



State of the art of specialized nutritional intervention in pediatric patients with autism spectrum disorder: a guideline

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DOI: <https://doi.org/10.54448/ijn26318>

Received: 04-25-2026; Revised: 06-28-2026; Accepted: 07-01-2026; Published: 08-11-2026; IJN-id: e26318

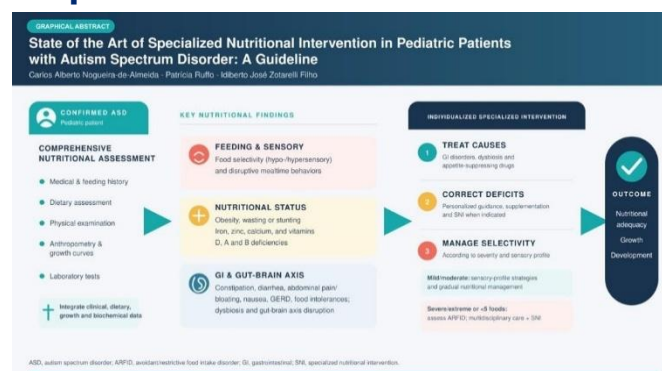
Editor: Dr Hind Mamoun Beheiry, MD, MPH.

Abstract

Autism Spectrum Disorder (ASD) is a complex and heterogeneous neurodevelopmental condition. The global prevalence of ASD has increased considerably in recent decades. Recent data from the United States estimate that 1 in 36 children is affected. Among the most significant health-related consequences of ASD are undoubtedly nutritional status disorders. In light of this, the present guideline outlines a nutritional treatment algorithm for ASD, with a focus on specialized nutritional interventions. The proposed algorithm enables an appropriate therapeutic approach that contributes significantly to improved health and quality of life, as well as to reducing family stress. Specialized nutritional intervention is necessary and serves as a simple, efficient method to help resolve a large proportion of nutritional issues in this patient group. Therefore, early nutritional intervention promotes healthier eating habits in children with ASD.

Keywords: Autism spectrum disorder. Algorithm. Nutritional treatment. Specialized nutritional intervention.

Graphical Abstract



Source: Own Authorship.

Introduction

Autism Spectrum Disorder (ASD) is a complex and heterogeneous neurodevelopmental condition characterized by persistent deficits in communication and social interaction, alongside restricted, repetitive patterns of behavior, interests, or activities [1]. The global prevalence of ASD has risen considerably in recent decades, impacting socioeconomic factors and public health [2]. ASD is increasingly encountered in medical practice. Recent data from the United States estimate that 1 in 36 children is affected [3]. Children with ASD exhibit deficits in communication and social interaction, as well as restricted, repetitive patterns of behavior, interests, or activities [4]. These alterations affect the entire body to some extent and have broad,

well-defined nutritional manifestations. A recent review by Nogueira-de-Almeida et al. [5] highlighted the most common nutritional repercussions, which are listed in Figure 1, taken from that publication.

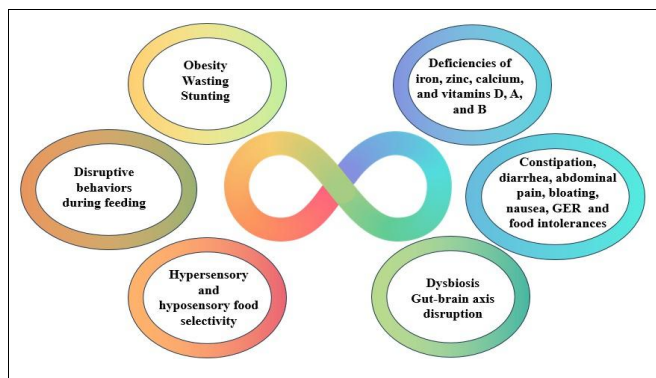


Figure 1. Nutritional problems associated with autism spectrum disorder (ASD). Source: Translated and adapted from Nogueira-de-Almeida et al. [3].

Food Selectivity and ASD

Food selectivity is a behavior characterized by the frequent or persistent refusal of certain foods, or entire food groups, due to characteristics such as taste, color, smell, consistency, or presentation [6]. Regarding ASD, among the aspects described in Figure 1, food selectivity stands out due to its high prevalence in this patient group, affecting 50% to 90% of them [7] and being 15 times more common in these children than in their neurotypical peers [8].

One of the most challenging aspects is that selectivity associated with ASD can manifest in two very distinct ways, involving either hypersensory or hyposensory characteristics [8-10]. The hypersensory profile is more common [11]; it leads to food refusal due to low tolerance for environmental stimuli [6] and the fact that patients perceive food characteristics in a very intense and uncomfortable manner [8]. Conversely, children with a hyposensory profile have great difficulty with the central processing of environmental information [12], making them less able to perceive flavors, smells, colors, noises, and textures [11]. In both cases, negative caloric balance, growth issues, and micronutrient deficiencies can occur; furthermore, in the presence of compulsive and repetitive behaviors—where a limited number of foods are consumed in large quantities—obesity may develop. The selectivity is often extremely severe, necessitating a differential diagnosis with Avoidant/Restrictive Food Intake Disorder (ARFID), a condition that frequently co-occurs with ASD.

Other manifestations with potential nutritional implications

In addition to food selectivity, other characteristics

described in Figure 1 contribute to the development of nutritional disorders in children with ASD. Disruptive behaviors during meals hinder the organization of family mealtimes and generate high levels of stress among caregivers and family members. Symptomatic gastrointestinal disorders can create negative associations with the act of eating, reducing intake and compromising digestion and absorption processes. Intestinal dysbiosis, in turn, often interferes with intestinal transit, affecting both nutrient intake and metabolism. Alterations in the gut-brain axis negatively impact mood and sleep, intensifying irritability - a common issue in these patients. Finally, micronutrient deficiencies can reduce appetite, alter sensory perception, and foster atypical behaviors, such as pica.

Major Clinical and Scientific Outcomes Supporting the Proposed Algorithm and Guideline

Problematic mealtime behaviors and poor diet quality are pressing concerns for children with ASD. Gray et al. (2024) [13] implemented and analyzed the "Autism Eats" program for children under 3 years of age with ASD. Healthy Eating Index (HEI-2015) scores were calculated based on 3-day food records. Problematic mealtime behaviors were assessed using the Brief Autism Mealtime Behavior Inventory; the Child Feeding Questionnaire was also utilized. A total of 51 participants completed the initial assessment, and 98% completed the 3-day food records and anthropometric measurements. Significantly higher levels of problematic mealtime behaviors were observed compared to the reference group (e.g., total score of 55.7 vs. 32.5; $p < 0.001$). Children with ASD exhibited lower HEI-2015 scores than those found in national data (e.g., total score of 59 vs. 62). A large proportion of the children (29%) had a weight-for-length $\geq$ 95th percentile. Therefore, early nutritional intervention impacts problematic mealtime behaviors and promotes healthier eating habits in children with ASD.

A retrospective observational study described the clinical, metabolic, and orthopedic manifestations of nutritional rickets in children with ASD. Patients were included if they exhibited clinical findings suggestive of rickets, laboratory evidence of vitamin D deficiency (with or without hypocalcemia), and radiographic findings consistent with the disease. Socioeconomic status was characterized using the Child Opportunity Index (COI) 2.0 based on residential zip code. A total of 11 patients (aged 4 to 16 years) met the inclusion criteria. All resided in neighborhoods located in the lowest COI quartile. All presented 25-hydroxyvitamin D levels < 10 ng/mL; eight had serum calcium < 7.0

mg/dL, and three experienced hypocalcemic seizures. Most patients improved with nutritional supplementation alone. At follow-up, serum calcium levels normalized in all patients; vitamin D levels normalized in four patients, remained low in six, and were undetectable in one patient. Serious complications included bilateral femoral neck fractures requiring open reduction and internal fixation, as well as deformities severe enough to require surgical intervention (osteotomy and guided growth). Thus, older children and adolescents with ASD and highly selective diets may develop severe nutritional rickets [14].

Also, Yildiz et al. (2026) [15] conducted a case-control study involving 118 children: 88 with ASD (DSM-5 criteria) and 30 healthy controls matched for age and sex. Based on Autism Behavior Checklist (ABC) scores, the patients with ASD were divided into Group I (ABC >60; n=48) and Group II (ABC ≤60; n=40). Levels of fibroblast growth factor 21 (FGF-21) and growth differentiation factor 15 (GDF-15) were measured using ELISA. Biochemical parameters, complete blood counts, plasma amino acids (LC-MS/MS), and urinary organic acids (GC-MS) were analyzed. FGF-21 levels were significantly elevated in the ASD group compared to controls ($p<0.0001$), whereas GDF-15 showed no difference ($p = 0.797$). The ASD group exhibited elevated levels of lactate, the lactate/pyruvate ratio, urea, AST, HDL, LDL, and lymphocyte and platelet counts, alongside reduced levels of pyruvate and serum and urinary creatinine ($p<0.05$). A reduction in essential and branched-chain amino acids was observed, while glycine and histidine levels increased ($p<0.05$). FGF-21 showed a weak yet significant correlation with markers of mitochondrial dysfunction and amino acid metabolism. ROC curve analysis indicated good diagnostic accuracy for FGF-21 regarding ASD (AUC=0.817), with a sensitivity of 98.9% and a specificity of 73.3% at a cutoff of 27.9 pg/mL. Urinary organic acids as methylmalonic acid, tiglylglycine, and 2-ketoisocaproic acid were significantly elevated ($p<0.05$). Thus, the authors reported that elevated serum FGF-21 levels in children with ASD are associated with metabolic alterations.

Finally, Cui et al. (2025) [16] conducted a systematic review to examine the intersection between rickets and ASD. All patients exhibited selective eating habits; the majority excluded dairy products and preferred potato-based foods. Musculoskeletal symptoms predominated, with common findings such as *genu valgum* (knock-knees), wrist widening, and metaphyseal irregularity (fraying). Seizures were the second most frequent reason for hospital admission, highlighting the importance of monitoring these

patients' neurological health. Calcium supplementation, primarily using calcium carbonate or calcium gluconate, was administered in all cases, and most patients showed normalization of biochemical markers, including serum calcium levels.

Assessment – Algorithm and Guideline

The algorithm shown in Figure 2 illustrates how the clinical assessment can be conducted.

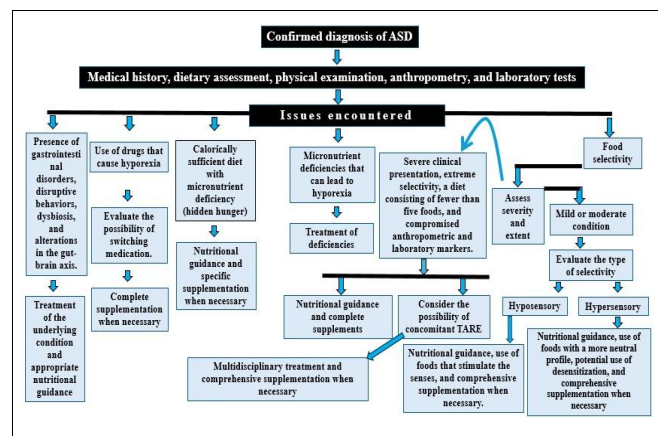


Figure 2. Nutritional treatment algorithm for ASD, focusing on specialized nutritional intervention. Source: Own authorship.

The first step is to confirm the ASD diagnosis. As this is not a simple process, it often entails assessment by multiple professionals. Once the suspicion is confirmed, the next step is to determine whether there are associated feeding difficulties. This is important because, although common, such difficulties may not necessarily be part of the clinical picture. If present, it is necessary to assess their profile and impact.

Anamnesis and dietary assessment

Dietary assessment aims to identify food intake patterns and compare them with current nutritional recommendations. This enables the identification of inadequate intake, whether insufficient or excessive, of energy, macronutrients, and micronutrients, as well as the characterization of the individual's eating habits. Consequently, it aids in diagnosing diet-related issues, allowing for the recommendation of appropriate treatment or nutritional guidance to minimize or correct such imbalances. Various dietary assessment methods exist for this purpose, but a 24-hour dietary recall is relatively simple and highly useful. Crucially, the results obtained should be compared against a reference standard, such as the food pyramid. Table 1 provides a concise, practical overview, based on the Brazilian Society of Pediatrics food pyramid [17], of how the diet observed during the assessment can be compared to the reference diet.

1. SIM NÃO	2. SIM NÃO	3. SIM NÃO	4. SIM NÃO
Figura 1. Você usa ou usa produtos à base de carne, subprodutos e restos, tais como arroz, peixe, farinha, macarrão, manteiga, biscoitos etc.? Essa grupo representa, basicamente, alimentos considerados de carboidratos especialmente a amido e que, portanto, fundamentalmente, fontes energéticas. Os produtos desse grupo representam 50% da dieta integral. O consumo adequado é recomendado pelo RDA em 40% da dieta, com base apenas na ingestão de carboidratos, e não na ingestão de proteínas e gorduras, bem como proteínas e açúcares livres, incluindo as cogonias. Apesar de ser a função de um carboidrato, ele não dá parte desse grupo. O consumo de 100% dos cereais desse grupo na forma integral pode apresentar algumas vantagens nutricionais, mas deve-se ter cuidado, devido ao fato de que alguns alimentos podem estar como quantidades de alguns minerais.	Figura 2. Você usa ou usa verduras e legumes? Verduras e legumes são fontes de vitaminas, minerais e fibras, além de antioxidantes. Também possuem proteínas, que ajudam a modular a microbiota intestinal. O baixo consumo desse grupo é causa frequente de constipação intestinal, devido às fibras. Quando esse grupo não é consumido, especialmente quando também há frutose não está presente na dieta, podem ocorrer deficiências vitamínicas.	Figura 3. Você usa ou usa frutas? Frutas são fontes de antioxidantes, além de fibras, vitaminas e minerais. Também possuem prebióticos, que ajudam a modular a microbiota intestinal. A falta de frutas na natureza por suas longas vidas e a escassez de carboidratos leva mais frutas para fazer sucos do que sucos com frutas. Assim, a natureza, além de naturezas efeitos metabólicos indesejáveis, quando esse grupo não é consumido, especialmente quando também as verduras e legumes não estão presentes na dieta, podem ocorrer deficiências vitamínicas e diabéticas.	Figura 4. Você usa ou usa leite, leite ou derivados? Laticínios fornecem proteínas de alto valor biológico e lipídios. Entretanto, sua função principal na infância refere-se à presença de cálcio de elevada biodisponibilidade, sendo a principal fonte dietética desse nutriente. A lactose do leite não é muito prebiótica. O baixo consumo pode levar à osteoporose. Para crianças com ingestão baixa de carne, os laticínios podem ser a cumprir o papel de principal fonte de proteínas e, nesse caso, a quantidade ingerida deve ser suficiente para uma boa absorção. Apesar de o leite conter lipídios saturados, eles são considerados de baixo poder aterogênico.

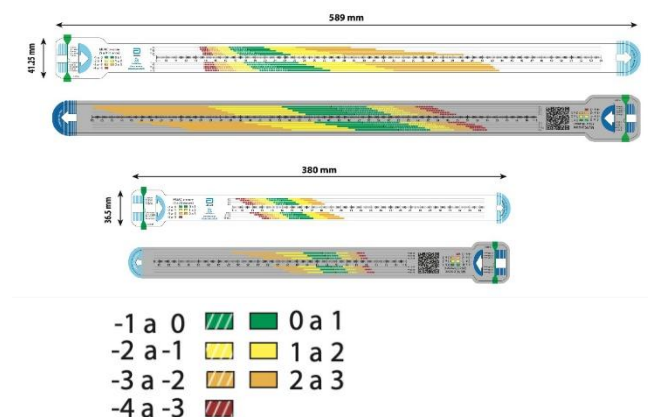
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Physical examination

Table 2. Nutritional abnormalities and associated nutrients.

Organ	Sign	Deficiency
General appearance	Emaciated, obese, edematous	Obesity, marasmus, kwashiorkor
Skin of the face and neck	Nasolabial seborrhea	Riboflavin, niacin
Mucous membranes	Pale	Anemia
	Petechiae, purpura	Ascorbic acid
	Scrotal and vulvar dermatitis	Riboflavin
	Symmetrical dermatitis of exposed areas, thickened friction areas	Niacin
	Follicular hyperkeratosis	Vitamin A
	"Crazy-paving" dermatitis	Vitamin A, protein
	Postural edema	Protein, thiamine
Subcutaneous tissue	Reduced	Protein-energy
Body hair	Change in color and texture; detaches easily	Protein-energy
	Brittle, dull hair; easily pulled out	Zinc
	Xerophthalmia, keratomalacia	Vitamin A
	Bitot's spots	Vitamin A
Eyes	Pericorneal congestion	Riboflavin
	Conjunctival pallor	Anemia
	Impaired vision in dim light	Vitamin A, zinc
Lips	Quelite angular ou escara	Niacin, riboflavin
	Queilose	Niacin, riboflavin
Gums and teeth	Acute periodontal gingivitis, dental caries	Ascorbic acid
	Loss of tooth enamel	Fluoride, zinc
Tongue	Smooth, pale, atrophic	Anemia
	Reduced taste sensitivity	Zinc
	Red, painful, denuded, edema	Niacin, riboflavin
Glands	Goiter	Iodine
	Parotid enlargement	Protein
Skeleton	Costochondral rosary	Vitamins C and D
	Cranial bossing, craniotabes	Vitamin D
	Epiphyseal widening, especially at the wrists	Vitamin D
Neurological	Loss of vibratory sensation and deep reflexes	
	Calf pain	Thiamine
Extremities	Pain on movement, frog-leg position	Vitamin C

The first step is to measure weight and height and calculate the body mass index (BMI). These data should be plotted on WHO growth curves [19]. Height and BMI values below a z-score of -2, or those showing a downward trend even if above -2, should be considered at-risk. In such cases, dietary intake of macronutrients and micronutrients may be insufficient. A highly efficient and simple strategy is the use of mid-upper arm circumference (MUAC) measurement [20]. Recently, MUAC data [21] validated against BMI [20, 22-24] have been produced, enabling rapid assessment of nutritional status using a single tape; in addition to taking measurements, the tape uses a color-coded system to provide an immediate diagnosis, indicating when values fall below a z-score of -2—thereby signifying insufficient dietary intake [22]. Figure 3 shows the MUAC tape.



Laboratory tests

Treatment

The treatment strategy, focusing on supplementation, is summarized in Figure 2. Specialized nutritional intervention (SNI) will be indicated at various stages. In this article, SNI refers to the use of a complete isocaloric supplement, defined as

a "supplement containing 1 kcal/mL, intended to provide all the nutrients a balanced diet would supply at a given energy intake, including a balanced mix of macro- and micronutrients" [27]. The first step is to conduct a comprehensive clinical assessment, including an evaluation of nutritional status, as discussed above. From this point, it is suggested that associated problems requiring specific treatment be identified. The main ones are described below.

Presence of gastrointestinal disorders, disruptive behaviors, dysbiosis, and gut-brain axis alterations

These problems are common in children with ASD and require specific treatment. Intense nausea, abdominal pain, gastroesophageal reflux, diarrhea, or constipation often leads to low food intake and must be addressed therapeutically. Disruptive behaviors significantly compromise mealtime, leading to family dynamic imbalances and intense stress. Similarly, specialized strategies implemented under professional guidance are needed to address this issue. While alterations in the gut-brain axis are difficult to confirm, the high prevalence of dysbiosis in this group makes their presence highly likely. Ideally, microbiota restoration can be achieved through dietary adjustments, though the use of prebiotics and probiotics may often be necessary [5]. If there is an associated caloric intake deficit, the concomitant use of SNI is indicated.

Use of medications that cause hyporexia

Medications frequently used for ASD can lead to a lack of appetite and low food intake. Examples include fluoxetine, atomoxetine, topiramate, methylphenidate, and lisdexamfetamine, among others. In such cases, once this adverse effect and its impact on nutritional health become evident, it is worth discussing the possibility of switching medications with the prescribing professional. If this is not possible, the child will likely require SNI [28].

Hidden hunger

"Hidden hunger" refers to situations where the diet provides sufficient calories but fails to ensure an adequate intake of micronutrients. In these cases, specific supplementation of the missing vitamins and/or minerals is required [29].

Micronutrient deficiency leading to hyporexia

Deficiencies in various micronutrients can lead to reduced appetite and/or hunger, resulting in insufficient food intake. Examples include thiamine,

cobalamin, vitamin A, zinc, and iron [30-32]. Treatment involves supplementing the deficient elements. In some instances, low vitamin and mineral intake co-occurs with low caloric intake. In such cases, the use of SNI can address both problems simultaneously, offering the advantage of prescribing a single product.

Food selectivity

The consequences of this restricted diet range from mild issues to severe cases of malnutrition, obesity, or specific vitamin deficiencies. While the strategy for a hyposensitive profile may involve hyper-stimulation through food (using strong seasonings and crunchy textures), the hypersensitive profile requires a more cautious and gradual approach, potentially involving desensitization therapy. There is no single formula for treatment, but the current consensus points to the potential need for a multidisciplinary team, including speech-language pathologists, psychologists, nutritionists, and physicians, and the involvement of the entire family unit to transform the mealtime environment [5]. Specific strategies for each profile can be reviewed in the recent publication by Nogueira-de-Almeida et al. [5].

In this context, the prescription of SNI can be extremely useful. In severe cases, SNI will certainly be necessary. In milder cases involving hypo- or hypersensitive profiles, caloric intake is often very low, making supplementation necessary to prevent malnutrition. The prescribed amount will always depend on the magnitude of the caloric deficit. For most patients, 400 mL/day is likely sufficient, though larger amounts may be required due to a drastic reduction in food intake. When ARFID (Avoidant/Restrictive Food Intake Disorder) is also present, it is crucial to implement multiprofessional therapy alongside the use of SNI.

Final considerations

Nutritional status disorders are undoubtedly among the most significant health-related consequences of autism spectrum disorder. In this context, an appropriate therapeutic approach can significantly improve health and quality of life, while also helping to reduce family stress. The use of specialized nutritional intervention is often necessary and serves as a simple, efficient way to help resolve many of the nutritional issues faced by this patient group.

CrediT

Author contributions: **Conceptualization; Data**

curation; Formal Analysis; Investigation; Methodology; Project administration; Supervision; Writing - original draft; Writing-review & editing- Carlos Alberto Nogueira-de-Almeida, Patrícia Ruffo, and Idiberto José Zotarelli Filho.

Acknowledgment

Not applicable.

Ethical Approval

Not applicable.

Informed Consent

Not applicable.

Funding

We appreciate Abbott Laboratories' sponsorship for the open-access publication of this scientific review article.

Data Sharing Statement

All referenced sources are accessible through the respective journals or public repositories.

Conflict of Interest

Author Patrícia Ruffo declares a conflict of interest with Abbott Laboratories. The other authors declare no conflicts of interest.

Similarity Check

It was applied by Ithenticate®.

Application of Artificial Intelligence (AI)

Not applicable.

Peer Review Process

It was performed.

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