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Original Research

Pediatric autism spectrum disorders and link to food and other allergies

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ABSTRACT:
Aim: The aim of the study was to investigate the link between specific food intolerances and autism spectrum disorders. **Methodology:** This study included 100 patients diagnosed as ASD who attended the phoniatrics clinic in Dubai hospital in the period from Jun 2017 to Jun 2019. The control group involved 50 typically developing children. The diagnosis and severity of autism confirmed by childhood autism rating scale (CARS) and DSM V criteria. Food Intolerance test analyses IgG antibody levels to 222 specific foods to ascertain which food a person might be intolerant to. **Results:** The outcome measures were the percentage of children with elevated IgG in different food items and the mean level of IgG in each food item. The percentage of ASD children with positive food intolerance were 96% for milk, 94% for egg white, 96% for casein, 62% for gliadin, 74% for oat and 80% for wheat. There was a significantly higher level of IgG concentration (U/ml) in ASD than control group. **Conclusion:** A high prevalence of food intolerance was identified in the ASD children. The results of the present study suggested the presence of food intolerance to multiple food items in children with ASD suggesting their possible roles in ASD etiology or symptomatology.
Keywords: Autism, autism spectrum disorders, diet therapy in autism, food allergy, food intolerance.

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INTRODUCTION

Autism spectrum disorders (ASDs) are complex developmental disorders with largely unknown etiologies. Although recent progress in genetics has defined various genetic diseases that manifest autistic features, this group only accounts for up to 10% to 15% of ASDs, which usually manifest as severe forms of autism.[1,2] For the remaining ASD patients, the diagnosis of ASD is based solely on subjective behavioral symptoms that can vary markedly over time and during development. Experts generally agree that there are at least two types of ASDs in terms of development: abnormal cognitive development evident from birth (classical autism) and developmental regression, usually between 18 and 24 months of age following apparently normal development (regressive autism).[3] In cases of regressive autism, parents often report an apparent temporal association between onset of regression and immune insults such as microbial infection or adverse reactions to medications. Apart from behavioral symptoms, certain medical conditions (eg, gastrointestinal [GI] symptoms) are present in many but not all ASD children.[4-6] The presence of comorbidities also affects the behavioral symptoms. Because of the high prevalence of GI symptoms and the apparent clinical improvement by dietary intervention frequently reported by parents, a link between GI abnormalities and the onset and development of ASDs has been posited. Improvement of behavioral symptoms is most commonly reported with a dairy- and wheat-free diet (the so-called casein-free, gluten-free [cf/gf] diet), leading to speculation about a high prevalence of food allergy (FA) in ASD children. In allergy/immunology practice, it is not unusual to be consulted for the evaluation of FA in an ASD child.[7,8] In most such cases, parents have many questions regarding laboratory testing and various intervention measures. These ASD patients are challenging for practicing allergists/ immunologists. First, due in part to their limited expressive language and other behavioral symptoms, it is more difficult to obtain a detailed history for FA and to perform a physical examination on children with ASD as opposed to normally developing children. It is also

difficult to provide medically sound and up-to-date information regarding treatment measures promoted by complementary and alternative (CAM) practitioners, which often lack rigorous scientific validation, especially when the parents are desperate for answers.[9] Interestingly, epidemiological studies have shown that the risk of ASD was elevated in the presence of maternal asthma and allergy during pregnancy. Recently, it was reported that the maternal allergy or asthma recorded during the second trimester of pregnancy was associated with a two-fold increased risk for ASD [10]; moreover, during the past several decades, the prevalence of autism has increased more than ten-fold. The estimated prevalence of autism in approximately three children per 10,000 in 1970 increased dramatically to one per 152 in 2007, as reported by the CDC.[11] Another recent study reported that the levels of all Th2 cytokines were significantly higher in children with autism spectrum disorder than in matched controls; however, no evidence indicated a skewing toward either Th2 or Th1.[12] Elevated serum IgE and eosinophils in peripheral blood have also been reported in children with ASD and are further evidences of an allergic response.[13,14] One of the simplest immunotherapeutic strategies is allergen avoidance. Behavioral symptoms in autistic children may be improved by excluding certain foods from their diets. This is due to potential immunologic reactivities to food allergens that lead to intestinal lesions in these patients.[15] Approximately 76% of autistic children had at least one gastrointestinal problem vs. 30% in healthy children, and 64% of autistic children had more than two GI symptoms. 18% of autistic children older than four were not toilet trained, vs. 2% of their siblings.[16] Libbey reported that mothers of individuals with autism possess antibodies that react with brain proteins. When these antibodies were passively transferred to pregnant non-human primates or rodents, the offspring exhibited behavioral and nervous system changes.[17] Research on autistic children with food allergies has been limited. There is little empirical evidence regarding the possible role of foods or additives causing behavioural disorders in children with autism. We hypothesize that allergen avoidance may lead to a decrease in certain behavioural disorders in autistic children with food allergies.

AIM OF THE PRESENT STUDY

The aim of the study was to investigate the link between specific food intolerances and autism spectrum disorders, by comparing the food Intolerance test in children with ASD and typically developing children without known food allergy or mental disorders.

METHODOLOGY

The study included 100 patients diagnosed as ASD in the period from Jun 2022- Apr 2023. The control group involved 50 typically developing children without known food allergy or mental disorders. Exclusion criteria were autism secondary to genetic syndromes; epilepsy; celiac disease, and ASD children on dietary regimen. The diagnosis of autism was carried out using the protocol of ASD assessment including; parent's interview, Checklist of ASD (CASD), clinical examination, diagnostic criteria of autism according to the Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM V) and childhood Autism Rating Scale (CARS) test. CASD is a 30-item parent or clinician checklist of autistic behaviors, set to the (DSM V), as a rapid test for diagnosis of ASD[1]. CARS test consists of 15 items rated on a 4-point scale. The CARS score can range from 15 to 60 points according to the severity of autism. The score categorized into non-autistic (15-29), mild to moderately autistic (30-36) and severely autistic (37-60 points). CNS Foodprint Test Kits: 16 pads of microarray slides from the same lot that contain 222 food proteins per pad were used. Each pad contains its own calibrators and controls. Positive control results must fall between 70-130 U/ml with a mean of 100 U/ml. The CNS Food-print Test results are revised and analyzed for several reactant food items and their level in U/ml. Reports of test results for each patient will show either elevated (≥30 U/ml), borderline (24-29 U/ml), or normal (<24 U/ml) IgG reactions in every tested food item. The independent sample Mann-Whitney U test was used for non-normally distributed data. Descriptive statistics expressed as frequency and percentage for nominal variables and the Pearson Chi-Square test were used to study significant differences between the 2 groups. A two-sided $p < 0.05$ was considered as statistically significant using SPSS 25.0.

RESULTS

The study included 100 patients with a diagnosis of ASD (82 males and 18 females). The mean age of the studied children was 5.3 years, and the age range was (2.4 -12 years). The control group was 50 normal children (29 male and 21 female) with a mean age of 7.1 years and age range (4.2 -12 years). ASD group children had a diagnosis of ASD and the CARS score mean was 35.6 ± 5.1. The severity of ASD was mild to moderate in 56 patients and severe in 44 patients. Food-print test results for the ASD children were gathered, and the repeating elevated IgG results for each food (> 30 U/ml) were counted and added together to see the number of times each type of food caused high IgG reaction. Foods that were elevated in 20% of the children or more were used. The reason for choosing frequencies 20 or above is that not every single elevated IgG causes a symptom; they must be frequent in most samples to be significant and to relate a condition to a symptom. It was revealed a significantly higher percentage of ASD patients with elevated IgG of egg white, casein, couscous, gliadin, oat, rice, bean, orange, Hazelnuts, pistachio, almond, and cashew in comparison to control group. There was

a significantly higher level of IgG concentration (U/ml) in ASD than the control group in egg white, milk, casein, couscous, gliadin, oat, rice, bean, orange and the 4 elevated nuts. There was also a significant positive correlation between age and the total number of food items with elevated IgG in each patient (r= .001). (Table 1)

Table 1- Level of IgG concentration (U/ml) in ASD and control group

Food variables	Group	Mean IgG level U/ml	Std. Deviation	T value	significance
Egg and non-veg products	ASD	76.0000	29.35261	5.452	.000
	control	48.5600	28.45057		
Milk and milk products	ASD	121.3200	35.03386	7.606	.000
	control	74.6400	36.22479		
Cereals	ASD	99.8200	37.37535	6.964	.025
	control	55.4400	35.58615		
Nuts	ASD	20.11391	27.5800	2.268	.069
	control	19.63318	19.7400		

DISCUSSION

Recent reports indicate that the prevalence of food allergies in children with autism was 14.0% vs. 3.5% in children without autism. Also, the prevalence of respiratory allergies in children with autism was 26.4% vs. 14.9% in children without autism.[18] The prevalence of positive SPT in our study was 7.7%; however, another study reported the prevalence of positive SPT in children with autism to be 14.9% vs. 9.8% in healthy and non-atopic controls matched for age, race, and gender. Gupta et al. reported increased serum IgE levels in children with ASD.[19] The nature of the underlying etiopathogenesis of Autism Spectrum Disorder is still unknown and yet to be uncovered. Recently some researchers have suggested that food peptides that leak from gut to blood might induce immunological reaction or toxic effects on the central nervous system through interacting with neurotransmitters. The previous studies' results must lead us to hypothesize a relationship between food intolerance and ASD.[20] The results of the present study suggested the presence of food intolerance to multiple food items in children with ASD. The IgG level was significantly higher in the ASD group in many food items, including milk, casein, gliadin, oat, rice, bean, orange, and nuts, in comparison to the control group, suggesting their possible roles in ASD etiology or symptomatology. Many children with ASD cannot properly digest peptides from proteins in their diet; peptides from milk, wheat, and eggs tend to be the most common problem.[21] Trajkovski et al found statistically significant higher plasma concentration of IgG antibodies against -lactalbumin, -lactoglobulin, and casein in participants with ASD. He concluded that the clinical correlation of positive allergy test results still unclear, but these children may represent a better candidate for dietary intervention.[22] In the present study, it was found that a large number of control children have elevated IgG for many food items, which may indicate food intolerance is common across a wide range of health issues. Further studies concerning follow up of ASD children after specific diet plans, according to food intolerance test results are needed, to show the effect of intolerant foods free diet on autistic behavior severity and level of IgG after the diet plan.

CONCLUSION

The results of the present study suggested the presence of food intolerance to multiple food items in children with ASD suggesting their possible roles in ASD etiology or symptomatology.

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