

Gastrointestinal Symptoms of Patients with Autism Spectrum Disorder

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Abstract

Background: Concern about possible GI dysfunction in ASD is intensified by high rates of feeding concerns and consequent medical sequelae in ASD. Etiological factors contributing to the pattern and prevalence of atypical intake in ASD remain elusive, but may involve pathophysiological processes in the GI tract. In this study, we evaluated the gastrointestinal symptoms of patients with autism spectrum disorder in Mashhad, Iran.

Methods: This is a cross-sectional study performed during September 2015 and April 2018 on patients referred to pediatric gastrointestinal clinics of Ghaem and Noor Hedayat centers by definite diagnosis of autism spectrum disorder (ASD). All subjects were interviewed to answer some questions about the gastrointestinal manifestations like constipation, chronic abdominal pain, diarrhea, recurrent vomiting, gastro-esophageal reflux, nausea, and agitation. For each patient a checklist was completed including demographic, history and physical examination variables.

Results: During the period of study, 46 definite ASD patients were enrolled in the study. The mean age of the participants was 7.72 ± 2.80 years (range: 2-16). Most of the patients were male (37, 80.4%). Diarrhea (occasional or chronic) was seen in six patients (13%) and constipation in 21 patients (45.7%). There was no significant difference between the gastrointestinal symptoms and gender or age of the patients ($P > 0.05$). An important finding in physical examination was tooth decay, which was found in 21 patients (45.7%).

Conclusion: GI symptoms, with the high prevalence in ASD patients, should be considered as major problems; and preventive strategies must be taken for resolving them. Constipation was the most prevalent symptom, which can be related to the nature of the disease or other mechanisms.

Key Words: Autism spectrum disorder, Constipation, diarrhea, Gastrointestinal symptom.

* Please cite this article as: Jafari SA, sedghi N, Khalesi M, Kianifar HR, Kiani MA, Chaichi Z, Derafshi R. ***** Gastrointestinal Symptoms of Patients with Autism Spectrum Disorder. Int J Pediatr 2022; 10 (4):15730-15736. DOI: **10.22038/IJP.2022.61877.4749**

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Received date: Dec.5,2021; Accepted date:Mar.17,2022

1- INTRODUCTION

Autism spectrum disorder (ASD) is a neurodevelopmental disorder, which displays in the first few years of life and involves severe deficits in social interaction and communication, with concomitant limitations in interests and severe attachment to routine or to repetitive or perseverative behaviors (1). It is predicted that it is rising in the children population markedly within the last decade (2). Because of the heterogeneity in its clinical manifestation and severity of ASD symptoms, it is indicated as “spectrum” (3). ASD is a multifactorial disorder with phenotype heterogeneity (4).

Concern about possible GI dysfunction in ASD is intensified by high rates of feeding problems and consequent medical sequelae in ASD. Children with ASD have a five-fold elevated risk of developing a feeding problem compared with their peers (5). Severe food selectivity (i.e., eating only a narrow variety of foods) is the most common feeding concern documented among children with ASD, predominantly in the form of strong preferences for starches, snack foods, and processed foods and a bias against fruits, vegetables, and proteins (6). However, feeding concerns in ASD are often overlooked in relation to other areas of clinical concerns, probably because selective eating patterns are not necessarily associated with the greater risks of compromised growth that trigger clinical attention in pediatric settings (5). Evidence suggests that atypical patterns of intake in ASD children place this population at risk for long-term nutritional or medical complications which are not captured by broad anthropometrics or analysis of overall energy intake, such as vitamin and mineral deficiencies (5) and compromised bone growth (7).

Etiological factors contributing to the pattern and prevalence of atypical intake in ASD remain elusive, but may involve pathophysiological processes in the GI

tract. In this study, we evaluated the gastrointestinal symptoms of patients with autism spectrum disorder in Mashhad, Iran.

2- METHODS

2-1. Study population

This is a cross-sectional study performed during September 2015 and April 2018 on patients referred to pediatric gastrointestinal clinics of Ghaem and Noor Hedayat centers by definite diagnoses of autism spectrum disorder (ASD).

2-2. Eligibility

Patients with definite diagnosis of ASD between 1-18 years old were included in the study. We excluded the patients who had no consent of their parents or guardians for participation.

2-3. ASD diagnosis

The participants of the study were diagnosed with ASD by psychologists. The diagnostic tools included the Autism Diagnostic Interview-Revised (ADI-R), and the Autism Diagnostic Observation Schedule-Second Edition (ADOS-2), both considered as an international gold standard in the ASD diagnostic process. ADI-R is a semi-structured interview with parents or caregivers that concerns development and current condition of a child. It covers three domains of symptomatology according to ICD-10: (A) social interaction, (B) social communication, and (C) repetitive and restricted behaviors and interests. Each domain provides a cut-off score to meet ASD criteria and allows evaluation of symptom severity. Final ASD diagnosis was made based on clinical evaluation; all children enrolled in the study had to meet criteria for ASD on both ASD diagnostic tools (8).

2-4. Study design

All subjects were interviewed to answer some questions about the gastrointestinal

manifestations like constipation, chronic abdominal pain, diarrhea, recurrent vomiting, gastro-esophageal reflux, nausea, and agitation. They also underwent physical examination and evaluated for anemia, oral exam, abdominal, cardiovascular, and lung exams. For each patient a checklist was, then, completed including demographic, history and physical examination variables.

2-5. Ethical considerations

All patients' parents were asked to complete written informed consent to participate in the study. This study was approved by the ethical committee of Mashhad University of Medical Sciences.

2-6. Statistics

Data was entered in SPSS software version 21. Descriptive data were presented in

percentages and frequencies. Chi square and Fisher exact tests were used for categorical variables analysis. For comparing the continuous variables, we used independent T-Test or Mann Whitney test. P values less than 0.05 were considered as significant.

3- RESULTS

During the study period, 46 definite ASD patients were enrolled. The mean age of the participants was 7.72 ± 2.80 years (range: 2-16). Most of the patients were male (37, 80.4%). Other demographic data are listed in **Table 1**.

Diarrhea (occasional or chronic) was seen in six patients (13%) and constipation in 21 patients (45.7%). Other gastrointestinal symptoms are seen in **Table 2**.

Table-1: Demographic data of the ASD patients

| Characteristics | Value |
|-----------------------|--|
| Age (mean± S.D) year | 7.72± 2.80 |
| Gender (n, %) | Male (37, 80.4) Female (9, 19.6) |
| Height (mean± S.D) cm | 123.32± 15.41 |
| Weight (mean± S.D) kg | 31.38± 7.40 |
| BMI (mean± S.D) | 19.59± 5.4 |
| BMI percentile (n, %) | <5 th percentile (1, 2.1) 5-85 th percentile (25, 54.3) 85-85 th percentile (5, 10.86) >95 th percentile (11, 23.9) |

Table-2: Frequency of gastrointestinal symptoms in ASD patients

| Gastrointestinal symptoms | N, % |
|---------------------------|----------|
| Diarrhea | 6, 13 |
| Constipation | 21, 45.7 |
| Abdominal pain | 6, 13 |
| Recurrent vomiting | 8, 17.4 |
| Nausea | 3, 6 |
| GER | 4, 8.7 |
| Agitation | 4, 8.7 |

There was no significant difference between the gastrointestinal symptoms and gender or age of the patients ($P>0.05$); the Fisher exact test revealed that there was no significant difference between gender and diarrhea ($P=1.0$), constipation ($P=0.264$), chronic abdominal pain ($P=0.581$), vomiting ($P=0.673$), nausea ($P=1.0$), GER ($P=0.571$) and agitation ($P=0.167$). An important finding in physical examination was tooth decay, which was found in 21 patients (45.7%).

According to Mann Whitney test results, there was no significant relationship between BMI and existence of none of gastrointestinal symptoms ($P>0.05$), including the mean BMI in patients with or without diarrhea ($P=0.681$), constipation ($P=0.421$), abdominal pain ($P=0.723$), recurrent vomiting ($P=0.508$), nausea ($P=0.902$), GER ($P=0.323$) and agitation ($P=0.323$).

4- DISCUSSION

In this study, we investigated the gastrointestinal symptoms in patients with ASD. The most common presentation of gastrointestinal symptoms in our study population was constipation. We also found that nearly half of our participants had tooth decay. We focused on the exact gastrointestinal symptoms without any other risk factors.

In a previous study similar to our results, it was demonstrated that GI symptoms were prevalent in ASD patients in different age-categories. They showed that individuals with ASD were more severely affected by GI problems than the controls: almost half of the children and adolescents with ASD suffered from GI symptoms several times per week or daily; in addition, subjects with ASD tended to present more GI problems than the controls. Moreover, they showed that food selectivity and mealtime problems are prevalent (9). Attention to GI problems is significantly less than behavioral or other clinical concerns

associated with ASD, in the view of health professionals and caregivers of individuals with ASD (4).

In line with our study, the main complaint was constipation and/or hard stools (9-13). In our study we did not evaluate the food consumption or diet patterns in the patients. In other studies, it was demonstrated that higher frequency of GI symptoms was associated with higher scores in more severe presentation of ASD symptomatology: social interaction, social communication, and repetitive and restricted behaviors and interests (9, 14, 15). Alterations of behavior, such as aggression, self-injurious activity, or sleep problems are often misleadingly attributed to be just “symptom of the autism” (10), but it is possible that behavioral impairments in ASD are exacerbated or even partially due to the underlying gastrointestinal problems (14). In a meta-analysis, it was indicative of greater risks for general GI symptoms among children with ASD than in those without ASD, showing that this population may be more prone to specific symptoms of abdominal pain, constipation, and diarrhea. The conventional standards correspond to a greater than threefold elevated risk of general GI concerns, constipation, and diarrhea between children with and without ASD and a “medium” effect size is attributed to a greater than two-fold elevated risk of abdominal pain (10). It means that ASD by the lower effect size can lead to more risks of abdominal pain. The existence of a GI pathology specific to ASD has not been established, and mechanisms of GI disorders in ASD are not fully explained. Questions also remain about the relative contribution of behavioral factors, such as toileting and feeding problems, to the observed association between diarrhea, constipation, and abdominal pain in ASD. It is estimated that more than 95% of childhood constipations may be functional, without

an underlying physiologic cause (16). Many children with ASD experience nonorganic toileting problems that may precipitate or play a role in the development of constipation, including absent or delayed acquisition of bowel training (17) and higher rates of problem behaviors related to changes in toileting routines (18). Fecal retention in ASD may also occur secondary to the difficulty with sensory stimuli, sensory processing, and motor problems, leading to altered gastrointestinal motility and defecation physiology (19). It is also possible that elevated rates of constipation may be related to the ubiquity of food selectivity in this population, as the dietary patterns, often associated with ASD, involve high intakes of processed food and low-fiber diets due to their resistance to the consumption of fruits and vegetables as the sources of providing natural laxative effects and decreasing intestinal transit time (20). Therefore, the interweaving effects of behavior, diet, alterations in feeding choices, perceived improvements or decrements in parents' and caregivers' functions with the alterations in diet, all point to the importance of broad-based, longitudinal, unbiased studies of feeding patterns, GI symptoms, and behavior (20).

GI symptoms seem to have a multifactorial basis (21). They also can be related to the microbiota residing in the GI system (22). Evidence shows that gut microbiota and its metabolites influence the brain via the gut–brain axis, i.e., a bidirectional communication between the gut and the brain through neural, endocrine, and immune mechanisms. In ASD, differences in abundance and composition of gut microbiota have been observed (23), and the altered signaling from gut to the brain has been suggested as a potential contributor to the development of ASD and its behavioral presentations. At the same time, altered gut microbiota may contribute to the GI problems associated with ASD (24).

In our study, we did not find any correlation between gender and the GI symptoms ($P>0.05$). However, in another study, it was shown that GI symptoms occurred in girls with ASD more commonly than in boys (9). There is growing evidence of gender differences in ASD symptoms (25). Kushak and Winter (26) suggested that intestinal microbiota, believed to interact with sex hormones, is a factor associated with higher ASD prevalence in boys. So, it might be hypothesized that gut microbiota can contribute to gender differences in GI symptoms, as well. However, the population of our study and the comparative study are limited for generalizing this hypothesis.

Our study focused on the GI symptoms in ASD patients without any comparison to a control group. Our sample size was small. We did not have laboratory findings in our investigation; and there was no Long-term follow-up which could be helpful in data interpretation. Moreover, we did not assess the feeding and diet of our patients or their behavioral scores' severity. More studies are needed to find evidence linking GI dysfunction with behavioral presentations of ASD and their probable mechanisms.

5- CONCLUSION

It is revealed that the GI symptoms in ASD patients have a high prevalence; and they should, hence, be considered as major problems and preventive strategies must be taken for resolving them. Constipation was the most prevalent symptom, which can be related to the nature of the disease or other mechanisms. Additional research is needed to clarify the etiology, prevalence, topography, and remediation of GI problems in ASD, with a consideration of the potential interwoven contributions of factors such as immune abnormalities, mucosal barrier dysfunction, gastrointestinal motility, feeding and toileting concerns, and the gut microbiome.

6- CONFLICT OF INTEREST

None.

7- ACKNOWLEDGEMENT

We appreciate the assistance of the Clinical Research Development Unit Of Akbar Hospital n performing this research.

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