



(REVIEW ARTICLE)



Autism spectrum disorder is associated with multifold risks in the process of pregnancy: Imbalance of nutritional, environmental and social behavioral aspects

Eileen Owan, Diane E Heck and Hong Duck Kim *

Department of Public Health, School of Health Sciences and Practice, New York Medical College, Valhalla NY, US.

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Abstract

Autism spectrum disorder (ASD) is characterized by qualitative impairments in social interaction, communication, and stereotyped behavior patterns. The cost burden for health coverage for ASD is focused on educational applied behavioral analysis and psychotropic drugs to decrease maladaptive behaviors and support learning and development. Determinants of either risk factors or prevention related to ASD covering environmental, social-behavioral, and genetic are still unknown. This review focuses on the multifold risks of Autistic disorder (ASD), including environmental, genetic, and food supplemental concerns and health policies and regulations.

Keywords: Autism spectrum disorder (ASD); Vitamin Supplements; Prenatal exposure and pregnancy; Environmental factor; Socio-economic factor; Prevention; Prediction

1. Introduction

Autism spectrum disorder (ASD) is a cognitive disability identified by persistent impairments with interaction, repetitive behaviors, and activities. [1] The increased risk of autism is associated with short interpregnancy intervals (IPI), the length of time between the end of one pregnancy and the beginning of gestation. Current knowledge and evidence-based study suggest environmental factors and socioeconomic relations are preventable contributors, but it is still debatable to ASD prevalence.

According to the University of Pennsylvania's Perelman School of Medicine in 2014, the cost of treating adults and children with autism in the United States is estimated at \$200- \$300 billion annually, including medical coverage focused on managing spectrum disorders, behavioral, educational interventions, alternative medicine, and dietary changes. A study carried out by Delobel-Ayoub (2015) found an excess risk of ASD in disadvantaged backgrounds indicating the prevalence associated with occupational class, maternal education, and household income.[1] The report also included immigrants and single-parent families, revealing that a higher prevalence among unemployed adults throughout pregnancy affects fetal development and health. As well as, a mother who is mentally exhausted, physically unhealthy, and un-nourished may be unable to have a healthy newborn. [2]

Environmental and sociocultural factors affect brain functions and are potential causes of autism. Toxic metals exist in different areas and originate from the air, water, and sewage sludge. For example, an estimated 60 to 65% of cases of autism occur as a result of prenatal, perinatal, and postnatal environmental factors due to exposure to environmental toxicants. Currently, several chemical toxicants are known to cause neurodevelopmental disorders. [3] According to Bolte, 2019 prenatal nutritional status is linked to brain development in the offspring and is a potential biologic basis for the association between short IPIs. [4] Although vitamin deficiency is associated with neural tube defects, folic acid,

* Corresponding author: Hong Duck Kim

Department of Public Health, School of Health Sciences and Practice, New York Medical College, Valhalla NY, US.

omega-3, probiotics, vitamins: C, A, D, B12, iron, and other elements are known to replace the missing nutrients and improve some of the symptoms of autism.[5] Folic increases during pregnancy because of increased demands from the fetus and required for DNA replication. [6] Before pregnancy, multivitamins and folic acid supplements reduce the risk of ASD in offspring. [7] Interestingly, more evidence-based findings suggest that taking folic acid, a typical prenatal vitamin for up to 12 weeks of gestation, reduces the susceptibility to ASD and protects against developmental and reproductive toxins.[8] It indicates the effectiveness of folic acid and vitamins on the mother and offspring. In this review, we discuss and delineate in-depth the following issues: 1. Correlation of the socio-economic relations and environmental relationship to autism; 2. Relationship between environmental factors and socioeconomic factors exposure; 3. Effectiveness of supplements in the prevention and control of autism.

2. Methods

Environmental and sociocultural factors affect brain functions and are potential causes of autism. Toxic metals occur in different areas and originate from the air, water, and sewage sludge. For example, an estimated 60 to 65% of cases of autism occur as a result of prenatal, perinatal, and postnatal environmental factors due to exposure to environmental toxicants. Currently, several chemical toxicants are known. All relevant research papers were used when performing the literature review to understand the connection of environmental factors and socio-economic relationships with autism spectrum disorder, the supplements, and public health regulations that influence the health issue. Information collected is from websites of institutions and organizations such as the U.S. Food and Drug Administration (FDA) in Counteract Program, World Health Organization (WHO), National Institutes of Health (NIH), and the Centers for Disease Control and Prevention (CDC) and PubMed.

3. Results

3.1. Correlation of the socio-economic relations and environmental relationship to autism

The compelling report provides an evidence-based review of the current knowledge about environmental risk factors in ASD using findings from published systematic reviews and meta-analyses.

According to Gaugler et al. (2014), ASD is associated with 40 to 50% of environmental factors. That is critical because the brain becomes more vulnerable due to immune dysregulation, oxidative stress, and nutrient deficiencies. [9] There is an association between environmental factors and ASD. [10] For example, a study of nearly 200 chromosomal defects reported environmental factors to estimate 40 to 55% off compared with 25 to 40% genetic factors of developing the autistic disorder. [11]

Although exposure to toxic waste, air pollutants, and polychlorinated biphenyls (PCBs) are known causes of neurodevelopmental disorders. [12] Population indicators of socioeconomic status are correlated with the health and development of children. Children whose mothers are educated with at least a high school diploma are more likely to have a diagnosis of autism compared to children of mothers without a degree. [13]

3.2. Relationship between environmental factors and socioeconomic factors exposure

Environmental pollutants and socioeconomic factors are associated with congenital disabilities. [14] Examples of environmental factors are maternal health, socioeconomic status, lifestyle, Etc. [15]

Children experience low birth weight, learning disabilities, and mental health problems due to their poor environment or socioeconomic status.[16] Therefore the nature of child development is beyond education and childcare but enriching environments during pre-and post-natal development. Therefore, policies and programs focused on reducing parental stress, enhancing the parent's emotional well-being, and providing community resources for parents and communities should be prioritized.[17] Prenatal care is the perfect example of preventive care. Inadequate prenatal care will lead to birth complications.

3.2.1. Fetal environment

Prenatal exposures, such as hormone alterations, obesity, hypertension, and infections, are considered in the etiology of ASD. The mother and fetus could compromise the fetal-maternal-placental system leading to adverse effects on the neurotransmitter, neuropeptide, and immune pathways. [4]

3.2.2. Toxic exposure

Multiple environmental chemicals are released indoors through furniture, building material, cosmetics, vehicles, and agricultural industries. Toxic metals occur in the air, soil, water, and plants. It impacts bodily functions and neurological and behavioral impairment. [4]

3.2.3. Gestational bleeding

Gestational bleeding is associated with fetal hypoxia. Fetal distress, hypertension, prolonged labor, and low Apgar score are associated with autism due to oxygen deprivation during brain development. Hypoxia increases dopaminergic activity, and there is evidence for dopamine overactivation in autism. [18]

3.2.4. Maternal immigration

Maternal stress is pivotal because of the demands of residing in a new country, limited social support, or stress resulting from economic or social factors. [18] The psychosocial environment and maternal stress are related to behavior development, including autistic features.

3.3. Effectiveness of supplements in the prevention and control of autism

Prenatal nutritional status is associated with the brain development of an offspring. Food insecurity is a leading cause of low nutritional status due to low income or other resources. Food insecurity is challenging to solve, and supplements and limited to no access to diet therapy are individuals with ASD exposed to all health issues. In addition, monitoring the micronutrient will improve the symptoms of children with ASD.[19]

3.3.1. Vitamin B12

Infants of vitamin B12-deficient breastfeeding mothers or infants are vulnerable between 6 and 12 months of age. In addition, it is associated with behavioral and developmental functioning. [19] Patients with autism could receive vitamin B12 replenishment to improve the symptoms of ASD because of its role in neurotransmitter function and neuronal metabolism. [5]

3.3.2. Omega-3 Fatty Acids

Omega-3 fatty acids are necessary for average growth and are essential to neurodevelopment. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) are essential for brain structure, function, and the treatment of neurodevelopmental disorders because they function on cell membranes.[20] Deficiency of Omega-3 fatty acids leads to abnormal development of the nervous system in childhood, hyperactivity, dyslexia, dyspraxia, and autistic disorder. [6]

3.3.3. Probiotics

Probiotics are microorganisms that reduce the overgrowth of bacteria and synthesize antioxidant substances. “gut-brain health” is associated with ASD. [20] The gut can influence gastrointestinal symptoms in individuals with ASD. According to Trudeau et al. (2019), Probiotic therapy could decrease the behavioral symptoms to levels similar to individuals without ASD.[21]

3.3.4. Vitamin D

Vitamin D is neuroactive and improves the development of the brain. The vitamin has a significant effect on neurotransmission. Vitamin D deficiency causes brain exposure to vulnerable pathogens [21]. Vitamin D deficiency is associated with autism, depression, attention deficit hyperactivity disease, Alzheimer’s disease, and Parkinson’s.[22]

3.3.5. The ketogenic diet

It provides energy from fat, proteins, and carbohydrates. During the diet, the body shifts from using glucose to retrieving energy from fatty acids in the blood.[6] KD is a nutritional intervention for behavioral symptoms associated with ASD, improves social interactions and communication, and reduces attention deficit hyperactivity disorder (ADHD), compulsive behavior, abnormal sleep, and decreased frequency of seizures. [23]

3.3.6. Folic acid

Folic acid supplements consumed could reduce the risk of offspring’s ASD.[24] Folic supplements are crucial for fetal neurodevelopment. The minimum folic acid dosage is estimated to be at least 400 µg daily.[25]

4. Discussion

A public health strategy on ASD is promoting the effectiveness and developing awareness on supplementation in limiting ASD in children to increase policy implications and public health interventions to reduce or eliminate the effects of environmental factors. [26]

Due to the presence of dysmorphic features that are lower in males than females and have a greater frequency of cognitive impairment [26] although parental age of both the father and mother is one of the most consistently identified perinatal risk factors for ASD. Indeed, boys are affected with ASDs more frequently than girls. Social determinants and environmental factors are associated with the pathogenesis of this disorder.

5. Conclusion

Overall, Prenatal, perinatal, and postnatal factors, exposure to toxicants, and infectious microorganisms are associated with autism. Further studies need to validate the connectivity between environmental factors, including supplemental effectiveness and risk of ASD during pregnancy or the developmental period of the brain.

Moreover, the possibility that folic acid and other supplements could influence the pathogenesis of autism is supported by the systematic review of studies on the relationship between this supplement and ASD, and it is a positive influence on the brain developmental process

Perspective and significance

According to the CDC, the average medical expenditure of a child with ASD exceeds the health cost of individuals without ASD. The costs include education, ASD-related therapy, and family-coordinated services. Is estimated to cost \$30,000 to \$66,000 per child. There is a need to reduce the cost of health care and increase the quality of life (QOL) following evaluation, monitoring, diagnosis, and exploration of the biomarker to predict risk surrounding community and environmental factors.

Compliance with ethical standards

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Disclosure of conflict of interest

It is declared that there is no conflict of interest.

References

- [1] Delobel-Ayoub Malika, Virginie Ehlinger, Dana Klapouszczak, Thierry Maffre, 4 , 5 Jean-Philippe Raynaud, Cyrille Delpierre, and Catherine Arnaud. Socioeconomic Disparities and Prevalence of Autism Spectrum Disorders and Intellectual Disability. Nov 2015.
- [2] Sun X, Auyeung B, Baron-Cohen S, Allison C. Parental concerns, socioeconomic status, and the risk of autism spectrum conditions in a population study. December 2014.
- [3] Grandjean P, Landrigan PJ. Developmental neurotoxicity of industrial chemicals. Lancet. 2006; 368: 2167-2178.
- [4] Bölte S, Sonya Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of autism spectrum disorder. Cellular and Molecular Life Sciences. 2019, 76: 1275–1297
- [5] Kawicka A, Regulska -Ilow B. How nutritional status diet and dietary supplements can affect autism. A review. Roczniki Państwowego Zakładu Higieny. 2013, 64(1): 1-12.
- [6] Levine SZ, Kodesh A, Viktorin A, Smith L, Uher R, Reichenberg A, Sandin S. Association of Maternal Use of Folic Acid and Multivitamin Supplements in the Periods Before and During Pregnancy With the Risk of Autism Spectrum Disorder in Offspring. JAMA Psychiatry. 2018, 75(2): 176-184.

- [7] Goodrich Amanda J., Heather E. Volk, Daniel J. Tancredi, Rob McConnell, Fred W. Lurmann, Robin L. Hansen, and Rebecca J. Schmidt. Joint Effects of Prenatal Air Pollutant Exposure and Maternal Folic Acid Supplementation on Risk of Autism Spectrum Disorder. Nov 2017
- [8] Gaugler T, Klei L, Sanders SJ, Bodea CA, Goldberg AP, Lee AB, Mahajan M, Manaa D, Pawitan Y, Reichert J, Ripke S, Sandin S, Sklar P, Svantesson O, Reichenberg A, Hultman CM, Devlin B, Roeder K, Buxbaum JD. Most genetic risk for autism resides with common variation. *Nat Genet.* Aug 2014, 46(8): 881-5.
- [9] Landrigan PJ. Review What causes autism? Exploring the environmental contribution. *Curr Opin Pediatr.* Apr 2010, 22(2): 219-25.
- [10] Bandim JM, Ventura LO, Miller MT, Almeida HC, Santos Costa AE. Autism and Möbius sequence: an exploratory study of children in northeastern Brazil. *Arq Neuropsiquiatr.* 2003, 61(2A): 181-5.
- [11] Hallmayer J, Cleveland S, Torres A, Phillips J, Cohen B, Torigoe T, Miller J, Fedele A, Collins J, Smith K, Lotspeich L, Croen LA, Ozonoff S, Lajonchere C, Grether JK, Risch N. Genetic heritability and shared environmental factors among twin pairs with autism. *Arch Gen Psychiatry.* Nov 2011, 68(11):1095-102.
- [12] Rossignol DA, Genuis SJ, Frye RE. Environmental toxicants and autism spectrum disorders: a systematic review. *Transl Psychiatry.* 2014, 4: e360.
- [13] Maureen S. Durkin, Matthew J. Maenner, F. John Meaney, Susan E. Levy, Carolyn DiGuseppi, Joyce S. Nicholas, Russell S. Kirby, Jennifer A. Pinto-Martin, Laura A. Schieve. Socioeconomic Inequality in the Prevalence of Autism Spectrum Disorder: Evidence from a U.S. Cross-Sectional Stud. 2019.
- [14] Amy MP, Suzan LCI, Ira BT, Frederick L, Katharine H, Gary MS. Air pollution, neighborhood socioeconomic factors, and neural tube defects in the san Joaquin valley of California. 2015.
- [15] López-Escobar Beatrice, Bogdan J. Wlodarczyk, Jose Caro-Vega, Ying Lin, Richard H. Finnell, Patricia Ybot-González. The interaction of maternal diabetes with mutations that affect folate metabolism and how they affect the development of neural tube defects in mice. 2019.
- [16] Conroy Kathleen, Megan Sandel, Barry Zuckerman. Poverty grown-up: how childhood socioeconomic status impacts adult health. 2010.
- [17] Hackman Daniel, Martha J Farah, Michael J. Meaney. Socioeconomic status and the brain: mechanistic insights from human and animal research. 2010.
- [18] Hannah Gardener, Donna Spiegelman, Stephen L Buka. Prenatal risk factors for autism: a comprehensive meta-analysis. 2018.
- [19] Mei Tan, Ting Yang, Jiang Zhu, Qiu Li, Xi Lai, Yuanyuan Li, Ting Tang, Jie Chen, Tingyu Li. Maternal folic acid and micronutrient supplementation is associated with vitamin levels and symptoms in children with autism spectrum disorders, reproductive. toxicology. 2019.
- [20] Yong-Jiang Li, Jian-Jun Ou, Ya-Min Li & Da-Xiong Xiang. Dietary Supplement for Core Symptoms of Autism Spectrum Disorder: Where Are We Now and Where Should We Go? 2017.
- [21] Trudeau MS, Madden RF, Parnell JA, Gibbard WB, Shearer J. Dietary and Supplement-Based Complementary and Alternative Medicine Use in Pediatric Autism Spectrum Disorder. *Nutrients.* 2019, 11(8): 1783.
- [22] Macova L, Bicikova M, Ostatnikova D, Hill M, Starka L. Vitamin D, Neurosteroids and Autism *Physiol. Res.* 2017, 66(3): S333-S340
- [23] Qinrui Li, Jingjing Liang, Na Fu, Ying Han, Jiong Qin. A Ketogenic diet and the treatment of autism spectrum disorder. 2021.
- [24] Xian Liu, Mingyang Zou, Caihong Sun, Lijie Wu & Wen-Xiong Chen. Prenatal Folic Acid Supplements and Offspring's Autism Spectrum Disorder: A Meta-analysis and Meta-regression. 2021.
- [25] Crider KS, Yang TP, Berry RJ, Bailey LB. Folate and DNA methylation: A review of molecular mechanisms and the evidence for folate's role. *Advances in Nutrition.* 2012, 1: 21–38.
- [26] Kristen Lyall, Lisa Croen, Julie Daniels, M. Daniele Fallin, Christine Ladd-Acosta, Brian K. Lee, Bo Y. Park, Nathaniel W. Snyder, Diana Schendel, Heather Volk, Gayle C. Windham, Craig Newschaffer. The Changing Epidemiology of Autism Spectrum Disorders. Dec 2016.