The Relationship Between Dietary Patterns and ASD

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Abstract. The dietary intake pattern of the mother when preparing for pregnancy, during pregnancy, and the nutritional exposure of the infant after birth have a bearing on the likelihood of the infant developing autism spectrum disorder (ASD). Many types of research have revealed a relationship between diet and the onset of ASD. However, it has not been established whether diet can be used to control the manifestation of ASD or in the prevention of ASD in unborn children. Therefore, there is an interest in ascertaining the main reasons for the relationship between dietary patterns and ASD. This paper analyzes studies about nutrition and its influence on ASD. In addition, the research explores the whole spectrum of environmental factors, namely external and internal ones, and their potential impact on an infant. Furthermore, the paper discusses the nutrition of the offspring and an approach to preventing the risk of ASD. The combination of different factors such as the mother's nutrition at various stages, the nutrition available to the infant, and the environment have been indicated in the results of the analysis to determine the level of risk for ASD in children. In this regard, further investigation of ASD prevention among infants is highly important and should be encouraged.

Keywords: Dietary Pattern, ASD, Malnutrition, Nutrient Deficiency.

1. Introduction

Autism spectrum disorder (ASD) can be viewed as a developmental and communication disability resulting from brain changes. Some individuals with ASD have a medically recognized problem, such as a genetic disorder. Other causes are currently unknown. Because ASD is a complex problem, it presents unique challenges for each field of medicine. The increasing prevalence of ASD currently affects 1 in every 44 children [1]. Nutritional screening and frequent assessment of children with ASD is an important clinical practice because it may help avert multiple risk factors that intensify the prevalence of malnutrition. Notably, eating foods containing gluten and casein has been associated with ASD in young children. Due to improper maternal nutrition, children often have food-related medical problems including gastrointestinal discomfort, inflammatory bowel disease, diarrhea, constipation, and acid reflux. Cases of ASD should also be evaluated from an environmental perspective, considering both internal and external factors. An accurate understanding of the nutritional risks inherent in children with ASD is of great value to the clinician responsible for nutritional surveillance and parents concerned about the influences of limited or restrictive diets [1]. Therefore, the paper considers gastrointestinal tract and immune system irregularities and neuropeptide disbalance and their function in the pathophysiology of ASD while examining the leading causes of the disorder. It also investigates whether it influences the manifestation of the disorder in children. In addition, risk characteristics enclose more senior parents, low birth weight, preterm birth, and usage of valproic acid or thalidomide during pregnancy.

2. Causes of ASD

The causes of ASD remain unknown to most professionals in the scientific community. However, its likelihood of occurring is positively associated with maternal deficiencies in nutrition (see Fig 1). Nevertheless, there is no evidence that nutrition is the predominant cause of unborn children developing ASD.

Numerous studies show that ASD is a consequence of multiple causes. Several factors that increase children's likelihood of developing ASD have been identified, including environmental, biological,

and genetic factors. However, investigations have shown that ASD can occur early in development as a disturbance in the average growth of the brain [2]. These disturbances may be due to defective genes that affect the evolution of the brain and control how brain cells propagate to each other. Some environmental aspects and associated disorders, such as gastrointestinal oddities and resistant imbalances, are involved in the pathophysiology of ASD [3]. One neuropathological manifestation of ASD is focal cortical dysplasia due to heterochromatic germ cell division, which causes germ cells to migrate abnormally to their target area. Irregular neuronal migration results in detached foci of thin cortical regions in the brains of individuals with ASD, particularly in the frontal lobe with smaller pyramidal and medial neurons [4]. These pathological findings are associated with sensory and motor deficits and seizures seen in ASD. The autistic epilepsy phenotype is linked to microcephaly, a pathological condition resulting from rapid brain development in the early stages, which leads to ASD. There is evidence of inflated total brain volume and altered gray matter volume in patients with ASD.

ASD is more common among premature infants. Nevertheless, numerous studies demonstrated that immunization to prevent transmittable diseases in preadolescents does not relate to the risk of ASD [2]. Studies on twins show that some people have a genetic propensity to autism. Research on identical twins has demonstrated that if one twin is impacted, there is a 36-95% chance that the other will also be affected. Families with one offspring with ASD have a greater chance of having another child with the same issues. Most of the genes associated with autism are implicated in chemical connections between neurons in the brain [2].

In some cases, parents and other family members of individuals with ASD may show minor barriers to social communication skills or display recursive behaviors. There is also proof that emotional disturbances, such as bipolar disorder and schizophrenia, are more common in families where one of them with ASD. In addition to genetic deviations inherited in almost all human cells, contemporary research has shown that genetic modifications can affect the chance of autism spectrum disorders development [2]. These mutations can occur naturally in a parent's sperm or egg or during fertilization due to a change in the deoxyribonucleic acid sequence or DNA, a human genetic material [2].

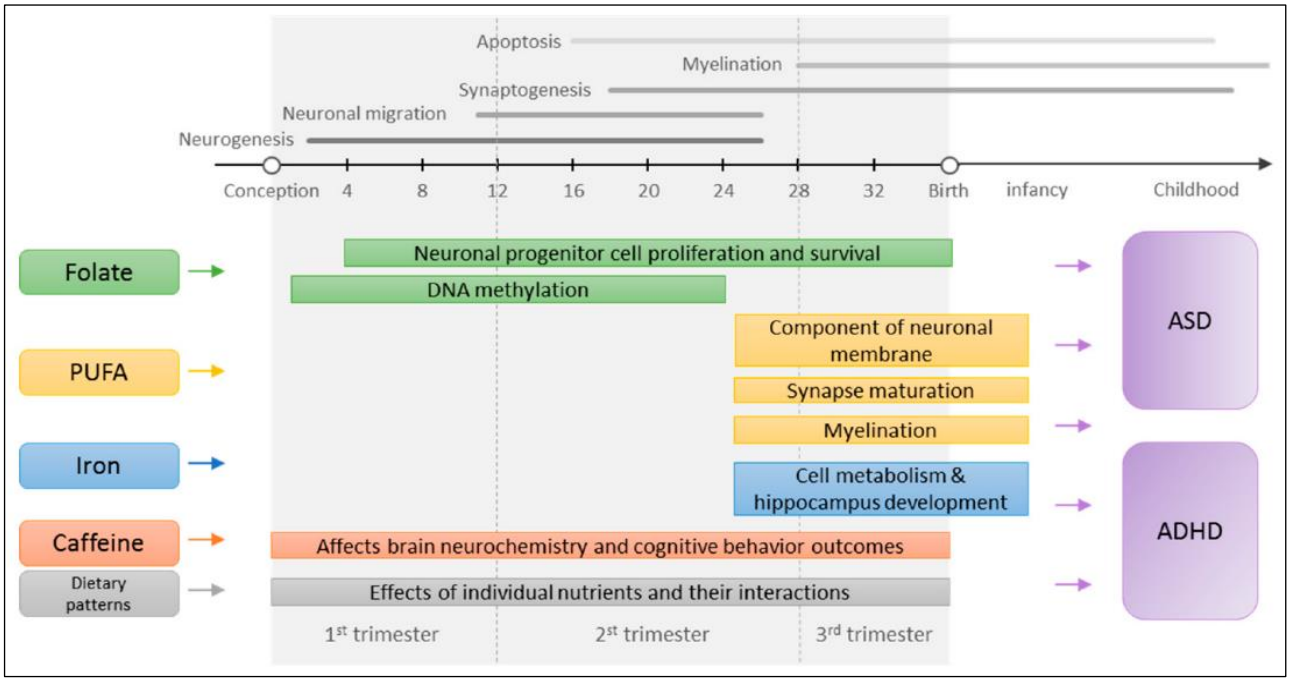


Fig. 1 The Effect of Nutrition on the Unborn Child During Various Stages of Gestation [5]

3. Relationship Between Nutrition and ASD

3.1. Maternal Nutrition

Maternal nutrition is essential for the embryo's brain development, and the parent's nutritional insufficiency is regarded as a risk aspect for schizophrenia, neural tube defects, and other neurodevelopmental disorders. During pregnancy, as the embryo's nutritional needs gradually increase, the mother's own nutritional deficiencies may affect the development of the fetal brain. This has directed the supposition that maternal diet may be a menacing element for ASD. Accordingly, maternal supplementation of folic acid or multivitamins was found to have an inverse relationship with the likelihood of ASD manifesting in the offspring [5]. A study with pregnant female rodents proved that maternal protein deficiency is comparable to ASD symptoms in the offspring [6]. Since the prenatal period is sensitive, great attention should be paid to the status of nutrients of an autistic child's mother. Although researchers have examined the significance of diet and nourishment in youngsters with ASD, the literature lacks a link between maternal nutrition and ASD in offspring [6]. Current proof regarding mothers taking folic acid, iron, and multivitamins in averting autism spectrum disorder (ASD) in their children is inconclusive.

Fatty acids are crucial for brain evolution. Studies of the correlation between maternal fatty acid intake and ASD risk have shown that insufficient omega-3 fatty acid intake is associated with significant risk [6]. In particular, antioxidants, vitamins, minerals, and trace elements are essential for the regular metabolism of neurotrophic facets [6]. For example, there is evidence that ASD is caused by vitamin D insufficiency during pregnancy as well as during infancy. Similarly, iron deficiency is more prevalent in children with ASD. Since multiple nutrients are needed for the development and proper functioning of the brain of children, the upkeep of appropriate nutritional status can be viewed as a key to ASD prevention.

Dietary guidelines often recommend that pregnant or lactating mothers take supplements to support dietary intake, mainly when essential nutrients are not fully obtained from the diet. The effectiveness of these supplements depends on the nutrient. For instance, studies of supplements with calcium have been said to reduce the incidence of preeclampsia and premature birth in pregnant women at high risk, with no improvement in neonatal outcomes. Zinc supplementation is also believed to have a positive effect on reducing preterm birth. Even though supplements appear to have advantageous effects, most studies are examining the effectiveness of supplements to determine how population and lifestyle considerations (e.g., maternal age, nationality, comorbid conditions, physical activity) are likely to interact with the reported outcome of pregnancy [6]. Hence, the mentioned recommendations must be considered and constructed with caution. Further studies are expected to consider aspects of demographics and lifestyle, plus other potential aspects that influence supplement absorption and outcomes (e.g., dosage, dietary source, and absorption method).

3.2. Role of Diet in the Incidence of ASD

Diet has a critical impact on the likelihood of developing ASD. There are two main diets recommended for women to prevent ASD. The first is a ketogenic diet which is based on the idea that abnormalities cause autistic behavior in carbohydrate metabolism in cells [7]. A ketogenic diet can also balance the process when mitochondria do not work as well as they should. A ketogenic diet is high in fat and low in carbohydrates and carefully controls protein levels. In an open study of 30 autistic children over six months, 60% showed various improvements in social interaction, hyperactivity, teamwork, and memory [7]. Several studies have compared the effects of ketogenic diets (such as the modified Atkins diet) to gluten-free or casein-free diets on ASD. As a result, the Children's Autism Rating Scale and Autism Treatment Evaluation Test scores in both diets show better results than children on regular nourishment.

The second is a monosaccharide diet. An easily digestible monosaccharide diet has been proposed as it circumvents some of the problems caused by the lack of enzymes required for carbohydrate metabolism. However, data on safety and efficacy are limited [6]. A general reduction in

carbohydrates may be an alternative to this approach. Adopting a diet for the individual symptoms of the disease depends on the patient's nutritional needs and food preferences. Experts emphasize that continuous observation of the diet plan and the status of nutrition of children affected by ASD is crucial [6]. ASD children had a diet with a high prevalence of energy and fat and low in fruits and vegetables. Similarly, consumption of lean meat of all types was associated with more increased consumption of fish and dietary fat [8]. Increased dairy product intake is also associated with enriched cereal and pasta consumption. They also frequently consumed products with low nutritional value, such as beverages, confectionaries, and snacks. Children with ASD have higher healthy titration response rates for energy, saturated fat, calcium, and vitamin C than controls and lower for iron, iodine, and B vitamins [8]. In conclusion, this highlights the need to assess dietary patterns and intake of nutrients in children with ASD to correct changes and prevent potential foodborne illnesses. It is also critical to start a proper diet for people with autism since their well-being suffers due to them being overweight, obese, or malnourished. Nevertheless, diet alone is often not enough to effectively treat ASD.

4. Factor Affecting ASD

4.1. Offspring Genetic and Nutrition

The internal genetic makeup of the offspring influences the likelihood of the child developing ASD. A child born in a family with a history of ASD has a high probability of developing the condition if the parent or the offspring is exposed to diseases that increase the risk of ASD [9]. Maternal nutritive status and body mass index during gestation have been indicated as environmental factors that affect brain growth via surplus or deficiency of micronutrients and growth factors and affect offspring neurodevelopmental outcomes [9]. In this regard, maternal obesity and low birth weight are connected with a major hazard of ASD. Maternal obesity activates the mother's immune system. It induces chronic inflammation of the uterine environment, which promotes the growth and differentiation of fetal nerve cells, leading to neurodevelopmental disorders in the offspring [9].

Moreover, maternal malnutrition can trigger a physiological pressure reaction that causes neuronal harm via the disproportionate release of proinflammatory factors (see Fig 2). The same can be stated about the continued malnutrition of the offspring. Supplementing calcium when preparing for pregnancy has reduced the chances of ASD in the offspring [10]. A study on children with confirmed ASD revealed a lower intake of fruits and vegetables, which denied them the needed calcium, iron, and B-complex micronutrients to help lower the incidences and exhibition of ASD behaviors [11]. Further, consumption of foods with gluten and casein results in a pronounced presentation of ASD in young children. Modifying nutrient intake to gluten-free and casein-free (GFCF) has been proven effective in controlling the condition and suppressing its manifestation [12]. Hence, a particular nutrition plan is suggested for children with ASD (see Fig 3).

Conceptual folic acid supplementation is generally considered to be an adequate backup for minimizing the risk of neural tubular lesions and some other disorders related to neuropsychiatry [8]. Li's analysis further tested the effect of prenatal folate intake during early pregnancy on the protection of fetal ASD. Even though there is lacking proof to confirm the idea that maternal folic acid intake due to gestation decreases the chance of ASD in children, the quantity of sample for analyses is small, and the results should be considered with caution. More population-based studies are urgently needed to determine and confirm when and at what level of folic acid intake is protective for the offspring with ASD. Thus, the optimal dose of folate is important for the health of pregnant women, safe childbirth, and fetal growth.

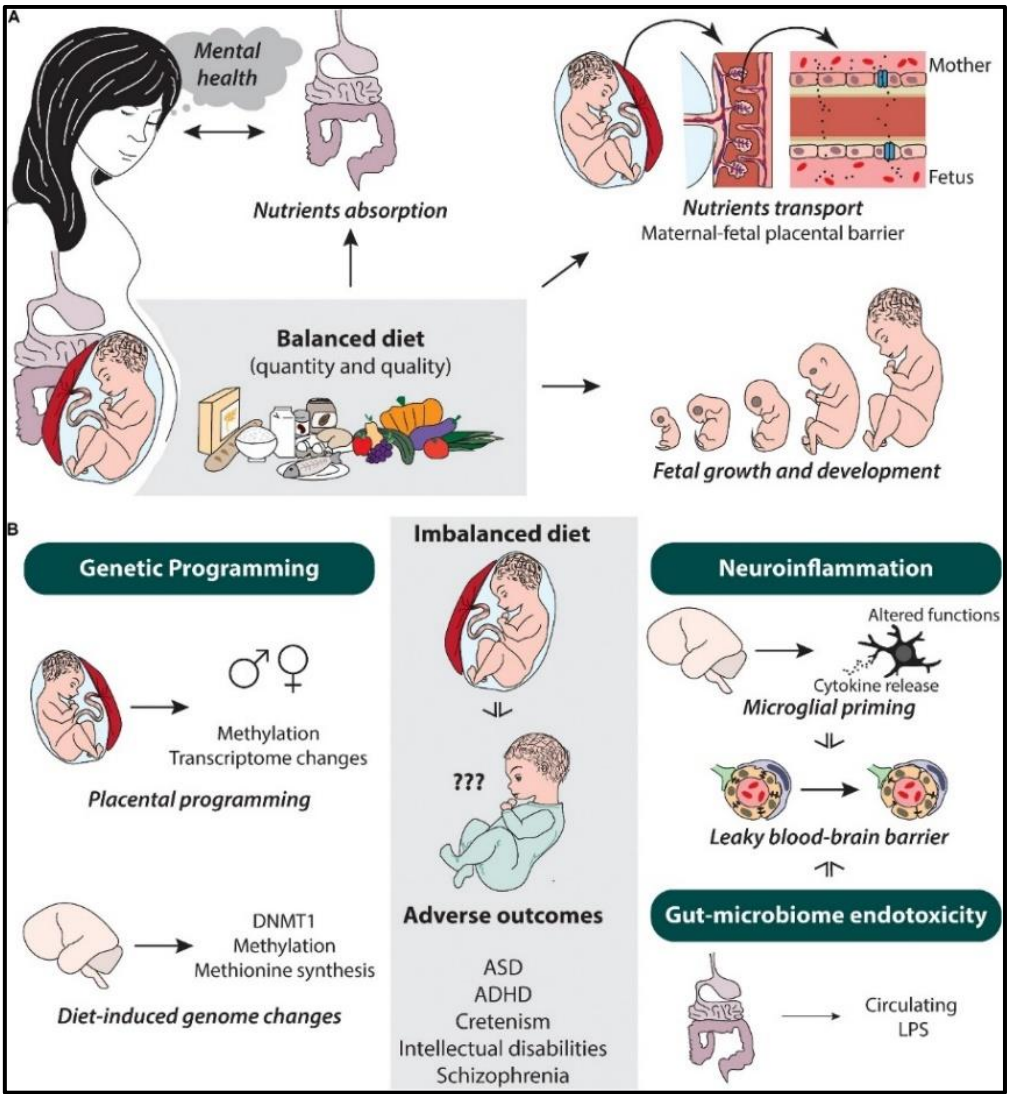


Fig. 2 A Diagram Showing the Maternal Impact on the Likelihood of Developing ASD [13]

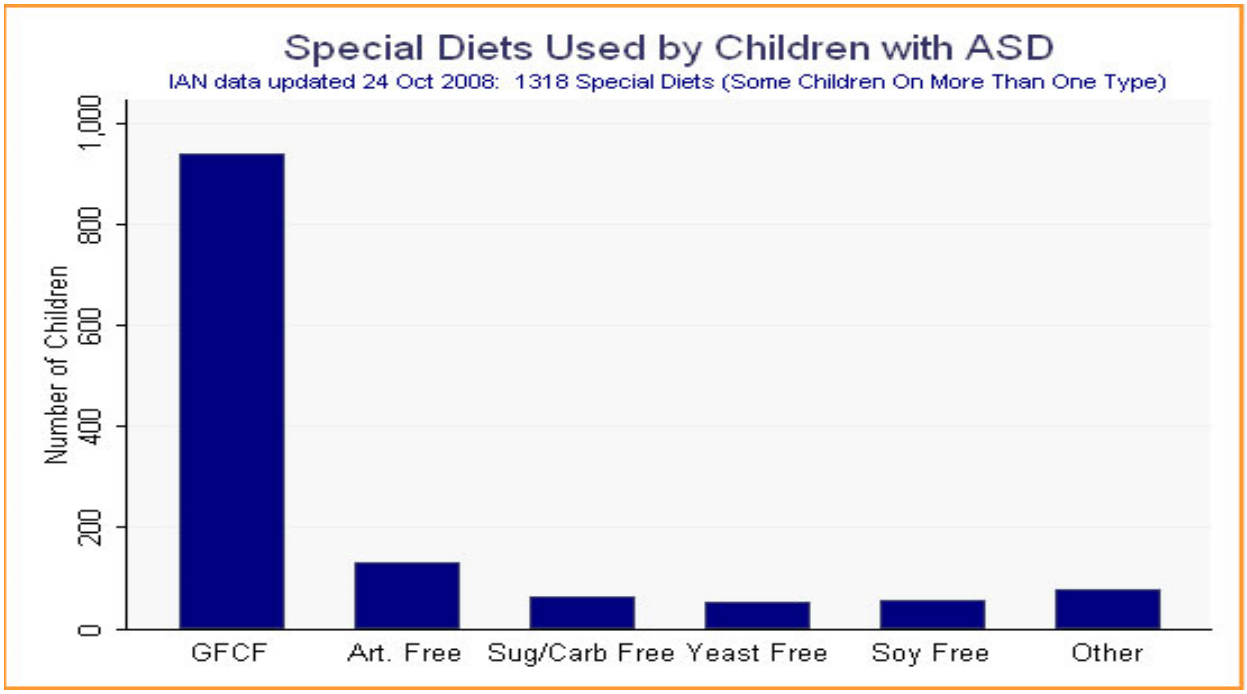


Fig. 3 A Graph Showing the Diets Recommended for Children with ASD [14]

4.2. Environment

Epigenetics and its complex mechanisms serve as the most memorable mediators of environment-genomic interactions. The environment to which an infant is exposed can influence the access and absorption of nutrients in the body between ages 0 and 3 years [9]. Although no single environmental factor is sufficient to cause ASD, a combination of them may be associated with the development of ASD. In genetically predisposed individuals, environmental risk factors combine or interact to create a threshold that can define dysfunction, causing ASD [9]. Early vulnerability to a combination of environmental factors, ranging from microorganisms, bacteria, and viruses to drugs, chemicals, and physical agents, during critical central nervous system evolution is linked to neurodevelopment, including ASD[15]. However, environmental factors are also connected with the way ASD cases are usually managed.

Some other conditions that may contribute to the development of ASD are conception when the parents are at an advanced age, contact with certain pesticides and living with air pollution, overweight, parents with diabetes or immunological disorders, premature birth, and difficulties during delivery. [16]. What is more, when these factors are combined with compromised nutrition, the risk for the onset of ASD increases. Epidemiological studies have shown that fetal vulnerability to chemical and toxic triggers, such as air pollution, pesticides, materials used in the plastics industry, and heavy metals, can raise the risk of ASD development [17]. Potential mechanisms unite the aforementioned environmental risk factors for ASD and include relations with genetic factors and epigenetic features that decrease the ability to detoxify xenobiotics and cause neuroinflammation and oxidative pressure. Probable roles include neurobiological and neurotransmitter changes and signaling pathway abnormalities [18]. Numerous tests have analyzed biological markers of children with ASD postnatally exposed to heavy metals, especially mercury, compared to children without ASD. Assessment of the breast teeth, especially enamel formed in the womb and persists for one year after birth, can also assist in determining prenatal exposure. One of the most investigated environmental factors is air pollution which plays a significant role in the pathogenesis of ASD.

Several research findings have found positive relationships in terms of vulnerability to environmental contaminants, such as PM2.5, PM10, NO_2, SO_2, CO, and O_3, and the development of neurodevelopmental disorders, including ASD [19]. The neurotoxic mechanisms of these contaminants are not fully comprehended. Nonetheless, inflammatory and oxidative pressure functions recreate a vital role in structural and operational modifications, impacting the central nervous system (CNS) and resulting in psychiatric disorders through epigenetic transformations in genes involved in these processes (see Table 1). Understanding the concept of the "critical time window" is another critical breakthrough in the search for the cause of ASD [19]. Symptoms often appear in infants' early years, suggesting they are more likely to develop before, during pregnancy, and in early life [19]. Studies of human pregnancy and early life suggest that air pollution exposure during fetal development and maturation of the central nervous system is associated with a systemic inflammatory response and may lead to neurodevelopmental disorders [19].

Table 1. External Environmental Factors Resulting in ASD

Class	Factors
Chemistry and toxicity	Air pollution, pesticides, plastic materials, and heavy metals.
Genetic factors and epigenetic features	Detoxification of xenobiotics, mediate neuroinflammation and oxidative stress, neurobiological and neurotransmitter changes, signaling pathway abnormalities, and inflammatory and oxidative stress.
Pollutants	PM2.5, PM10, NO_2, SO_2, CO, and O_3

5. Conclusion

The research has illustrated that healthy nutrition of the mother before pregnancy, preparation for pregnancy, during pregnancy, and shortly after the birth of the offspring has a significant effect on the likelihood of developing ASD. In addition to the mother's nutrition, the nourishment available to infants from birth to at least three years can also determine whether they will acquire ASD. The internal and external environment to which an infant is exposed determines the likelihood of developing ASD. The internal environment factors entail the infant's genetic makeup, including the effects of the mother's behavior during the prenatal period. The external environment factors mainly refer to the pollutants and chemicals that the infant is exposed to at an early age, among other risk factors. The significance of this study is in its insights into nutritional approaches that should be followed to lower the probability of ASD development in children from early development. However, the main limitation of this study is that there is no solid scientific explanation for ASD incidences, particularly in infants. As a result, the available information is based mainly on observations and theories. Thus, there is a solid basis for further research regarding ASD prevalence and risk factors among infants.

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