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*Review*

# Nutrition-related autism causes

Autism causes

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**Abstract**

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by significant delays in interaction and communication, as well as restrictive interests. With increasing prevalence rates worldwide and in Türkiye, ASD has become a topic of extensive study. Although the exact cause remains unknown, research has explored various factors, including the potential impact of nutrition a critical environmental factor influencing brain development.

The term "nutrition" here refers not only to a child's diet after birth but also to maternal nutrition before and during pregnancy. Studies suggest that maternal diet during these periods plays a significant role in a child's development. Moreover, individuals with ASD may experience nutritional deficiencies due to selective eating habits or gastrointestinal issues, which can further exacerbate symptoms. On the other hand, such deficiencies might also contribute to the onset of autism.

This review aims to examine the relationship between nutrition and the development of ASD and to evaluate the potential effects of nutrition on autism formation or symptom management.

**Keywords**

autism spectrum disorder, food supplements, diet, nutrition, nutrition therapy

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## Introduction

Autism Spectrum Disorder (ASD) is a lifelong neurodevelopmental disorder that begins in early childhood and is characterized by deficits in social communication skills, repetitive behaviors, and restricted areas of interest. Autism is generally noticed within the first three years of life, with behaviors such as lack of eye contact, failure to respond to being called, attention deficits, and difficulties in non-verbal communication. These signs may not be recognized in very young children but become more apparent as the child begins to speak. Clinically, ASD is a heterogeneous condition, meaning it manifests differently among individuals, with varying severity.[1-3]

The general prevalence of autism has significantly increased in recent years, and the National Health Statistics Unit has reported the most recent prevalence rate of 1 in 36.[4] According to a study conducted in 11 states in the United States (USA), where the sample group consisted of children under the age of 8, the prevalence of autism is 17 per 1,000.[5] In Türkiye although the exact prevalence within the general population is unknown, it is estimated to be similar to the global average.[6]

There are various studies conducted by institutions in Türkiye regarding the number of individuals with ASD. According to these studies, the total number of individuals diagnosed with ASD is reported to be 107,834.[6,7] Autism is 4.5 times more common in males, and the condition tends to be more severe in female children.[8]

### *Nutrition and Autism*

The exact cause of autism remains unknown, but biological, genetic, and environmental factors likely contribute. Epigenetics, the interaction between environment and genes, plays a significant role in central nervous system development. While genetic factors are implicated in 10-20% of Autism Spectrum Disorder (ASD) cases, genetic susceptibility may increase vulnerability to environmental risk factors or alter genetic expression.[2,3]

Key environmental risk factors associated with ASD include:

- Nutrition
- Maternal metabolic issues
- Infections
- Neurotoxic agents
- Air pollution
- Advanced parental age
- Vaccines
- Vitamin D deficiency

Particularly studied factors include medications, heavy metals (e.g., lead, mercury), pesticides, polybrominated diphenyl ethers, and polycyclic aromatic hydrocarbons.[6]

ASD, a neurodevelopmental disorder, is considered a brain development disorder. Brain development begins shortly after conception and continues into early adulthood, with rapid growth during the first 1,000 days. Nutrition plays a vital role in gene expression during this period. Research shows that the timing, severity, and chronicity of nutritional deficiencies can uniquely affect brain development, cognition, and behavior.[9]

Given the rapid rise in ASD prevalence, evidence suggests nutrition may influence its development, highlighting the need for further investigation.[10]

The Importance of Oxidative Stress and Antioxidants in Autism

Free radicals are high-energy compounds with unpaired electrons in their outer orbitals. Due to their tendency to pair their unpaired electrons, the high energy they produce can damage biological structures, such as proteins, lipids, nucleotides, and coenzymes.[11] Most reactive oxygen species (ROS) are free radicals. The cell is protected from oxidative stress caused by ROS by cellular antioxidants such as reactive nitrogen species (RNS).[12] When the level of ROS exceeds the cell's antioxidant capacity, oxidative stress occurs. Oxidative stress is a mediator of brain damage, stroke, and neurodegenerative diseases. Studies have shown that oxidative stress plays a role in the pathogenesis of many neuropsychiatric disorders, including Alzheimer's disease, Parkinson's disease, schizophrenia, bipolar disorder, and autism.[14] Therefore, controlling ROS production is essential for maintaining normal cellular function. An increase in ROS in the central nervous system can lead to a decrease in the number of brain cells, which is thought to contribute to the development of autism.[11,12]

Antioxidant mechanisms that prevent oxidative stress include detoxified metabolites, antioxidant enzymes, proteins, vitamins, and minerals.[13] Therefore, a diet designed considering the balance between free radicals and antioxidants could play an important role in the treatment or prevention of autism progression.[11,14]

Exogenous (externally sourced) antioxidants that can be obtained from the diet include α-Tocopherol (Vitamin E), β-carotene (Vitamin A), ascorbic acid (Vitamin C), and folic acid (Vitamin B9).[14] Few studies have investigated the increased vulnerability to oxidative stress in ASD. Previous studies have shown that endogenous antioxidant defense is inadequate in ASD, suggesting that exogenous antioxidants could play a critical role in preventing oxidative stress in autism.[15]

### *Vitamin and Mineral Deficiencies and Autism*

Vitamin and mineral deficiencies are often associated with autism, potentially due to intestinal permeability, food selectivity, or specific diets, and they can affect neurofunctional development. Addressing these deficiencies is believed to help alleviate autism symptoms. Recent literature indicates that vitamin and mineral supplementation has become popular in autism, with oral supplementation showing potential to improve the nutritional and metabolic status of children with autism.[15-18]

Studies have shown that children with autism often have lower levels of vitamins such as pantothenic acid, biotin, folate, vitamin B-12, vitamin D, and E in their serum. Mineral concentrations like lithium, calcium, magnesium, iodine, chromium, and selenium are also lower compared to healthy children.[16]

Vitamin B6, or pyridoxine, is important, but it must be converted into its active form, Pyridoxal 5-phosphate (P5P), for proper utilization. Low conversion rates of pyridoxine to P5P contribute to neurobehavioral disorders in autism.[17] Vitamin B6 plays a role in synthesizing neurotransmitters like serotonin, GABA, dopamine, norepinephrine, and epinephrine, which are often found to be imbalanced in autism.[19,20] Magnesium and zinc also affect Vitamin B6 utilization, thus influencing autism symptoms.[17,21]

Vitamin C is an antioxidant that plays a crucial role in neurotransmitter synthesis and reducing oxidative stress in

children with autism.[17-19] Vitamin B12 and folate are essential for central nervous system development, and their deficiencies are commonly observed in autism. Vitamin B12 deficiency, in particular, has been linked to eating difficulties and neurological issues in children with autism.[18,22]

Folate metabolism abnormalities in children with autism are significant, with issues in folate transport to the brain due to autoantibodies blocking folate receptors.[23] Early detection of these autoantibodies may be crucial for preventing or managing autism.[24]

Vitamin D also plays a neuroprotective role, and its deficiency has been linked to neuropsychiatric disorders like autism[18,25] Iron deficiency, commonly seen in children with autism, can lead to sleep and nervous system disorders.[18,26,27]

### *Omega-3 Fatty Acids*

Omega-3 fatty acids are critical for brain development and nervous system function.[19,27] A deficiency may disrupt neural development, potentially contributing to autism in childhood. Research suggests omega-3 supplementation could benefit individuals with Autism Spectrum Disorder (ASD). Studies have identified an imbalance in the omega-3/omega-6 fatty acid ratio in ASD patients, with elevated omega-6 and reduced omega-3 levels.[28,29]

The evidence on omega-3's impact on autism symptoms remains mixed, warranting further investigation into its role and potential deficiency in ASD.

### *Prebiotics and Autism Spectrum Disorder (ASD)*

Postnatal development is closely linked to the microbiome, highlighting the strong connection between the gut and brain. While autism's exact causes remain unclear, the gastrointestinal system significantly influences its development.[30,31]

Individuals with autism often exhibit abnormal digestive health, including "leaky gut" syndrome caused by mucosal inflammation and abnormal bacterial metabolites, which disrupt the intestinal barrier. Neuroactive compounds from the gut that cross the blood-brain barrier may also contribute to cognitive and behavioral changes, linking gastrointestinal health to neurodevelopmental disorders.[32]

Studies suggest that improved gut health may reduce autism symptoms. Interventions such as gluten-free and casein-free diets, multivitamins, prebiotics, and probiotics have shown promise. Probiotics, such as Lactobacillus and Bifidobacterium, may improve intestinal permeability and stabilize behavioral abnormalities. Preclinical and clinical findings suggest probiotics can enhance gastrointestinal health, though their effects on autism symptoms remain uncertain.[33]

Both prebiotics and probiotics play critical roles in neuroimmune processes by regulating gastrointestinal microbiota, the immune system, and the nervous system. Prebiotics serve as fuel for probiotics, while probiotics influence gut health; their synergistic relationship forms synbiotic foods. Synbiotic products enhance gut health by preventing issues like leaky gut and immune dysfunction.[34]

In summary, probiotics and their combination with prebiotics have gained attention as potential therapies for improving gastrointestinal health and symptoms in individuals with autism.

### *Maternal Nutrition During Pregnancy and Lactation and Its Relationship with Autism*

Brain development begins in the womb and continues until approximately age 21. External factors during this period can lead to pathologies such as attention deficits, autism, and intellectual disabilities.[35-37] Maternal nutrition plays a vital role in fetal brain development, with macronutrients supporting structural growth and micronutrients essential for myelination, synaptogenesis, and neurotransmitter functions. Maternal malnutrition has been linked to impaired brain development, and conditions such as obesity, diabetes, and hypertension increase the risk of neurodevelopmental disorders, including autism.[19,38-41]

Deficiencies in nutrients such as folic acid and vitamin D are particularly associated with an increased risk of Autism Spectrum Disorder (ASD). Maternal vitamin D deficiency, especially during the first trimester, may lead to cognitive dysfunction, language delays, and a heightened risk of autism. This risk is more pronounced in high-latitude regions where ultraviolet B radiation is limited.[18,42] However, the mechanisms linking vitamin D deficiency and ASD remain unclear.

Heavy metal exposure from the mother can also affect fetal brain development. Metals like lead, mercury, and arsenic can cross the placenta or be transferred through breastmilk, disrupting brain tissue and increasing the risk of developmental delays, hyperactivity, and autism. Lead exposure from the 12th week of pregnancy has been shown to cause chronic brain damage and impair the blood-brain barrier. Expectant and breastfeeding mothers are advised to minimize exposure to heavy metals found in food, cookware, and the environment.[43,44]

The link between autism and gluten/casein is tied to increased peptide levels, which interfere with brain signaling pathways. Avoiding gluten and casein during pregnancy and early childhood may help reduce autism risk, as suggested by some studies.[45]

### *The Relationship Between Breastfeeding and Autism*

Early environmental factors during prenatal and perinatal periods are linked to autism. While many cases of Autism Spectrum Disorder (ASD) are associated with these factors, some infants develop ASD symptoms later, indicating potential post-birth contributors.[46]

Breastfeeding is a key factor. The WHO and the American Academy of Pediatrics recommend exclusive breastfeeding for the first six months and continued breastfeeding for at least one year. Breast milk, rich in vitamins and minerals, strengthens the immune system and positively impacts brain development, cognition, and mental health. Breastfeeding directly from the mother may act as a protective factor against ASD.[46,47]

Evidence on breastfeeding's role in ASD is mixed. Some studies associate longer breastfeeding durations with reduced ASD risk, while others report no significant link.[48] For example, a study of 88 autistic children and 61 healthy controls found shorter breastfeeding durations in the ASD group but no statistically significant difference overall. However, children with severe ASD had significantly shorter breastfeeding durations, and a negative correlation was noted between breastfeeding duration and ASD severity.[49]

Bittker and Bell (2018) found that longer breastfeeding durations reduced ASD risk.[50] Similarly, Schultz et al. reported that formula-fed infants lacking DHA/ARA supplementation were more likely to develop ASD. Breast milk's immune-protective components, such as immunoglobulin A (IgA), and formula with DHA/ARA supplementation were linked to better immune function.[51] Conversely, a 2015 study by Husk and Keim found no relationship between breastfeeding and ASD.[47]
Overall, most studies suggest a potential protective role of breastfeeding in ASD, though findings are inconsistent. Further research is needed to clarify this relationship.[52]

### *Ethics Approval*
This study is a narrative review of previously published literature. Ethical approval was not required.

### *Statistical Analysis*
No statistical analysis was performed, as this study is based on a review of existing literature.

### *Reporting Guidelines*
This manuscript is a narrative review and does not follow a specific reporting guideline.

### *Limitations*
As a narrative review, this study did not employ a predefined systematic search strategy. Differences in study design, sample size, and outcome measures across the literature, together with the currently evolving evidence base and the limited availability of large, high-quality randomized controlled trials, may influence the strength of the conclusions.

### *Conclusion*
Today, nutrition plays a significant role in the treatment and prevention of many diseases. The positive effects of adequate and balanced nutrition on brain development have been proven. With the increasing prevalence of ASD, nutrition, as an environmental factor, has been linked to autism. The frequent occurrence of vitamin and mineral deficiencies in children with autism suggests that these deficiencies may contribute to autism. Improvements in autism symptoms following the correction of these deficiencies support this theory. Studies have also shown that maternal malnutrition or obesity before and during pregnancy can lead to the development of autism. Although deficiencies in vitamin D and folic acid in the mother have been linked to the development of autism, the exact mechanisms remain unclear. Furthermore, the consumption or supplementation of prebiotics and probiotics to address common gastrointestinal issues in autism, as well as a diet rich in antioxidants to reduce oxidative stress, have shown potential in preventing autism or alleviating symptoms. Research indicating that breastfeeding can act as a protective factor against the development of autism-like symptoms or reduce existing autism symptoms exists, but there is no conclusive information regarding the optimal duration of breastfeeding. Although many studies have explored the relationship between nutrition and autism, the results remain inconclusive. The differences and uncertainties in the findings suggest that more research is needed. It is believed that addressing nutritional deficiencies in individuals with autism may alleviate symptoms, improve cognitive function, and have positive effects on behavior. Therefore, a personalized, adequate, and balanced nutrition plan should be recommended for individuals with autism, taking into account their specific health issues.

***Ethics Declarations***
*Ethical approval was not required as this study is a review of previously published literature.*

***Animal and Human Rights Statement***
*No human participants or animals were involved in this study.*

***Informed Consent***
*Not applicable.*

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*No new data were generated or analyzed in this study.*

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*The authors declare no conflict of interest.*

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*The authors declare full responsibility for the scientific content and integrity of this review article.*

***Abbreviations***
*ARA: Arachidonic Acid*
*ASD: Autism Spectrum Disorder*
*DHA: Docosahexaenoic Acid*
*IgA: Immunoglobulin A*
*P5P: Pyridoxal 5-Phosphate*
*RNS: Reactive Nitrogen Species*
*ROS: Reactive Oxygen Species*

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