

## Association of Gastrointestinal Problems and Behavioral Disorders in Children with Autism Spectrum Disorders in Pediatrics and Psychiatry Outpatient Clinics in Suez Canal University Hospital

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### ABSTRACT

**Background:** Dysfunction of gastrointestinal tract (GIT) is one of the most frequent problems in children with autism spectrum disorder (ASD). **Objectives:** To assess the propagation of GIT problems in autism spectrum disorder kids and its correlation with their behavioral problems. **Patients and Methods:** This case-control study included 50 children with ASD matched with 50 healthy kids with the same age and gender. Parents of children with autism spectrum disorder and typically developed children, were interviewed to fill out the checklists about their behavior and GIT symptoms, then the collected data were tabulated and analyzed using SPSS version 26 software.

**Results:** All autism spectrum disorder group had significantly greater produce of the following symptoms: vomiting, constipation, soiling, reflux, and abdominal pain than typically developed group, with statistically significant differences. Also, autism spectrum disorder group had significantly longer duration of constipation, soiling, reflux, and abdominal pain than typically developed group. Medication used showed statistically significant difference among study groups as more than half autism spectrum disorder group used laxatives. Autism spectrum disorder had significantly greater mean values than typically developed group on the following CBCL scales: withdrawn, somatic complaints, anxious, social, thought, attention, aggressive behavior, internalizing problem, externalizing problem, and total problem, while delinquent behavior was significantly higher among typically developed than autism spectrum disorder group. **Conclusions:** Children with autism spectrum disorder are at greater risk of some behavioral and GIT problems which need a special care as compared to typical development (TD) children.

**Keywords:** Gastrointestinal Problems, Behavioral Disorders, Autism Spectrum, Pediatrics.

### INTRODUCTION

Persistent impairment in reciprocal social communication and relationships and confined, repetitive patterns of behaviors or interests are hallmarks of autism spectrum disorder, a complex neurodevelopmental disease <sup>(1)</sup>. Many children with ASD often have co-occurring medical disorders that impact various areas of their bodies. One of the most common issues in children with autism spectrum disorder is dysfunction of the GIT. A recent meta-analysis found that compared to typically developing children, children with autism spectrum disorder are four times more likely to have general gastrointestinal (GI) difficulties, more than three times more likely to suffer diarrhea and constipation, and twice as likely to experience stomach discomfort <sup>(2,3)</sup>.

A lot of research has been done on the types and prevalence of GIT problems in kids with ASD. Children with autism spectrum disorder have a reported prevalence of nine percent to 91 percent for abdominal pain or discomfort ranges between two percent to forty-one percent for stomach pain or discomfort, six percent to forty-five percent for constipation, three percent to 77 percent for diarrhea, and eight percent to nineteenth percent for chronic diarrhea <sup>(4)</sup>.

A substantial amount of new research has demonstrated the significance of the gut as an autism trigger in recent years. Gastrointestinal dysfunction is often linked to increased tantrums, irritability, aggressive behavior, and sleep difficulties in children

diagnosed with ASD. Furthermore, for some ASD patients, short-term antibiotic therapy that modifies the gut's bacteria may result in a transient improvement in behavioral symptoms <sup>(5,6)</sup>.

The objective of the present research was to look at the frequency of gastrointestinal symptoms in kids with ASD as well as their association with behavioral issues.

### PATIENTS AND METHODS

This case control study was performed in Pediatrics and Psychiatry Clinics in Suez Canal University Hospital and included 100 children distributed as 50 children with autism spectrum disorder and 50 typical development controls with the following inclusion and exclusion criteria:

**Inclusion Criteria for the cases:** Age 4 to 14 years, no usage of any type of antifungal or antibiotic drugs within the last month, diagnosis of autism, or Asperger's by a psychiatrist by using the CARS evaluation method.

**Exclusion criteria for the cases:** Children with any surgical GIT problems such as hernias, tracheoesophageal fistula, and children with attention deficit disorders (ADD/ADHD).

**Inclusion criteria for the control group:** Age 4 to 14 years, no usage of any type of antifungal or antibiotic drugs within the last month, and in good physical and mental health.

**Exclusion criteria for the control group:** Family history of autism in 1<sup>st</sup> or 2<sup>nd</sup> degree relatives, and children with any surgical GIT problems.

**Methods:**

The entire study subjects were subjected to the following:

- 1) Personal history (Socio-demographic data), Detailed history of the ASD (Childhood Autism Rating Scale (CARS) score, onset of diagnosis, current and previous medications), Past development history especially history of use of spoon and toilet control.
- 2) GIT problems (frequency and duration).
- 3) The Child Behavior Checklist (CBCL) was completed by the primary caregiver at each time point to evaluate presence of child internalizing (i.e., depression, anxiety) and externalizing symptoms (i.e.: emotional and behavioral problems).

The Arabic version used in this research was translated and used in previous studies (7).

The assessment yields scores for 7 syndrome scales:

- Anxious/Depressed, Emotionally Reactive, Withdrawn , Somatic Complaints, Attention Problems, Aggressive Behavior, and Sleep Problems.
- Furthermore, the CBCL 1½-5 and CBCL 6-18 provide scores for three summary scales, including Internalizing, Externalizing, and Total Problems.

The Internalizing Problems score is derived by aggregating the scores obtained from the 4 syndrome scales: Anxious/Depressed, Emotionally Reactive, Withdrawn, and Somatic Complaints.

On the other hand, the Externalizing scale is formed by combining scores obtained from the syndrome scales of Aggressive Behavior and Attention Problems. Sleep Problems Syndrome Scale, CBCL 1½–5, is a stand-alone measure. The Total Problems score is calculated based on a total of sixty-seven items that make up the seven syndromes, thirty-two items that indicate other problems (such as chewing inedibles), and one additional item provided by the parent or caregiver. If the parent or caregiver reports more than one additional problem, only the item with the highest score is included in the Total Problems score.

**Ethical considerations:**

**An informed consent was taken from each parent/legal caregiver. The consent included: Aim of the research, a clear explanation of the goal that the average person can understand. No harmful maneuvers were used. All data were confidential. All investigations were used in the research only. An identified person to whom the patient was return to any time for any explanation. According to the findings of the research, the parents of each and every patient were informed. The parents or the caregivers of the patients have the right to withdraw from the research at any moment without providing a reason. The Helsinki Declaration was followed throughout the study's conduct. The study was approved by the Ethics Board of Suez Canal University.**

**Statistical analysis**

All statistical calculations were done using SPSS (statistical package for the social science; SPSS Inc., Chicago, IL, USA) version 22. Quantitative data were statistically described in terms of mean ± SD and median (range) when not normally distributed. Qualitative data were statistically described in terms of frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables was done using student t test for normally distributed data and Mann Whitney U test for non-normally distributed data. For comparing categorical data, Chi square (χ<sup>2</sup>) test was performed. The level of significance was calculated according to the following probability (P) values: P<0.05 was considered statistically significant.

**RESULTS**

Table 1 shows demographic and clinical data of the study groups. The mean age of the study group was 8.3±1.89 years. Males were predominant in both groups. ASD group had significantly delayed age of spoon use and toilet training than normal group. Restricted diet distribution showed insignificant difference between study groups.

**Table 1: Demographic and clinical features of participants in autism spectrum disorder and typically developed groups.**

Baseline characteristics	Autism Spectrum Disorder group (n=50)	Typically developed group (n=50)	P value
Age (years), Mean ± SD	8.3±1.89	8.8±2.17	0.222
Gender (n%)			0.401
1. Male	44(88%)	41(82%)	
2. Female	6(12%)	9(18%)	
Age at the time of spoon use (years), Mean ± SD	3.9±1.0	2.5±0.5	<0.001
Age at the time of toilet training (years), Mean ± SD	4.0±0.8	2.6±0.5	<0.001
Restricted diet (n%)			0.059
1. Gluten-free	3(6%)	0(0%)	
2. Soy-free	0(0%)	0(0%)	
3. Casein-free	0(0%)	4(8%)	
4. No	41(82%)	42(84%)	
5. Uncertain	6(12%)	4(8%)	

In table 2, ASD group had mean age at disease diagnosis of 4.1 years with mean CARS score of 35.4. More than half of study group (60%) had mild to moderate autistic disorder.

**Table 2:- Clinical criteria of the disease among the autism spectrum disorder group (n=50).**

Disease criteria	(n=50)
CARS score Mean ± SD Median (Range)	35.4 ± 4.0 35(30-45)
CARS severity Mild-Moderate Severe	30(60%) 20(40%)
Age at the time of diagnosis (years) Mean ± SD Median (Range)	4.1 ± 1.0 4(3-6)

1. Quantitative variables are presented as mean ±SD, qualitative variables are presented as number and percentages.
2. Abbreviations: CARS; childhood autism rating scale.

Table 3 shows that, all ASD group had significantly higher number of children with vomiting, constipation, soiling, reflux and abdominal pain than TD group with statistically significant differences. Also, ASD group had significantly longer duration of constipation, soiling, reflux and abdominal pain than TD group with statistically significant variance.

**Table 3:- Frequency and duration of the GI symptoms in ASD and typically developed groups.**

GIT problems	Autism Spectrum Disorder group (n=50)	Typically developed group (n=50)	P value
<b>Vomiting frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%) Often (>50%) Uncertain	0(0%) 37(74%) 11(22%) 0(0%) 2(4%)	4(8%) 42(84%) 4(8%) 0(0%) 0(0%)	<b>0.012</b>
<b>Diarrhea frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%)	2(4%) 40(80%) 8(16%)	6(12%) 40(80%) 4(8%)	0.222
<b>Constipation frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%) Often (>50%)	2(4%) 4(8%) 16(32%) 28(56%)	20(40%) 27(54%) 3(6%) 0(0%)	<b>&lt;0.001</b>
<b>Soiling frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%)	5(10%) 39(78%) 6(12%)	44(88%) 6(12%) 0(0%)	<b>&lt;0.001</b>
<b>Reflux frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%) Often (>50%) Uncertain	10(20%) 34(68%) 4(8%) 0(0%) 2(4%)	27(54%) 23(46%) 0(0%) 0(0%) 0(0%)	<b>&lt;0.001</b>
<b>Abdominal pain frequency (n%)</b> Never Rarely (<10%) Sometimes (10% - 49%) Often (>50%)	0(0%) 7(14%) 38(76%) 5(10%)	14(28%) 32(64%) 4(8%) 0(0%)	<b>&lt;0.001</b>

1. Fisher exact test. \*Statistically significant as p<0.05, GIT; gastrointestinal.

This chart (Figure 1) shows that All GIT symptoms are more frequent in autism spectrum disorder group than the TD group.

In table 4, medication used showed statistically significant difference among study groups as more than half ASD group used laxatives while only 12% in TD group used laxatives. ASD group used more medication than TD group.

**Table 4:- Medications for GIT problems used in autism spectrum disorder and typically developed groups.**

Medications	Autism Spectrum Disorder group (n=50)	Typically developed group (n=50)	P value
Ranitidine	4(8%)	6(12%)	<b>&lt;0.001*<sup>1</sup></b>
Metronidazole	6(12%)	4(8%)	
Laxatives	26(54%)	6(12%)	
Other	18(36%)	19(28%)	
Not applicable (no medications)	20(40%)	31(62%)	

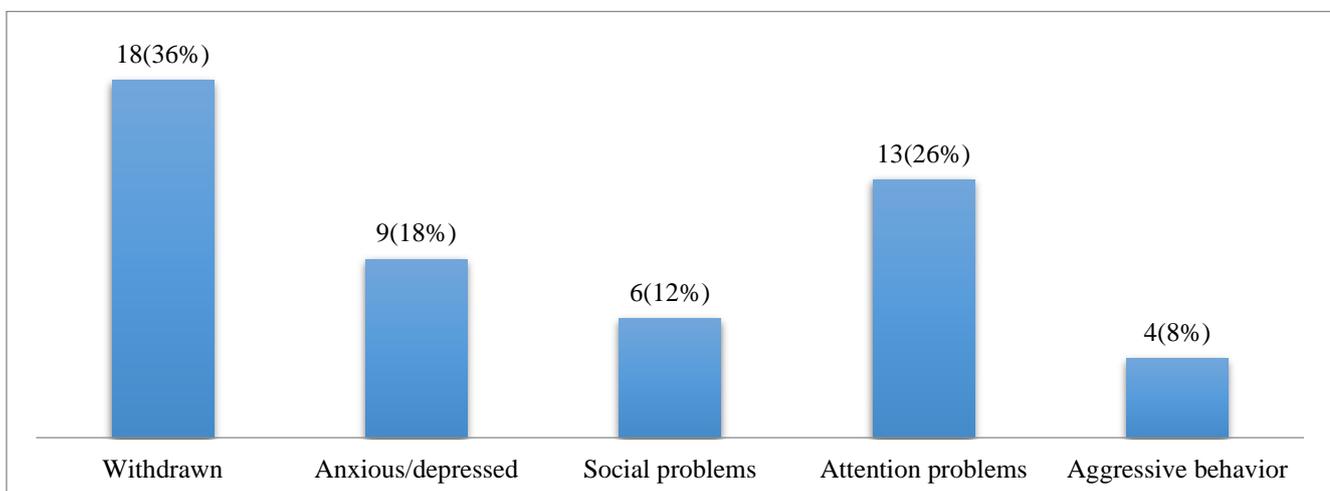
1. Fisher exact test. \*Statistically significant as p<0.05, GIT; gastrointestinal.

Table 5 shows that ASD had significantly higher mean values than TD group on the following CBCL scales: somatic complaints, withdrawn, social problems, anxious, thought disturbance, attention problems, aggressive behavior, internalizing problem, externalizing problem, and total problem, while delinquent behavior was significantly higher among TD than ASD group.

**Table 5: Comparison of the means of the CBCL scales in children with autism spectrum disorder and typical developed groups.**

CBCL Scales	Autism Spectrum Disorder group (n=50)	Typically developed group (n=50)	P value
Withdrawn	8.7±2.6	1.7±1.5	<0.001*
Somatic complaints	3.9±1.8	1.3±1.0	<0.001*
Anxious	8.9±3.5	3.3±1.5	<0.001*
Social problems	7.9±2.6	1.4±1.3	<0.001*
Thought disturbance	3.9±2.3	0.8±0.8	<0.001*
Attention problems	12.1±4.5	2.4±1.1	<0.001*
Delinquent behavior	2.0±1.9	3.7±2.4	<0.001*
Aggressive behavior	10.5±6.4	7.7±3.1	0.006*
Internalizing problem	21.4±6.3	6.2±2.6	<0.001*
Externalizing problem	22.6±10	10.1±3.8	<0.001*
Total problem	57.9±18.9	22.1±7	<0.001*

In figure 2, among ASD group 18 had withdrawn, which was the most common behavioral problem.



**Figure 2: Distribution of behavioral problems among ASD group (n=50).**

In table 6, only soiling showed significant difference among patients with behavioral problem, while vomiting, diarrhea, constipation, reflux and abdominal pain showed insignificant difference.

**Table 6:- GIT problems distribution among CBCL scales among children with autism spectrum disorder group (n=50).**

		Withdrawn n=18	Anxious/ depressed n=9	Social problems n=6	Attention problems n=13	Aggressive behavior n=4	P-value
Vomiting	Rarely	13	9	4	7	4	0.181 <sup>1</sup>
		72.2%	100.0%	66.7%	53.8%	100.0%	
	Sometimes	5	0	2	4	0	
		27.8%	0.0%	33.3%	30.8%	0.0%	
	Uncertain	0	0	0	2	0	
		0.0%	0.0%	0.0%	15.4%	0.0%	
Diarrhea	Never	0	0	2	0	0	0.072 <sup>1</sup>
		0.0%	0.0%	33.3%	0.0%	0.0%	
	Rarely	16	7	2	11	4	
		88.9%	77.8%	33.3%	84.6%	100.0%	
	Sometimes	2	2	2	2	0	
		11.1%	22.2%	33.3%	15.4%	0.0%	
Constipation	Never	0	0	2	0	0	0.066 <sup>1</sup>
		0.0%	0.0%	33.3%	0.0%	0.0%	
	Rarely	4	0	0	0	0	
		22.2%	0.0%	0.0%	0.0%	0.0%	
	Sometimes	4	5	0	5	2	
		22.2%	55.6%	0.0%	38.5%	50.0%	
Often	10	4	4	8	2		
	55.6%	44.4%	66.7%	61.5%	50.0%		
Soiling	Never	0	0	2	3	0	0.022* <sup>1</sup>
		0.0%	0.0%	33.3%	23.1%	0.0%	
	Rarely	16	7	2	10	4	
		88.9%	77.8%	33.3%	76.9%	100.0%	
	Sometimes	2	2	2	0	0	
		11.1%	22.2%	33.3%	0.0%	0.0%	
Reflux	Never	2	3	2	3	0	0.344 <sup>1</sup>
		11.1%	33.3%	33.3%	23.1%	0.0%	
	Rarely	14	4	4	8	4	
		77.8%	44.4%	66.7%	61.5%	100.0%	
	Sometimes	0	2	0	2	0	
		0.0%	22.2%	0.0%	15.4%	0.0%	
Uncertain	2	0	0	0	0		
	11.1%	0.0%	0.0%	0.0%	0.0%		
Abdominal pain	Rarely	2	0	2	3	0	0.092 <sup>1</sup>
		11.1%	0.0%	33.3%	23.1%	0.0%	
	Sometimes	13	9	4	10	2	
		72.2%	100.0%	66.7%	76.9%	50.0%	
	Often	3	0	0	0	2	
		16.7%	0.0%	0.0%	0.0%	50.0%	

## DISCUSSION

In the current study, the mean age of the 50 patients was  $8.3 \pm 1.89$  years. Males were predominant in both groups with statistical insignificant difference. ASD group had significantly delayed age of spoon use and toilet training than normal group. That comes in agreement with other studies <sup>(8)</sup>.

In this study, All ASD group had significantly higher children suffering from vomiting, constipation, soiling, reflux and abdominal pain compared to TD group with statistically significant differences. Also, ASD group had significantly longer duration of constipation, soiling, reflux and abdominal pain than TD group with statistically significant differences.

It was found that in comparison with the control group, 84.1 percent of children with ASD had GIT clinical symptoms <sup>(9)</sup>. On the other hand, **Black et al.** found that gastrointestinal tract disorders were just as common in kids with autism spectrum disorder as in a control group, with nine percent versus nine percent of cases, respectively, based on a review of hospital records <sup>(10)</sup>.

The likelihood of GI symptoms is higher in children with ASD compared to children without ASD, according to a meta-analysis of individual research. The 2014 systematic review by **McElhanon et al.** included 2,215 kids with autism spectrum disorder from fifteen trials. The analysis included four clinical variables: vomiting, diarrhea, constipation, and abdominal pain. The meta-analysis found that compared to control groups, children with autism spectrum disorder were more likely to have vomiting (odds ratio [OR] 4.42), diarrhea (OR 3.63), constipation (OR 3.86), and abdominal pain (OR 2.45) <sup>(11)</sup>.

The present research found that "abdominal pain" and "constipation" were the most often reported gastrointestinal disorders. Parents of TD children likewise reported these gastrointestinal symptoms most often, but ASD individuals rated them more frequently and for longer durations than their TD peers. Patients with ASD were differentiated from TD controls based on the degree of gastrointestinal problems rather than their kind. The most often mentioned gastrointestinal (GI) problems in literature were constipation and abdominal discomfort <sup>(8)</sup>.

Milk intake was identified by **Doshi-Velez and colleagues** as the most robust predictor of constipation in individuals with ASD. This matter could become better understood in the future if researchers consider things like dietary quality, water consumption, medicine, physical activity levels, sensory profile, and other environmental variables that may contribute to constipation <sup>(12)</sup>.

This cohort's high diarrhea prevalence (96 percent of ASD children) is consistent with previous studies that found 75.6 percent of ASD participants to have diarrhea <sup>(13)</sup>.

It is reasonable to wonder if there is an association among the severity of ASD symptoms and the prevalence of digestive problems in kids diagnosed with ASD. Common behavioral traits in children with autism spectrum disorder may be symptoms of digestive problems. Some common facial indications of gastrointestinal problems in autistic children include grimacing, teeth gritting, and excessive chewing. Symptoms may be accompanied by vocalizations as crying, yelling, or delayed echolalia. Parents and caregivers may observe motor actions related to the abdominal region, such as the kid placing their own hands or items (such as chairs or tables) on the stomach. Abdominal behaviors are a general term for these actions. In addition to or instead of typical motor movements, there may also be facial expressions and actions involving the abdomen <sup>(13)</sup>.

In the current study, Among ASD group 18(36%) had withdrawn, 9(18%) had anxiety/depression, 6(12%) had social problems, 13(26%) had attention problems and 4(8%) had aggressive behavior. Vomiting, diarrhea, constipation, reflux, and abdominal pain showed insignificant differences amongst cases with behavioral problem while only soiling showed significant difference as  $p=0.022$ .

Children suffering digestive problems are at a higher risk of exhibiting psychological illnesses, including anxiety, behavioral problems, and other psychological symptoms. Prior research has examined the correlations among gastrointestinal symptoms and symptoms of ASD. According to **Maenner et al.**, there is no correlation among the occurrence of gastrointestinal disorders and two specific behaviors often seen in individuals with ASD: stereotypic/repetitive behaviors and self-injurious behaviors <sup>(14)</sup>.

The research conducted by **Gorrindo et al.** found a strong correlation among gastrointestinal dysfunction and sleep difficulties as well as food intolerance. However, there was no observed association between GI dysfunction and irritability or aggressiveness. The research found that functional constipation was the most prevalent gastrointestinal problem in children with ASD, accounting for eighty-five percent of cases. Furthermore, there was a substantial correlation among functional constipation and language impairment in these children. The study also examined the connections between behavioral issues and GI symptoms in children with different subtypes of autism spectrum disorder, such as high-functioning autism and atypical autism with delayed neurodevelopment. Functional constipation (FC) was the most prevalent GID in ASD. Odds for constipation were significantly associated with younger age, increased social impairment, and lack of expressive language <sup>(15)</sup>.

Among a group of 95 children diagnosed with high-functioning autism and IQ scores greater than eighty, a significant majority (sixty-one percent) had at

least one gastrointestinal symptom. There were no significant differences in autistic symptom severity, adaptive behavior, or overall internalizing or externalizing issue scores among children with and without gastrointestinal difficulties. Nevertheless, those with GI problems had significantly elevated levels of emotional disorders <sup>(16)</sup>.

**Mouridsen *et al.*** found that children diagnosed with atypical autism and an IQ below seventy had a greater likelihood of experiencing gastrointestinal issues detected in a hospital setting compared to those with an IQ above seventy. In general, children with atypical autism had a similar occurrence rate of gastric, intestinal, and hepatic disorders compared to the control group <sup>(17)</sup>.

## CONCLUSION

In order to develop gastrointestinal treatments for people with ASD at any point in their lives, it is necessary to assess how the associations among these symptoms change with age and developmental stages. This study adds to the development of evidence relating ASD with co-occurring conditions.

## DECLARATIONS

- **Consent for publication:** I attest that all authors have agreed to submit the work.
- **Availability of data and material:** Available
- **Competing interests:** None
- **Funding:** No fund
- **Conflicts of interest:** no conflicts of interest.

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