presence or absence of GI symptoms or conditions. Therefore, none of the prior autism studies reported the association between ID and the certainty regarding presence or absence of GI symptoms.

In light of this research gap, the objective of this study was to examine differences in the parental certainty and odds of reporting GI signs and symptoms among autistic children with and without ID. In line with our previous research (Calliope Holingue, Poku, Pfeiffer, Murray, & Fallin, 2021), we make a distinction between GI signs and symptoms as follows: *symptoms* are phenomena that can only be described by the person feeling them. These include abdominal pain, nausea, or a burning sensation in the throat or chest. These symptoms are not directly experienced by anyone else. However, *signs* can be observed by someone else either visibly (e.g., witnessing diarrhea, vomiting, clammy skin, or someone clutching their abdomen) or with a tool (e.g., temperature, blood pressure, techniques to detect blood in the stool which is not visible to the human eye). Although we recognize there is heterogeneity in how these terms are used clinically (Cox, Ray, Jensen, & Diehl, 2014), we feel this precise distinction is import in the context of autism, as *signs* rather than *symptoms* may be more readably detected by caregivers of autistic individuals, especially in the presence of intellectual disability, language impairments, and interoceptive difficulties. In this study, we hypothesized that among individuals with co-occurring ID: (1) parental uncertainty would be heightened, and (2) GI signs and symptoms would be more common.

METHODS

Participants

Data from this study were obtained from an urban, outpatient ASD specialty clinic in the Mid-Atlantic region of the United States, between 2010 and 2019, which provides medical, psychological, speech-language pathology, occupational, and social work services. The inclusion criteria consisted of children 6–17 years old (a) who received an ASD diagnosis at the clinic; (b) had non-missing information about ID diagnosis; (c) whose caregivers provided written consent to join the institutional review board-approved research registry, which allows use of their medical records for research purposes (consent rate 80%; Kalb et al., 2019); and (d) whose parents completed the Background and History form, described further below.

Measures

As this is an ASD specialty clinic, most patients who are seen are evaluated for autism, and other conditions as indicated. Most evaluations are team-based, and diagnostic teams consist of a diagnostic physician (e.g., psychiatrist, developmental pediatrician, neurologist) or licensed psychologist, in combination with an occupational therapist, speech language pathologist, or social worker. The evaluation process included review of available school and medical records, taking a developmental, medical, and family history, diagnostic interview, behavioral testing/questionnaires when indicated (e.g., cognitive, adaptive, receptive/expressive language, sensory) and qualitative observation of play/interaction skills. Most patients also are assessed with the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2; Lord et al., 2000). Information gathered during the evaluation was used to inform a clinical best-estimate diagnosis (CBE) according to DSM-IV/DSM-5 criteria, the gold standard for autism diagnosis. Notably, there is an extremely high concordance between our CBE diagnoses and ADOS-2 classifications at our center, which is consistent with research from an external group

highlighting a concordance of 90% for clinical diagnoses of ASD by developmental-behavioral pediatricians with versus without the ADOS-2 (Barbaresi et al., 2022).

Diagnoses of ID are also based on DSM-IV/DSM-5 criteria and are informed by (1) standardized cognitive (IQ) testing, such as the Wechsler Intelligence Scale (Wechsler & Kodama, 1949), Stanford Binet IQ test (Terman & Merrill, 1937), or Differential Ability Scales (DAS-II) (Elliott, Murray, & Pearson, 1990) and/or developmental assessment, in which milestones are evaluated, typically assessed using the Capute Scales (O'Connor Leppert, Shank, Shapiro, & Capute, 1998) also known as Cognitive Adaptive Test/Clinical Linguistic and Auditory Milestone Scale (CAT/CLAMS) (Note that recent cognitive/developmental evaluations from school or other outside sources are utilized if available and appropriate); (2) questionnaire- or interview-based measures of adaptive function, such as the ABAS-3 (Harrison & Oakland, 2015) or Vineland-II (Sparrow, Balla, & Cicchetti, 2005); (3) review of available school or medical records, and (4) direct observation of the child.

Given that the evaluations in this study come from a clinical center, a wide range of assessment and evaluation tools are used by the clinical team, depending on the clinical indication as well as the provider's expertise and preferences. Quantitative information about the frequency of which assessment tools were used is unfortunately not available for this study.

Prior to scheduling, demographic information was collected from the electronic medical record (child age, sex, race, and parental education). At diagnostic intake, parents were asked to endorse whether their child had experienced or displayed a range of signs or symptoms related to GI problems in the past 3 months ("Please answer the following regarding any stomach or abdominal problems [child name] has had in the past three months"). These data were gathered via the clinic's electronic Background and History form. Response options were "unsure," "no," and "yes." The exact wording of the signs and symptoms ascertained are listed in Table 2. They include subjective symptoms such as abdominal (belly) pain and nausea, observable signs such as diarrhea, and behavioral indicators that might indicate GI distress (Buie et al., 2010), such as tilting head to the side and arching back, or refusing many foods that the patient would eat in the past.

Statistical analysis

First, we described the frequency of GI signs and symptoms in the total ASD sample and separately among individuals with and without co-occurring ID. Chi-square tests were used to assess whether the frequency of response options (yes, no, unsure) differed between the two groups for each of the GI signs/symptoms. Next, multivariable logistic regression models were used to assess the association between having co-occurring ID and parental uncertainty of each of the GI signs/symptoms. In this analysis, parental responses of "yes" and "no" were considered "certain," and responses of "unsure" were considered "uncertain." Lastly, multivariable logistic regression models were used to assess the association between having co-occurring ID and each of the GI signs/symptoms. For this analysis, each model excluded children whose parents were uncertain (response of "unsure") regarding the presence or absence of that particular GI symptom or sign. *p*-Values <0.05 were considered statistically significant. All analytic variables were non-missing for at least 97% of study participants, with exception of parental education, which was missing in 11% of participants.

RESULTS

Participants

The final analytic sample consisted of 308 children with an ASD diagnosis. Of these children, 110 (36%) had a co-occurring ID diagnosis. Participants' demographic information is provided in Table 1. All children were between the ages of 6–17 years (mean = 10.79, SD = 3.55). Most (64.3%) did not have co-occurring ID. The majority of children were male (80.84%), White (51.33%), or Black/African-American (26.33%), and had parents with a bachelor's (28.73%) or Graduate degree (37.09%). There were no sociodemographic differences between ID groups. There was only one observation per child.

Frequency of GI signs/symptoms and parental uncertainty

The signs/symptoms parents in the total sample were most unsure about were abdominal pain (13.07%) and other GI/tummy symptoms (14.19%). In both the groups with and without ID, most parents reported their children did not have each of the GI signs or symptoms (see Table 2). The most common signs or symptoms overall were constipation (32.25%), abdominal pain (21.24%), and refusing to eat many foods that they would eat in the past (19.34%). About half of parents (49%) reported their child experiences any of the GI signs/symptoms (mean 0.94 symptoms out of possible 9). About a third (30%) of parents reported they were uncertain about the presence of at least one of these signs/symptoms (mean 0.77 symptoms out of possible 9).

Differences in frequency of GI signs/symptoms and parental uncertainty by ID status

The signs/symptoms that were not significantly different in terms of parental uncertainty between the two groups

TABLE 1 Participant Characteristics.

	Total ($n = 308$)	ASD without ID ($n = 198$)	ASD with ID ($n = 110$)	p-Value
Child age (years)	10.79 (3.55)	10.75 (3.52)	10.87 (3.61)	0.79
Child sex				
Female	19.16	17.68	21.82	0.46
Male	80.84	82.32	78.18	
Child race				
White	51.33	54.40	45.79	0.40
Black/African-American	26.33	23.32	31.78	
Multiracial or other race	14.33	13.99	14.95	
Asian	8.00	8.29	7.48	
Parent education				
High school or less	16.00	15.05	17.98	0.93
Trade or Associates Degree	18.18	18.28	17.98	
Bachelors	28.73	29.57	26.97	
Graduate	37.09	37.10	37.08	
Insurance				
Public	19.61	16.67	25.00	0.11
Private	80.39	83.33	75.00	

Abbreviations: ASD, autism spectrum disorder; ID, intellectual disability.

were constipation, diarrhea, refusal of many foods would eat in the past, regurgitating food and chewing it again, retching, spitting up 2 or more times per day, and tilting head to side and arching back. However, four signs/symptoms had significantly higher uncertainty in the autistic group with ID: abdominal pain, bloating, nausea, and other GI/tummy symptoms (Table 3).

There were significant differences in the frequency of response options (unsure, no, yes) between the groups for abdominal (belly) pain, bloating, nausea, and other GI/tummy symptoms (Table 2). Using the logistic regression models, none of the signs/symptoms were significantly different between the two groups, with the exception of "other GI/tummy symptoms," which was significantly higher in the autistic group with ID compared to the autistic group without ID (Table 4).

DISCUSSION

The goals of this study were to assess whether ASD with co-occurring ID, relative to ASD without ID, is associated with a higher likelihood of parent-reported GI signs/symptoms, and/or a greater degree of uncertainty regarding the presence of these symptoms.

Our first finding is that ASD with ID was associated with a significantly higher likelihood of uncertainty regarding the presence of abdominal pain, nausea, bloating, and other GI/tummy symptoms. Conversely, parents of autistic children with ID did *not* report greater uncertainty regarding the following signs/symptoms: constipation, diarrhea, refusing foods, regurgitating foods and chewing it again, retching, spitting up, and tilting head/arching back. The finding may be because the latter symptoms may be assessed more objectively by parents, especially if they are very involved in the toileting process and mealtimes. Nausea and bloating, on the other hand, refer to internal sensations. It may be the case that parent- or self-report measures of GI symptoms, especially ones that are essentially internal sensations, are not always adequate alone in the ID population, particularly in minimally verbal or nonverbal individuals, or those with greater cognitive disability. Other sources of information (e.g., clinician exam, imaging, stool samples, heart rate variability) may be needed to supplement these tools in a subset of the ID population (Holingue et al., 2022). There are also growing efforts to examine links between potential risk factors (e.g., anxiety) and GI symptoms using more objective measures, such as heart rate variability, cortical response to stress, and stress-associated cytokines (Ferguson et al., 2017; Ferguson et al., 2016). It should also be noted that no single GI measure is likely to assess GI symptoms accurately and reliably in every individual on the autism spectrum. Rather, multiple versions are needed that account for a person's age, language level, and neurodevelopmental functioning more broadly.

Our second finding is that among parents who reported they were certain regarding the presence of specific GI signs/symptoms in their children, almost all signs/symptoms were not significantly different in the ASD with ID group, suggesting that co-occurring ID is not overwhelmingly associated with greater GI symptomology. However, all the analyses suggested a positive

TABLE 2 Prevalence (%) of gastrointestinal signs and symptoms.

		Total ($n = 308$)	ASD without ID ($n = 198$)	ASD with ID ($n = 110$)	*p*-Value
Abdominal (Belly) pain	Unsure	13.07	6.06	25.93	<0.001
Abdominal (Belly) pain	No	65.69	69.70	58.33	
Abdominal (Belly) pain	Yes	21.24	24.24	15.74	
Bloating	Unsure	10.86	6.12	19.44	<0.001
Bloating	No	77.63	83.16	67.59	
Bloating	Yes	11.51	10.71	12.96	
Constipation	Unsure	8.14	7.07	10.09	0.42
Constipation	No	59.61	62.12	55.05	
Constipation	Yes	32.25	30.81	34.86	
Diarrhea	Unsure	6.62	6.12	7.55	0.89
Diarrhea	No	79.14	79.59	78.30	
Diarrhea	Yes	14.24	14.29	14.15	
Nausea	Unsure	9.24	5.64	15.74	<0.01
Nausea	No	76.90	78.46	74.07	
Nausea	Yes	13.86	15.90	10.19	
Other GI or tummy symptoms	Unsure	14.19	11.17	19.81	<0.01
Other GI or tummy symptoms	No	79.21	84.77	68.87	
Other GI or tummy symptoms	Yes	6.60	4.06	11.32	
Refuse many foods that the patient would eat in the past	Unsure	5.57	4.06	8.33	0.26
Refuse many foods that the patient would eat in the past	No	75.08	77.16	71.30	
Refuse many foods that the patient would eat in the past	Yes	19.34	18.78	20.37	
Regurgitated food and chewed it again	Unsure	5.28	4.06	7.55	0.35
Regurgitated food and chewed it again	No	93.40	94.92	90.57	
Regurgitated food and chewed it again	Yes	1.32	1.02	1.89	
Retching	Unsure	5.57	4.06	8.33	0.16
Retching	No	92.13	92.89	90.74	
Retching	Yes	2.30	3.05	0.93	
Spit up 2 or more times a day	Unsure	5.28	5.10	5.61	0.23
Spit up 2 or more times a day	No	90.76	92.35	87.85	
Spit up 2 or more times a day	Yes	3.96	2.55	6.54	
Tilted head to the side and arched back	Unsure	7.28	6.12	9.43	0.56
Tilted head to the side and arched back	No	90.07	91.33	87.74	
Tilted head to the side and arched back	Yes	2.65	2.55	2.83	

Note: Table 2 summarizes the prevalence and frequency of uncertainty for each GI sign and symptom.
Abbreviations: ASD, autism spectrum disorder; GI, gastrointestinal; ID, intellectual disability.

association (i.e., increased prevalence) between co-occurring ID and GI symptoms. It is likely increased uncertainty and sample size limited the power needed to detect statistical significance (e.g., bloating, spitting up).

We did find that "other GI/tummy symptoms" were significantly elevated in the ASD with ID group. Unfortunately, we did not have open-ended text responses from parents to better understand what symptoms these may refer to. We hypothesize that these may reflect symptoms such as flatulence, heartburn, incontinence, pain during bowel movements, and abdominal pain, diarrhea, or vomiting in relation to specific food intake. More research is needed to identify what these other symptoms are so that we can include them in GI questionnaires and obtain more information about their prevalence in this population.

We are not able to identify the origin or cause of the GI symptoms assessed in this study. Symptoms can either be due to an "organic" GI condition (e.g., inflammatory bowel disease, celiac disease) or a disorder of gut-

TABLE 3 Results of multivariable logistic regression models examining association between having ASD with ID (versus ASD without ID) on the odds of parental uncertainty regarding GI signs and symptoms.

Outcome	OR	95% CI%	*p*-Value
Abdominal (Belly) pain	5.42	(2.68, 11.58)	<0.001
Bloating	3.70	(1.77, 8.08)	<0.001
Constipation	1.48	(0.63, 3.37)	0.36
Diarrhea	1.25	(0.48, 3.13)	0.64
Nausea	3.12	(1.42, 7.14)	0.01
Other GI or tummy symptoms	1.97	(1.02, 3.78)	0.04
Refuse many foods that the patient would eat in the past	2.15	(0.80, 5.89)	0.13
Regurgitated food and chewed it again	1.93	(0.69, 5.39)	0.20
Retching	2.15	(0.80, 5.89)	0.13
Spit up 2 or more times a day	1.10	(0.37, 3.06)	0.85
Tilted head to the side and arched back	1.60	(0.65, 3.84)	0.29

Note: Odds ratios and 95% Confidence Intervals and corresponding *p*-values are shown for the association between the main predictor (ASD with ID vs. ASD without ID) and parental uncertainty for each GI symptom or sign, in multivariable logistic regression models. Each line represents a separate model.

TABLE 4 Results of multivariable logistic regression models examining association between having ASD with ID (vs. ASD without ID) on the odds of GI signs and symptoms.

Outcome	OR	95% CI%	*p*-Value
Abdominal (Belly) pain	0.78	(0.41, 1.43)	0.43
Bloating	1.49	(0.70, 3.07)	0.29
Constipation	1.28	(0.77, 2.12)	0.35
Diarrhea	1.01	(0.50, 1.97)	0.98
Nausea	0.68	(0.31, 1.38)	0.30
Other GI or tummy symptoms	3.43	(1.36, 9.10)	0.01
Refuse many foods that the patient would eat in the past	1.17	(0.64, 2.11)	0.60
Regurgitated food and chewed it again	1.95	(0.23, 16.44)	0.51
Retching	0.31	(0.02, 1.86)	0.28
Spit up 2 or more times a day	2.70	(0.84, 9.32)	0.10
Tilted head to the side and arched back	1.15	(0.23, 4.81)	0.85

Note: Odds ratios and 95% Confidence Intervals and corresponding *p*-values are shown for the association between the main predictor (ASD with ID vs. ASD without ID) and each GI symptom or sign, in multivariable logistic regression models. Each model excludes children whose parents indicated they were uncertain regarding the presence or absence of that particular GI symptom or sign.

brain-axis (e.g., irritable bowel syndrome, cyclic vomiting syndrome) (Drossman & Tack, 2022). By definition, disorders of gut-brain axis are defined by the Rome IV criteria as requiring the absence of an organic disorder that explains these symptoms (Rome Foundation, 2021). Given there was no GI testing reported in this study, it is not possible to know the etiology of these symptoms or underlying condition.

Our study should be interpreted in the context of some strengths and limitations. In terms of limitations, we only had parent report items on GI symptoms. Research in the general pediatric population with inflammatory bowel disease suggests that children as young as three can provide valuable data on their symptom severity, when provided with age-appropriate tools (Diederen et al., 2018; Kolho, 2016; Lee et al., 2011; Vernon-Roberts et al., 2019). It is possible that some parents in this study consulted with their children when filling out this questionnaire; however, we do not know the degree to which this occurred. We also had a limited number of items about GI signs/symptoms and are missing information regarding other symptoms (e.g., flatulence, heartburn, incontinence, pain during bowel movements) as well as information about medical assessments (e.g., blood and laboratory testing for inflammatory bowel disease, gluten intolerance, etc.). Lastly, we may be underpowered, given some of the large confidence intervals.

This study also has several strengths. First, our analytic sample comes from a clinically and demographically

diverse patient population. Further, ASD diagnosis was confirmed by a licensed clinician using a reference standard measure. ID was clinically confirmed as well, although IQ and adaptive behavior data were not available to incorporate into the analysis of the current study. Lastly, the inclusion of the "unsure" option for the GI items enabled us to describe the prevalence of GI signs/symptoms more accurately to interrogate whether ID is associated with certainty.

Overall, our findings suggest that children with co-occurring ASD and ID may have a similar likelihood of GI symptoms, but parents are less certain about the presence of these symptoms when their children have co-occurring ID. Difficulty with assessing GI symptoms in the ASD population has been previously discussed (Buie et al., 2010; C. Holingue et al., 2022; Calliope Holingue et al., 2018; Calliope Holingue et al., 2021; Margolis et al., 2019). Our findings align with this broader body of research and additionally indicate that co-occurring ID may compound established issues of poor measurement of GI signs and symptoms. Ultimately, this may lead to lower detection of GI symptoms, delayed care, inappropriate treatment, and further morbidity. We urgently need more attention to the development, adaptation, evaluation, and refinement of GI questionnaires for this population.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

The research was approved by the Johns Hopkins Medicine Institutional Review Board.

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