

A systematic review of the effect of nutritional status on autism spectrum disorder

Felipe G. Santiago,¹ Eduardo D. S. Lyra,¹ Patrícia da Silva Pantoja^{2*}

Abstract

Autism spectrum disorder (ASD) is a neurodevelopmental disorder that includes deficits in social interaction, communication and behavior, whose exact cause remains unknown. Its symptoms, such as food selectivity, food refusal and resistance to new habits affect children's ability to consume food. The aim of this study is to answer the following questions: Do children with ASD have a different nutritional and behavioral profile from neurotypical children? Are dietitian interventions capable of bringing benefits in terms of improvements in behavior, communication and socialization status? The methodology used was a systematic review. The authors produced two guiding questions; defined keywords; researched for papers in databases; applied inclusion and exclusion criteria; and analyzed the data obtained from papers that answered the guiding questions. The results revealed 27 publications in the Pubmed, Lilacs, and Capes databases that included keywords cross-referenced between ASD and gluten free, eating behavior, casein-free, nutritional status, food selectivity, vitamin deficiency, nutritional strategy. An analysis of 16 papers in Pubmed, 6 papers in Lilacs and 5 papers in Capes showed that

1. Escola de Saúde Pública do Ceará. Fortaleza, Ceará, Brazil.
2. University of Memphis. Tennessee, United States of America.

*Correspondence address:

E-mail: pdnewman@memphis.edu

ORCID: <https://orcid.org/0000-0002-4621-7059>

BJHBS, Rio de Janeiro, 2024;23(1):10-21

DOI: 10.12957/bjhbs.2024.85192

Received on 19/01/2024. Approved on 03/04/2024.

33.3% of the works had been published in Brazil. Randomized clinical trials (RCT) and cross-sectional studies were the most used methodologies. The analysis concluded that non-nutritional interventions have been effective in modifying unsatisfactory behaviors. Also, a combination of dietary and social/behavioral interventions is effective in circumventing food selectivity, thereby improving food acceptance.

Keywords: Nutrition, Autism, Public Health.

Introduction

ASD is defined as a neurodevelopmental disorder whose peculiarities include deficits in social interaction and communication as well as restricted or repetitive behavior or interests. Other important characteristics of ASD are limited repetitive patterns, stereotyped movements, activities and interests. Although the exact cause of ASD is unknown, genetic, environmental and immunological factors are thought to play a role in its pathogenesis.¹

With nutritional transition in Brazil over the years, several advances have been made in controlling energy-protein malnutrition, but the consequences of micronutrient deficiency have become the most important public health concern, especially among children. Studies have shown that children's usual diet is insufficient to meet 100% of their micronutrient needs,

especially for the minerals iron, zinc and calcium. Children with neurodevelopmental disorders are at risk of developing nutritional deficiencies.^{2,3}

In line with the International Classification of Diseases (ICD) - 11th revision (ICD 11), the Diagnostic Statistical Manual of Mental Disorders - DSM-5 made the codes previously assigned within Global Developmental Disorders unique and currently integrates autism spectrum disorder as code 6A02. The revision also removed the subcategories and levels of classification, typifying the condition only in relation to functional language impairment and intellectual disability.⁴

ASD causes a disability in the development of individuals' neurological systems and affects their ability to communicate, interpersonal relationships and behavior. It is accompanied by a diversity of functional alterations in which it is possible to notice a series of specific characteristics among children on this spectrum, varying in degree, from mild to debilitating. Among these characteristics, we can highlight the restricted and repetitive standardization of activities and interests, which prevents ASD sufferers from participating in new activities that are not routine, and affects their food consumption in a similar way.^{5,6}

The most relevant characteristics observed in children with ASD are mainly associated with poor development of language and social interaction, as well as a succession of gastrointestinal disorders, such as low production of digestive enzymes and inflammations of the intestinal wall, which intensify the symptoms of those with the disorder.⁷

Based on these symptoms, we can classify three categories of behavior that affect the autistic child's eating profile: food selectivity, food refusal (due to a resistance to trying new foods), and indiscipline during meals, a cause that is very characteristic of childhood and the disorder itself. These conditions cause autistic children to have a tiring diet with limited variety, probably leading to nutritional deficiencies.⁸

Methodology

This study was carried out using the systematic literature review methodology, which consisted of the following steps: production of a guiding question; analysis by searching for articles in literature databases with the definition of keywords, databases and application of the criteria defined for the selection of articles; and, as a last step, evaluation and analysis of the data obtained from the selected papers.

The guiding questions were divided in two stages: First, do children with ASD have a different nutritional and behavioral status than neurotypical children? Second, are dieticians' interventions capable of bringing benefits in terms of improved behavior, communication and socialization status?

The study was conducted between April and May 2020. The inclusion criteria for the studies were: original articles, studies on nutritional status, eating behavior and nutritional strategies in children with ASD, the withdrawal of gluten and/or casein, and those that fit the objective of the review, indexed in the LILACS (Latin American and Caribbean Health Sciences Literature), PUBMED and CAPES databases.

The search for papers used combinations of the following keywords, considered to be descriptors in DeCS (Health Sciences Descriptors) and MeSH (Medical Subject Headings): autistic disorder; autism spectrum disorder; infants; nutritional; casein; gluten-free; nutritional status;

eating behavior; gluten-free diet; and vitamin deficiency. The terms were cross-referenced as descriptors and as words in titles and abstracts.

The following inclusion criteria were used: studies involving children with ASD, aged between 0 and 12 years; cohort studies; cross-sectional studies; case series; randomized clinical trials (RCT); descriptive observational studies that included case reports, cross-sectional studies and case-control studies. We excluded literature review articles, theses, dissertations, duplicate articles, and articles whose full content was unavailable, as well as studies of children with chronic non-communicable diseases, non-autistic children, and other audiences, the elderly, athletes, animals, studies that refer to other types of diets, children of mothers with eating disorders and guidelines.

Results and discussions

Our results initially revealed 8 scientific papers in the LILACS database, 119 papers in the PUBMED database and 36 papers in the CAPES database for exploratory reading of abstracts. Twenty-seven papers were selected based on the inclusion and exclusion criteria, which were then read in full. After analysis, articles presenting aspects that answered the guiding question of this review were included in the object of study (Figure 1).

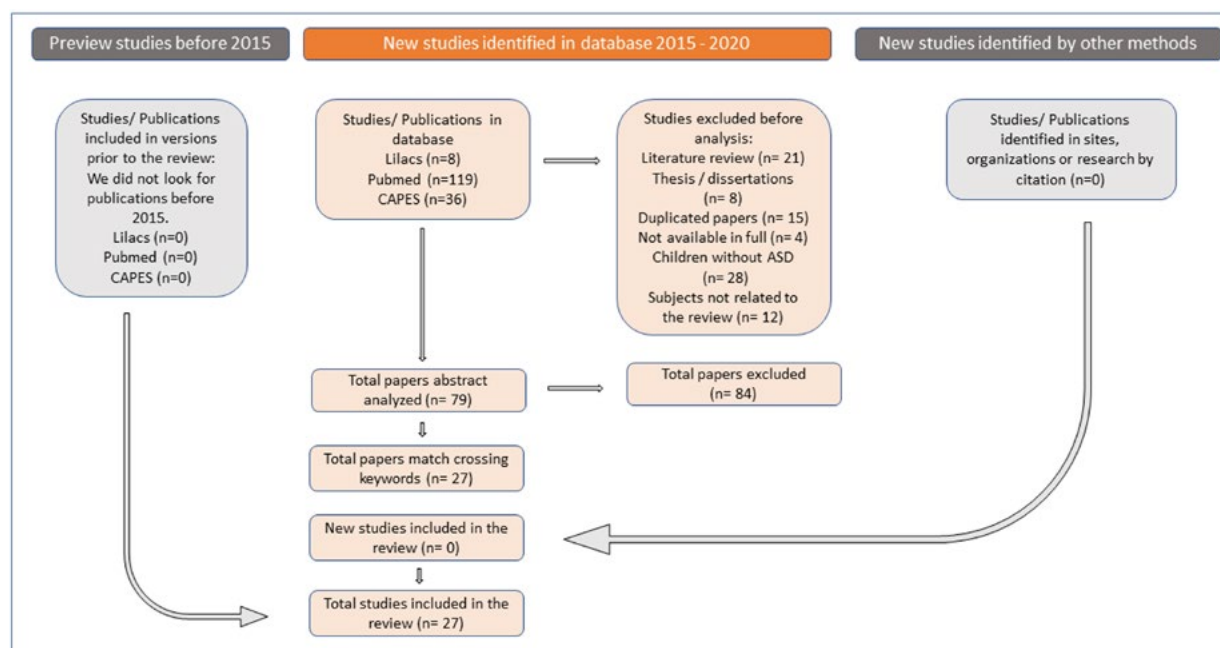


Figure 1. Systematic review flowchart

Source: The authors (2020).

The stages of this process are described in Table 1. Crossing keywords and database we found: ASD / gluten free appeared in 8 of the publications found in Pubmed, 3 in Lilacs and 1 in CAPES. ASD / eating behavior appeared in 2 of the papers selected in Pubmed but in none of the other databases. ASD / casein free appeared in only 3 papers, all of which in Pubmed. ASD / nutritional status appeared in 3 publications in Pubmed, 1 in Lilacs and 2 in CAPES. ASD/ food selectivity appeared in 2 papers in Lilacs. ASD / vitamin deficiency appeared in 1 paper in Pubmed and CAPES. ASD / nutritional strategy appeared in only 1 paper in the CAPES database (Table 1).

Table 1. Distribution of bibliographic publications obtained from the Pubmed, Lilacs and CAPES databases, according to the keywords selected, Brazil, 2020

Database	Keywords cross-referenced at the same time (as words in the abstract and descriptors)	Number of publications found	Abstracts analysed	Papers selected for analysis
PUBMED	ASD / gluten free	38	20	7
	ASD / eating behavior	30	8	2
	ASD / casein free	25	4	3
	ASD / nutritional status	24	10	3
	ASD/ food selectivity	0	0	0
	ASD / vitamin deficiency	2	2	1
	ASD / nutritional strategy	0	0	0
LILACS	ASD / gluten free	3	3	3
	ASD / eating behavior	0	0	0
	ASD / casein free	0	0	0
	ASD/ nutritional status	1	1	1
	ASD/ food selectivity	2	2	2
	ASD / vitamin deficiency	2	2	0
	ASD / nutritional strategy	0	0	0
CAPES	ASD / gluten free	3	3	1
	ASD / eating behavior	6	5	0
	ASD / casein free	7	7	0
	ASD / nutritional status	7	3	2
	ASD / food selectivity	2	2	0
	ASD / vitamin deficiency	5	4	1
	ASD / nutritional strategy	8	3	1

Source: The authors (2020).

A wide range of studies, comprising 27 publications, was selected. In terms of location, the countries with the highest number of studies were Brazil and the USA (29.6%) with an equal number of papers, as shown in Table 2, thereby demonstrating widespread interest in this subject.

Regarding the design of the methodology, the studies analyzed had a higher prevalence of RCTs and cross-sectional clinical trials (25.9%), followed by quantitative publications (14.8%) (Table 3).

In terms of sample size, the studies showed an adequate number of individuals for the research designs, ranging from 1 to 538 child participants.

Table 2. Number of publications according to the country in which the study was conducted

Country	Number of publications (N)	Percentage (%)
Brazil	8 (eight)	29.6
USA	8 (eight)	29.6
Spain	2(two)	7.4
Poland; Iran; Indonesia; Belgium; Germany; Italy; Canada, Egypt	1 each country	3.7 each

Source: The authors (2020).

Table 3. Types of studies found, 2020

Methodology	Samples selected (N)	Percentage (%)
RCT	7 (seven)	25.9
Cross-sectional	4 (four)	14.8
Quantitative	2 (two)	7.4
Qualitative	2 (two)	7.4
Group analysis	1(one)	3.7
Case-control	3 (three)	11.1
Meta-analysis	2 (two)	7.4
Multiple project	1(one)	3.7
Action project	1(one)	3.7
Opinion article	1(one)	3.7
Systematic review	2 (two)	7.4
Methodological study	1(one)	3.7

Source: The authors (2020).

The research aimed to use cautious reliable methods, which enable improved verification of the variables in the studies, demonstrating a valid repercussion to the impact of gluten-free and dairy-free diets on children and their problems, including micronutrient deficiency.

The verification of nutritional markers was conducted using quantitative and qualitative methods, namely: biochemical tests with serum quantification of vitamins and micronutrients; and anthropometric parameters, such as BMI (body mass index), W/H (weight-for-height index), TSF (triceps skinfold). These were essential to obtain consistent data and assess possible negative nutritional repercussions.

Table 4 presents the articles selected for the review, with their authors, date and country of publication, aims and main conclusions. In order to answer the research question of the article and in line with the publications found, the studies encompass three subtopics, namely: nutritional profile of children with ASD; eating behavior of children with ASD; and nutritional strategies for children with ASD.

Table 4. Distribution of references included in the systematic review, according to year of publication, country, authors, objectives and conclusions of the article, Brazil, 2020

Country, author and year	Objective of the paper	Description of the study	Main conclusions
Brazil Caetano, M. V & Gurgel, D. C. 2018.	To assess the nutritional status and food consumption of children with autism spectrum disorder (ASD).	Quantitative, descriptive, exploratory and cross-sectional.	Most of the children with autism spectrum disorder who were assessed were overweight and obese. The limited and repetitive food menu revealed a high level of inadequate intake of vitamins (A and B6) and the mineral calcium, showing a link with high consumption of foods rich in calories and poor in micronutrients.
Brazil Rocha G. S. S. et al. 2019	To analyze the possible presence of food selectivity behaviors in children with autism spectrum disorder (ASD).	Descriptive, exploratory quantitative field research.	The participants analyzed in the study present eating behaviors that are prone to food selectivity. The study showed the risk of nutritional deficiencies, especially in micronutrients, given that the childhood phase has a direct long-term influence on an individual's life. For this reason, nutritional monitoring and necessary interventions are required to ensure the correct nutrition of children with autism spectrum disorders.
Brazil Almeida, A. K. A. et. al. 2019	To analyze consumption of ultra-processed foods among children with ASD and its association with nutritional status.	Cross-sectional.	In natura or minimally processed foods were the basis of the diet of the children studied. Despite this, higher consumption of ultra-processed foods was associated with excess weight in children with ASD.
USA Sharp, W. G. et al. 2019	To evaluate the feasibility and initial effectiveness of a structured parent training program for children with autism spectrum disorder and food selectivity.	16-week RCT study.	The MEAL Plan appears to be feasible and its preliminary results are encouraging. If further study replicates these results, the MEAL Plan could expand treatment options for children with autism spectrum disorder and moderate food selectivity.
USA Peverill, S. B. S. et al. 2020	To examine the developmental progression of eating problems over four time points in preschoolers with ASD.	Group path analysis.	Most of the children's eating problems disappeared as they grew older, but some of them developed chronic problems.
Egypt El-Rashidy, O. et al. 2017	To analyze ketogenic diet versus gluten-free casein-free diet in autistic children	Prospective case-control.	Although the results were satisfactory, the number of subjects used was small and lacked multicentricity, since only a single location was used. Further studies were necessary,
Spain Leiva-García, B. et al. 2019	To evaluate the relationship between eating problems and oral health in children with autism spectrum disorder.	Observational case-control.	Food rejection and limited food variety were associated with an increased prevalence of malocclusion and altered Community Periodontal Index scores in children with ASD.
Poland Piwowarczyk, A., Horvath, A., Pisula, E. et al. 2020	To determine whether a gluten-free diet compared to a gluten-containing diet influences the functioning of children with autism spectrum disorders.	RCT, controlled and blinded study.	No differences were found between the groups with regard to autistic symptoms, inappropriate behaviors, or intellectual abilities after the intervention. A GFD compared to a GD did not affect the functioning of children with ASD.
Iran Ghalichi, F.; Ghaemmaghami, J.; Malek, A.; Ostadrahimi, A. 2016	To investigate the effect of a gluten-free diet (GFD) on gastrointestinal symptoms and behavioral indices in children with ASD.	RCT	GFD may be satisfactory for managing gastrointestinal symptoms and behavioral indices in children with ASD.

Table 4. Distribution of references included in the systematic review, according to year of publication, country, authors, objectives and conclusions of the article, Brazil, 2020 (cont.)

Country, author and year	Objective of the paper	Description of the study	Main conclusions
Indonesia Pusponegoro, H. D. et al. 2015	To determine the effect of gluten and casein supplementation on maladaptive behavior, severity of gastrointestinal symptoms and intestinal fatty acid binding protein excretion (I-FABP) in children with ASD.	Double-blind RCT	The administration of gluten-casein in children with ASD for one week was not sufficient to increase maladaptive behavior, the severity of gastrointestinal symptoms or urinary I-FABP. The effect of prolonged administration or other enterocyte mechanisms corroborated damage in ASD, which should be explored.
USA Hyman, S. L. et al. 2015	To obtain information on the safety and efficacy of a gluten-free / casein-free (GFCF) diet.	Double-blind, placebo-controlled challenge study	Dietary challenges had no statistically significant effects on measures of physiological functioning, behavior, problems or symptoms of autism, although these findings should be interpreted with caution due to the small sample size. The study does not provide evidence to support the general use of a GFCF diet.
Brazil Rosa, M. S. & Andrade, A. H. G. 2016	To trace the nutritional profile of children with ASD in Arapongas - PR.	Cross-sectional study	The conclusion is that children with autism spectrum disorder require continuous nutritional monitoring because of excess weight and obesity.
USA Mieurau, S. B. & Neumeyer, A. M. 2019	To examine possible direct and indirect roles for metabolism in the main symptoms of ASD, as well as evidence of metabolic dysfunction and nutritional deficiencies.	Systematic review with meta-analysis	More research is needed to test metabolic and nutritional interventions for efficacy in treatment of the main symptoms of ASD.
USA Hilman H. 2019	To evaluate the effects of video modeling on the food selectivity of three children with an autism spectrum disorder in a home environment.	Multiple baseline experimental project	The researcher suggests that the video modeling intervention was responsible for an increase in food acceptance.
USA Peterson, A. K.; Piazza, C. C.; Volkert, V. 2016	To apply treatment for food selectivity in children with autism spectrum disorders.	Complex RCT	A potential generalization effect of the treatment during ABA M preceded by SOS ABA was found.
Belgium Ostashchenko, E.; Deliens, G.; Durrleman, S.; Kissine, M. 2020	To explore whether children with autism show selectivity in social learning.	Complex RCT	Children with autism showed reduced attention to speakers' faces compared to the control group.
Brazil Cordeiro, D. A. M. & Silva, M. R. 2016	To describe strategies for implementing nutritional behaviors in autism spectrum disorder.	Action research	The resulting data lead us to believe that it is important to develop a nutritional guideline for the treatment of people with autistic disorder.
Brazil Kummer, A. et al. 2015	To evaluate the frequency of excess weight and obesity in children with ASD and ADHD.	Quantitative study	Children with ADHD and ASD are more likely to be obese or overweight than children without ADHD disorder.
USA Sathe, N.; Andrews, J. C.; Mcpheeters, M. L.; Warren, Z. E. 2017	To evaluate the efficacy and safety of dietary interventions or nutritional supplements in ASD.	Meta-analysis	Little evidence exists to support the use of nutritional supplements or dietary therapies for children with ASD.

Table 4. Distribution of references included in the systematic review, according to year of publication, country, authors, objectives and conclusions of the article, Brazil, 2020 (cont.)

Country, author and year	Objective of the paper	Description of the study	Main conclusions
Germany Lange, K. W.; Hauser, J.; Reissmann, A. 2015	To discuss the role of GFCF diets in the treatment of autism.	Opinion article	The evidence to support the therapeutic value of this diet is limited and weak. A GFCF diet should only be administered if an allergy or intolerance to gluten or nutritional casein has been diagnosed.
USA Polfuss, M. et al. 2016	To explore parents' perspectives on how their child's ASD attributes impact nutrition, physical activity, screen time behaviors and obesity risk.	Qualitative study	The strategies extracted from the parents' narratives promoted both healthy and unhealthy weight-related behaviors. The main conclusion of this study is that some parents did not follow the HCP guidance when they realized that the HCP did not understand their specific situation.
Spain Marí-Bauset, S. et al. 2015	To compare anthropometric values, nutrients, healthy consumption, healthy eating index and variety of foods with ASD.	Case-control study	A RCT is needed to explore the long-term effects of this diet on anthropometric and nutritional status as well as on behaviors in children with ASD.
Brazil Monteiro, M. A. et al. 2019	To identify and analyze the scientific evidence of nutritional interventions for children and adolescents with ASD.	Systematic review	Although some authors have shown progress in the symptoms associated with autism in individuals with this disorder who have undergone nutritional interventions, scientific evidence to support their use in children and adolescents with ASD is limited.
Italy Peretti, S. et al. 2019	To update current knowledge on maternal nutrition as a determinant of the risk of ASD in offspring.	Systematic review	Several studies have attempted to show a possible relationship between nutritional status and autism. In this review, the authors emphasized the limits and benefits found in the main current empirical studies that have examined the role of maternal diet during pregnancy and diet of ASD children as modifiable risk factors underlying the development or worsening of autism symptoms.
Brazil Lázaro, C.P. & Pondé, M. P. 2019	To construct the items and establish the content and construct validity of the Autism Eating Behavior Scale.	Methodological study	The scale aims to identify the dimensions of eating behavior that are altered, providing a more specific direction for therapy, and can also be used to measure the progress of treatment.
Canada Trudeau, M. S.; Madden, R. F.; Parnell, J. A.; Gibbard, W. B.; Shearer, J. 2019	To describe the use of supplement-based CAM therapies in children with ASD aged between 4 and 17.	Cross-sectional study	The use of complementary therapies in children with ASD is endemic and highlights the need for further research into public health education surrounding safety and efficacy.
Brazil Magnanin, T. 2019	To discuss the importance of a multi-professional approach to food selectivity in children with ASD.	Qualitative study	The activities proposed in the study are recommended for use in the family environment, at school and by the health team, thus becoming part of these children's routine.

Source: The authors (2020).

Nutritional status of children with autism spectrum disorder

The preparation of a group's nutritional profile can be used to improve how the group is treated. A quantitative, descriptive, exploratory and cross-sectional study conducted with 26 chil-

dren in the city of Limoeiro do Norte, Ceará, Brazil, showed that children with ASD have high levels of excess weight and obesity as well as inadequate vitamin and mineral intake.⁹

In another study with identical methodology, sharing the same objective of assessing excess weight in children with ASD and, in this case, attention deficit and hyperactivity disorder, Kummer and colleagues (2015)¹⁰ concluded that a sample of 69 patients with ASD is at greater risk of being overweight and obese compared to children without developmental problems from the same community.

In a study conducted in Arapongas, Goiás, Brazil, Rosa and Andrade (2018)¹¹ also found that children with autism spectrum disorder require continuous nutritional monitoring because they are overweight and obese.

Thus, these papers suggest that once the children have a nutritional disorder, obesity is one of the patterns that needs to be monitored to prevent excess weight. A healthy nutritional profile must be established for children with ASD.

Eating behavior of children with autism spectrum disorder

The reality that children with autism deserve special attention when it comes to food does not seem far-fetched, considering the developmental disorders and selectivity that may be present.²⁴ Almeida and colleagues, 2019¹² carried out a cross-sectional study in São Luís, Maranhão, Brazil, on a sample of 29 children, with the objective of analyzing the consumption of ultra-processed foods. They found that fresh or minimally processed foods were the basis of the diet of the children studied and that high consumption of ultra-processed foods was associated with excess weight in children with ASD.

In a multicenter study conducted in Canada with long-term group analysis, Peverill and colleagues, 2018,¹³ showed that children lost bad habits over time and naturally improved their nutritional status. In a complex study using RCT methodology, Ostashchenko and colleagues 14 (2020) showed that selective food behavior seems to be a social trait and that the promotion of family health is relevant to ASD children compared to the control group.

In a qualitative study conducted with the parents of autistic children, Polfuss and colleagues, 2016¹⁵, aimed to determine how their children viewed the eating behavior of this type of client. In an innovative approach, the authors inferred that strategies extracted from the parents' narratives promoted both healthy and strange behaviors that could conveniently be related to weight. Also, according to the authors, some parents did not follow the recommendations and guidelines, since this could infer a bad prognosis for the eating behavior of children with ASD, leading to excess weight and obesity, as mentioned in studies on nutritional status.

Through a complex RCT study, Peterson and colleagues, 2016¹⁶, demonstrated, through Applied Behavior Analysis (ABA), the existence of selective behavior in ASD. Thus, the results corroborated our initial hypothesis, that children with ASD have a different nutritional and behavioral status from neurotypical children and this status is a possible contributor to excess weight/obesity or nutrition disorders.

Nutritional strategies for children with autism spectrum disorder

Several interventions are mainly based on a gluten-free and casein-free perspective. In a randomized clinical trial with 80 children conducted in Iran, Ghalichi and colleagues (2016)¹⁷

concluded that gluten-free diets (GFD) may be helpful in the management of gastrointestinal symptoms and behavioral indices in children with ASD.

In this perspective, the findings of Puspongoro and colleagues, 2015¹⁸ in another randomized clinical trial with 74 children conducted in Indonesia, contrast with the study by Ghalichi and colleagues, 2016¹⁷. Using a double-blind approach, gluten and casein were inserted into the diet, with the result that the administration of gluten-casein in children with ASD for one week was not sufficient to increase maladaptive behavior, severity of gastrointestinal symptoms or urinary I-FABP. The possibility of prolonged administration or other enterocyte mechanisms leading to ASD damage should be explored.¹⁸

Following this same line of clarifying the impact of gluten-free and casein-free diets, a study using RCT methodology conducted with 66 children with ASD for 30 weeks showed that the interventions did not present statistically significant effects on measures of physiological functioning, behavior, problems or symptoms related to autism. Although these findings should be interpreted with caution due to the small sample size, the study does not provide evidence to support the generalized use of the gluten-free and casein-free (GFCS) diets.¹⁸

Given the fact that ASD presents non-specific behavior and is sometimes refractory to nutritional interventions, studies with different methodologies should be conducted. At this juncture, Hilman,¹⁹ implemented a home video modeling intervention during dinner for three participants that used a multiple baseline experimental design. The results suggested that video modeling was effective in increasing food acceptance, but food acceptance was higher for all three participants when reinforcement with the ABA scale was added.¹⁹

Through an action research project, Cordeiro and Silva²⁰ showed that the inclusion of a guide to nutritional guidelines for the treatment of people with ASD is worthwhile, in addition to reinforcing the perspective of the unknown etiology of ASD. The interventions proposed by the authors showed the heterogeneous nature of interventions involving autism.²⁰

Despite showing different studies with evidence base, studies using meta-analysis should be considered, In 2017, a meta-analysis within a systematic review found scant evidence to support the use of nutritional supplements or dietary therapies for children with ASD. Priority should therefore be given to studies at the top of the evidence pyramid. In such cases, it is worth mentioning that numerous different interventions will show differences between the groups in terms of autistic symptoms, inappropriate behaviors or intellectual abilities after the gluten diet intervention. A GFD compared to a gluten diet (GD) did not affect the functioning of children with ASD.²¹

In a systematic review with meta-analysis, Mieurau and Neumeyer²² attempted to examine possible direct and indirect roles for metabolism in core ASD symptoms, as well as evidence of metabolic dysfunction and nutritional deficiencies. Their conclusions infer that more research is needed to test metabolic and nutritional interventions for efficacy in treating the main symptoms of ASD.²²

In another systematic review with 18 studies, 16 of which were RCT, Monteiro and colleagues, 2020²³ categorically infer that, although numerous studies on interventions can be found, more comprehensive scientific evidence to support drastic changes in the diet of ASD patients is still lacking. Despite this, the authors concluded that there is no point in changing GFD and GFCS diets since their impacts are uncertain.^{26,28-30} At this juncture, within the conclusions

imposed for this study, there is still uncertainty among the publications about interventions. The findings of the study corroborates the conclusions of other authors.^{25,33-34}

Conclusions

The analysis of the studies in question demonstrated that adherence to gluten-free or casein-free diets by children with ASD confers wider benefits in the prevention of diseases such as cardiovascular diseases, neoplasms and maladaptive processes. Although some studies make a case for the removal of gluten and casein from diets, others do not encourage such a discussion.

What can be observed is that non-nutritional interventions, as discussed in the review, have been effective in reducing unsatisfactory behaviors.^{25,33-34} Once this becomes a practice, dietary intervention in conjunction with social/behavioral interventions is one way to improve food acceptance by circumventing food selectivity.

This systematic review identified the nutritional repercussions of a GFCS diet on children on the autistic spectrum. We also included micronutrients, such as vitamins (A and B6) and the mineral calcium, whose levels have been shown to be insufficient or suboptimal in patients in the studies included in this review.

In this respect, one can infer those new studies with a high level of scientific evidence, i.e. RCTs and meta-analyses, are needed, with larger samples of participants, in order to discuss interventions and better characterize dietary selectivity profiles and behavior.

Acknowledgements

The authors would like to thank School of Public Health in Ceará (ESP-CE) and General Hospital of Fortaleza (HGF) for support in a residency program in neurophysiology.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

References

1. Ranjan S, Nasser JA. Nutritional status of individuals with autism spectrum disorders: do we know enough? *Adv in Nutr.* 2015;6(4):397-407. DOI: <https://doi.org/10.3945/an.114.007914>
2. Pedraza DF, Queiroz D. (2011). Micronutrientes no crescimento e desenvolvimento infantil. *Rev. Bras. Cresc. desenvol. Hum* [online]. 21(1), 156-171.
3. Cermak SA, Curtin C, Bandini LG. (2010) Food selectivity and sensory sensitivity in children with autism spectrum disorders. *J Am Diet Assoc.* 110(2):238-46.
4. World Health Organization (2018): WHO releases new International Classification of Diseases (ICD 11). Available from: [https://www.who.int/news/item/18-06-2018-who-releases-new-international-classification-of-diseases-\(icd-11\)](https://www.who.int/news/item/18-06-2018-who-releases-new-international-classification-of-diseases-(icd-11)). Accessed in July 30th 2023.
5. Leal M, Nagata M, Cunha N de M, Pavanello U, Ferreira NVR. Terapia nutricional em crianças com transtorno do espectro autista. *SAU [Internet]*. March 10th 2017;1(13). Available from: <tps://portaldeperiodicos.unibrasil.com.br/index.php/cadernossaude/article/view/2425>
6. Lázaro, C.P. & Pondé, M. P. (2017). Narratives of mothers of children with autism spectrum disorders: focus on eating behavior. *Trends in Psychiatry and Psychotherapy* [online]. Vol. 39, n. 3.
7. Kahathuduwa CN, Dhanasekara CS, Wakefield S, et al. Autism spectrum disorder is associated with an increased risk of development of underweight in children and adolescents: A systematic review and meta-analysis. *Research in Autism Spectrum Disorders.* 2022 Jun;94:101969.
8. Johnson CR, Handen BL, Mayer-Costa M, Sacco K. Eating Habits and Dietary Status in Young Children with Autism. *Journal of Developmental and Physical Disabilities.* 2008 Jun 17;20(5):437-48.
9. Vanuza Caetano M, Cordeiro Gurgel D. Perfil nutricional de crianças portadoras do transtorno do espectro autista.

- Revista Brasileira em Promoção da Saúde. 2018 Feb 28;31(1):1–11.
10. Kummer A, Barbosa IG, Rodrigues DH, Rocha NP, Rafael M da S, Pfeilsticker L, et al. Frequency of overweight and obesity in children and adolescents with autism and attention deficit/hyperactivity disorder. *Revista Paulista de Pediatria* [Internet]. 2016;34(1):71–7. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4795724/>
 11. Rosa S, Helena A. Perfil nutricional e dietético de crianças com transtorno espectro autista no município de Arapongas Paraná. *Revista Terra & Cultura: Cadernos de Ensino e Pesquisa*. 2019 Oct 18;35(69):83–98.
 12. Almeida AKDA, Fonseca PCDA, Oliveira LA, et al. Consumo de ultraprocessados e estado nutricional de crianças com transtorno do espectro do autismo. *Revista Brasileira em Promoção da Saúde*. 2018 Oct 31;31(3).
 13. Peverill S, Smith IM, Duku E, Szatmari P, Mirenda P, Vaillancourt T, et al. Developmental Trajectories of Feeding Problems in Children with Autism Spectrum Disorder. *Journal of Pediatric Psychology* [Internet]. 2019 Sep 1 [cited 2021 Oct 22];44(8):988–98. Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6705712/>.
 14. Ostashchenko E, Deliens G, Durreleman S, Kissine M. An eye-tracking study of selective trust development in children with and without autism spectrum disorder. *J. Exp. Child Psychol*. 2020 Jan 1 [cited 2020 Dec 8];189:104697.
 15. Polfuss M, Johnson N, Bonis SA, et al. Autism Spectrum Disorder and the Child's Weight-Related Behaviors: A Parents' Perspective. *Journal of Pediatric Nursing*. 2016 Nov;31(6):598–607.
 16. Peterson KM, Piazza CC, Volkert VM. A comparison of a modified sequential oral sensory approach to an applied behavior-analytic approach in the treatment of food selectivity in children with autism spectrum disorder. *Journal of Applied Behavior Analysis*. 2016 Jul 23;49(3):485–511.
 17. Pusponogoro HD, Ismael S, Firmansyah A, Sastroasmoro S, Vandenplas Y. Gluten and casein supplementation does not increase symptoms in children with autism spectrum disorder. *Acta Paediatrica*. 2015 Aug 30;104(11):e500–5.
 18. Alamri E. Efficacy of gluten- and casein-free diets on autism spectrum disorders in children. *Saudi Medical Journal*. 2020 Oct 6;41(10):1041–6.
 19. Hilman H. Modelagem de Vídeo em Casa sobre Seletividade de Alimentos de Crianças com Transtorno do Espectro do Autismo. *Terapia Física e Ocupacional em Pediatria*. (2019) 39(6): 629–41.
 20. Cordeiro DA de M, Silva MR da. Estratégias para implementação de condutas nutricionais no transtorno do espectro autista: um relato de experiência. *Revista Corixo*. June 2018;(6).
 21. Sathe N, Andrews JC, Mcpheeters ML, et al. Nutritional and Dietary Interventions for Autism Spectrum Disorder: A Systematic Review. *Pediatrics*. 2017;139(6):e20170346.
 22. Mieurau SB, Neumeyer AM. Metabolic interventions in Autism Spectrum Disorder. *Neurobiology Of Disease*. 2019;132:04544.
 23. Monteiro MA. Autism spectrum disorder: a systematic review about nutritional interventions. *Revista Paulista de Pediatria* [online]. 2020;38.
 24. Rocha GSS, Júnior FCM, Lima NDP, et al. Análise da seletividade alimentar de pessoas com Transtorno do Espectro Autista. *Revista Eletrônica Acervo Saúde*. 2019; 24:.e538.
 25. Sharp WG, Burrell TL, Berry RC, Stubbs KH, McCracken CE, Gillespie SE, et al. The Autism Managing Eating Aversions and Limited Variety Plan vs Parent Education: A Randomized Clinical Trial. *The Journal of Pediatrics*. 2019 Aug;211:185-192.e1.
 26. El-Rashidy O, El-Baz F, El-Gendy Y, Khalaf R, Reda D, Saad K. Ketogenic diet versus gluten free casein free diet in autistic children: a case-control study. *Metabolic Brain Disease*. 2017 Aug 14;32(6):1935–41.
 27. Leiva-García B, Planells E, Planells del Pozo P, Molina-López J. Association Between Feeding Problems and Oral Health Status in Children with Autism Spectrum Disorder. *Journal of Autism and Developmental Disorders* [Internet]. 2019 Sep 5;49(12):4997–5008. Available from: <https://link.springer.com/article/10.1007/s10803-019-04211-w>
 28. Piwowarczyk A, Horvath A, Pisula E. Gluten-Free Diet in Children with Autism Spectrum Disorders: A Randomized, Controlled, Single-Blinded Trial. *J Autism Dev Disord*. 2020;50:482–90.
 29. Hyman SL, Stewart PA, Foley J, et al. The Gluten-Free/Casein-Free Diet: A Double-Blind Challenge Trial in Children with Autism. *J Autism Dev Disord*. 2016;46(1):205-220.
 30. Lange KW, Hauser J, Reissmann A. Gluten-free and casein-free diets in the therapy of autism. *Current Opinion In Clinical Nutrition And Metabolic Care*. 2015;18(6): 572-75.
 31. Marí-Bauset S, Lopis-González A, Zazpe-García I, et al. Nutritional status of children with autism spectrum disorders (asds): a case-control study. *J Autism Dev Disord*. 2015;45(1): 203-12.
 32. Peretti S, Mariano M, Mazzocchetti C, et al. Diet: the keystone of autism spectrum disorder? *Nutr Neurosci*. 2019; 22(12):825-39.
 33. Trudeau MS, Madden RF, Parnell JA, et al. Dietary and Supplement-Based Complementary and Alternative Medicine Use in Pediatric Autism Spectrum Disorder. *Nutrients*. 2019;11: 1783.
 34. Magnanin T. (2019). *Autismo: Comer para nutrir bem*. Ed. Do autor. Criciúma, SP.