REVIEW ARTICLE

The Autism Spectrum Disorder (ASD) and what Association with Gut-brain axis, Probiotic and other Related Factors?

Z JAHAN[a], MM CHOWDHURY[b]

Abstract:

Autism spectrum disorder has precipitously mounted globally since the early 1990s. The Autism rise in amount has flashed fears of an autism epidemic. Autism spectrum disorder (ASD) is a complex developing condition. Although ASD can be an enduring disorder, early diagnosis and treatments can improve a person's symptoms and daily functioning. Study shows that 1 in 54 children has been diagnosed with autism spectrum disorder (ASD); it is a spectrum form, which means that all persons with autism represent certain difficulties. Since there is no specific diagnostic test, experts are still hunting for accurately what causes autism. The core features must be present in early development, like obstacles in social communication and interactions and restricted interests or repetitive behaviors. Multi F factors influence autism spectrum disorder, like gut-brain health, Microbiome dysfunction in the gastrointestinal tract, autoimmune disease, etc. Many research study findings are that probiotics may help diminish the inflammatory condition and modulate the Gastrointestinal problem and behavioral abnormality in ASD. Exclusive breastfeeding has the lowest risk of autism spectrum disorder; it decreases the 76 % chances of ASD. A proper supplement like folic acid during the first-trimester act as protective against ASD.

Material and method: Relevant articles and literature were retrieved from different journals and web pages to find out the Autism details and how it related to various factors.

Keywords: Autism, gut-brain health, probiotic, early screening, protective supplements, social awareness.

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Introduction:

Autism spectrum disorder (ASD) is a matter of sweating nowadays.

Developmental disability and difficulties in social, communication and behavioral skills are remarkable challenge[1].

The study shows 1 in 54 children has been diagnosed with autism spectrum disorder (ASD), as per CDC's Autism and Developmental Disabilities Monitoring (ADDM). ASD is associated with all kinds of socioeconomic, racial, and ethnic groups. ASD is four times more common in the case of boys[2].

In the 1940s, autism was primarily designated, but very diminutive was known about it until the last few decades. It is a spectrum from, which means that, while all persons with autism represent specific difficulties, this condition may disturb them in distinct ways and to innumerable extents. Some of them can live independently, but others may show learning disabilities and may need special support entire life[3].

The autism trend has been precipitously mounting since the early 1990s globally. The prevalence of autism in the United States also has climbed progressively since scholars first began tracking it in 2000. The rise in the amount has flashed fears of an autism epidemic. Although researchers are actively developing such tests, there is no specific diagnostic test like a blood test or brain scan.

The core features must be present in early development, like obstacles in social communication and interactions and restricted interests or repetitive behaviors. Clinicians trust observations of a person's behavior to diagnose the condition[4]. Many factors influence autism

a. Dr. Zakia Jahan, Director, 3715 72nd Street, Apt # 35 Jackson Heights, NY 11372 646-851-3824.

b. Md Monzur Chowdhury, Managing Director of Center for Global Autism Awareness

Address of Correspondence: Md Monzur Chowdhury, Managing Director of Center for Global Autism Awareness, E-mail: monzurmgt@gmail.com

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spectrum disorder, like gut-brain connection, gut health, probiotics, etc.

Probable Causes:

The grounds of autism or its advances are still in the dark and not fully understood, although many factors are included. Each individual may have an exclusive set of causes and different elements that interact to express the same set of symptoms. Possible causes of autism may be Microbiome dysfunction in the gastrointestinal tract, autoimmune disorder, toxin and heavy metal, undiagnosed hypothyroidism, Methylation pathways disorder, co-infection such as viral, parasitic, Lyme[5].

Signs and Symptoms of Autism Spectrum Disorders

ASD instigates before the age of 3 years and can last all over the life. Even though over the period, symptoms may progress. Until the age of 18 to 24 months, some children with ASD gain new skills and meet developmental milestones criteria. Then they stop gaining new skills or drop the skills they once had.

Difficulties with social communication and interaction and restricted or repetitive behaviors or interests are updated criteria for diagnosing ASD. It is essential to consider that some people who don't struggle with ASD might also have some of these symptoms. These characteristics symptoms can make life very challenging and struggling for people with ASD. Some examples of social communication and social interaction are related to avoiding or does not keep eye contact, does not respond to a name by nine months of age, by 18 months of age does not point or looking at what you mean, doesn't like to play or avoid pretending game. Case in point of restricted or repetitive interests and behaviors are Lines up toys or other objects and getting disappointed in any change of order Repeating words or phrases repeatedly (i.e., echolalia). Hand flapping, rocking, and spinning in circles are Obsessive or odd behaviors. Other symptoms are delayed language skills, delayed movement skills, Gastrointestinal issues (e.g., constipation), etc.; for more details, symptoms significant to visit CDC website[6].

Early screening and treatment therapy:

Early screening test and surveillance for monitoring child development is essential. CDC's Learn the Signs. Act Early the program has developed free materials, including CDC's Milestone Tracker app, to guide and help parents observe children's development and detect when there is a matter of concern and if more evaluation screening is needed. Autism-specific screening should be done at the age of 18- and 24- or 30-month visits or whenever a situation is expressed7. Since no specific treatment is known yet after close observation, evaluation of symptoms, and test results, various targeted specific therapies are applied to address each patient's exact need and symptoms. According to progress and improve treatment can be modified. Address underlying infection and health conditions like thyroid dysfunction, and Research shows that different specific probiotic strains have a significant positive impact that improves the gut microbiome. For example, specific probiotic strains are critical to addressing chronic inflammation, and other strains are targeted to enhance cognitive and mental dysfunction. Eating naturally anti-inflammatory foods, nutritious diet recommendations, like a gluten-free and casein-free diet, and evidence-based supplements.

Specific Therapies to progress genetic pathways and genetic expression. Some natural herbs support and improve detoxification pathways. Some evidence shows the positive benefit of Methyl B12 and glutathione injections[5].

According to individualized aides, a Person with autism needs speech therapy, occupational therapy, social skills training, and physical therapy. Specialized classrooms, other social support, and sometimes even technical schools are required for most children with ASD[3].

Gut Factor:

Among autistic children's most common health complaints is a gut health problem. Still, now lots of Research is being conducted on this issue. Before diving into deep thoughts, did we ever think? Why do we feel a butterfly sensation in the stomach or tummy ache when we are excited or stressed and tensed! These sensations spring from our gut, indicating our brain and heart are coupled. Recent research studies findings that the brain affects our gut health and soul may even influence and touch our brain health. The communication and connection system between the gut and brain is called the gut-brain axis. This connection network communicates with each other both physically and biochemically and other different routes. The nervous system is a vital way to connect, with around

100 billion neurons in the human brain. Neurons are cells; they help the body to act and behave8. Exhilaratingly, our gut contains 500 million neurons connected with the brain via a nerve in the nervous system9. The vagus nerve signifies the vital component, establishing the connections between the brain and the gastrointestinal tract that maintain body functions, including control of mood, digestion, and other vital responses[10]. One animal study found that stress declines the signs sent through the vagus nerve and also causes gastrointestinal problematic[11]. The gut-brain axis is a bifacial transmission network links the enteric (gastrointestinal) and central nervous systems. This communication network is associated with anatomical, but it also ranges to include endocrine, hormonal, and immunological paths. The hypothalamic-pituitary-adrenal (HPA) axis, neuron within the gastrointestinal (GI) tract, autonomic nervous system all connect the gut and the brain,

permitting the brain to intestinal stimulus activities, and the gut to influence mood, cognition, and mental health[12] Researchers and some study findings point that a cause of autism is the same gene mutation in the brain and gut, and that was the first identified as a reason of autism, also causes gut dysfunction. Because study findings show brain and heart share many of the same neurons and share autism-related gene mutations[13], approximately it has been 60 years since autism spectrum disorder was first identified. Nowadays, the number of cases has soared. The United Nations approximations that up to 70 million people worldwide are of the autism spectrum, and no identified cause or cure found yet. Some research studies have found that up to 90 percent of autistic children struggle with gut-related health problems. According to the CDC, autistic children experience chronic diarrhea and constipation more than 3.5 times than they usually develop compeers[14].

Genetic factor:

The exact underlying cause for ASD is still not known. It is most likely an amalgamation of multiple genetic and environmental (nongenetic) factors. Study shows that approximately 20-40% of underlying genetic disorder has contributed to ASD. Chromosome abnormality or single gene disorder can encompass added health issues like PTEN Hamartoma Tumor syndrome). chromosome microarray and fragile X testing is the most common recommended test. The chromosome microarray helps to detect missing or extra small pieces of chromosome substantial that cause hundred known genetic syndromes. This chromosome microarray test has about a 5-15% chance to get positive results associated with ASD[15].

Environmental factor:

In the USA prevalence of autism per 10 000 individuals is between 45 and110. The prevalence of autism is currently estimated to lie between 45 and 110 per 10 000 individuals in the USA. Common hypothesized risk factors for autism include high parental age, poor parental education, male sex child, positive family history. Various speculation findings that environmental risk factor influences autism[16].

Since autism is multifactorial, that is influenced by genetics, neurological and environmental factors. It is not entirely impossible to prevent autism. Ecological factors are mostly attention enchanting to scientists because prevention is possible by evading them. So many environmental risk factors act as a stimulus of autism pathogenesis by producing their epigenetic effects on gene expression. Prenatal, natal, and postnatal categories under this factor and linked to the pathogenesis of autism. Exposing to the damaging environmental factors can alter the nature and measure of developmental gene expression in the crucial period of gestation and embryo forming period, increasing the danger of genomic imprinting diseases such as autism. This factor can alter DNA methylation in the next-generation organism.

There is a link between parental psychiatric history, mental disorders, mother's depression with child autism. Like the parental history of schizophrenia increased triple time risk of autism. Various medication use in the first trimester is associated with autism, such as anti-psychiatric, anti-epileptic, as well as valproic acid, leads to fetal valproate syndrome and other medication like as thalidomide, a painkiller, misoprostol, a prostaglandin analog gastric ulcer, â2-adrenergic agonists such as terbutaline to treat asthma[17].

Study shows prenatal psychiatric medication can raise the 68% risk of autism. Maternal prenatal drug uses causes a 46% increased risk of fetus autism[18].

Anti-pyretic or Analgesic paracetamol is widely used; it shows immune dysregulation and initiates oxidative

stress in humans. Additionally, it is inveterate that paracetamol (acetaminophen) can persuade apoptosis and necrosis observed in autistic brains[19].

The fetal risk of autism is also associated with natal risk factors like preterm (<35 weeks) and post-term pregnancy (>42 weeks. Fetal complications related to hypoxia, including fetal distress, umbilical-cord difficulties, raise the chance of autism. Postnatal risk factors have critical parts in vulnerability to autism. Low birth weight, jaundice, and postnatal infection are vital risk factors. Below than 2500 g measured as low birth weight and allied with a two-fold increase in the risk of autism[17].

Familial socioeconomic factor:

Other studies also indicate strength link between highly educated parents and the incidence of autism[17]. Many studies evaluated the association between parental education and jeopardy of child autism and confirmed the connection between low level of parental education and risk of autism[20].

Financial struggle factor: The diagnosis of child autism forces parents to face emotional and financial stress. Research from the University of Missouri says most parents don't immediately consider it a financial problem. They face major financial struggles later. Since autism has a shockingly immense impact on society, more economic support from non-profit organizations and governmental organizations should stand next to the autism-diagnosed family. It is essential to support and provide help to families to cope with the thoughtful financial life changes they may face. A family with having a child with autism associated with financial problems should seek assistance from financial advisors. So, they can provide advice to help families think deeply about utilizing available resources and the implications of spending all their giving up work money on various therapies or providing ideas to care for a child when another track could be available[21].

Benefits of probiotics for autism:

Probiotics are live micro-organisms, which, when directed in suitable amounts, confer a health benefit on the host[22]. The microbiota-gut-brain axis has been newly documented as a significant modulator and helpful for neuropsychiatric health. Probiotics recently named "psychobiotics" may stimulate brain activity and role. Other study findings also improve the behavioral movement of children with autism spectrum disorder (ASD)[23]. Many research study findings are that probiotics may help diminish the inflammatory condition and modulate the Gastrointestinal problem and behavioral abnormality in ASD. It decreases the gut barrier penetrability and reduces inflammation, producing cytokines and other immunomodulatory effects. According to Wang et al., administration of oral probiotics during pregnancy trimester averts autism-related behaviors in offspring by hindering the manufacture of pro-inflammatory interleukin 6 (IL-6) and IL-17a s in both maternal serum and fetal brains[24]. Probiotics are a significant and side-effect-free dietary product that can treat GIS and ASD symptoms by modifying dysbiosis, tumbling inflammation, and strengthening depleted immunity. A probiotic-containing diet helps to improve neural function, brain function via a mechanism of microglial-induced synaptic pruning and the formation of new synapses[25]. Other study's findings Lactobacillus case containing probiotics drinking has revealed beneficial and positive effects on mood and cognition in volunteers by influences on neuronal function[26]. In a research study using ASD mice as a model, probiotics have shown promising results, reducing autism and mood-related symptoms by restoring microbiota balance, strengthening the GI barrier via the tightening of intercellular adhesions[27]. The Food and Drug Organization (FAO) and WHO provide proper guidelines for an actual estimation of the use of probiotics as a diet or as a food supplement[28].

Possible treatment of autism with probiotics has been projected. Since autistic children also recurrently struggle with other GI disorders[29].

Protective supplements against autism-related behavior:

During the 1st month of pregnancy and three months before pregnancy taking unsaturated fatty acids and folic acid can protect against autism in mothers and infants. During the early trimester of pregnancy, maternal folic acid supplementation is beneficial and causes less behavioral abnormality in offspring at 18 months of age[30]. It also decreases the chance of severe language delay at age 3years[31]. Supplements can develop verbal and attention competence at four years of age[32] lesser

scores of infantile hyperactivities at age eight years[33] and predominantly diminution the risk of autism[34].

Breast feeding benefits:

Recent study findings are that nutritional status in newborns, significantly the length of breastfeeding, plays a vital role in the pathogenesis of autism spectrum disorder and protective effect against the risk of ASD. Exclusive breastfeeding decreased the risk of autism spectrum disorder; it reduced the 76 % chances of ASD the risk with exclusive breastfeeding [39].

Improvement of Social awareness is vital for early recognition and intervention of ASD:

Some research study findings suggest that public awareness about ASD is vital and needs improvement. Extensive misconceptions and misrepresentation were recognized, which can be focused on by attentive educational campaigns[35]. For raising and enhancing autism awareness, educational campaigns and focused initiative steps should be taken by NGO and governmental organizations. Those developmental steps can be effective and sustainable public health solutions for disseminating beneficial information to affected families. They will be helpful to improve the quality of life of autistic children and their families[36.] Some evidence findings are that such inadequate awareness and understanding about autism-related disorders involve the public, teachers, and healthcare professionals[37].

In the pilot study, researchers have established that a clinician-determined virtual learning platform for autism spectrum associated young adults shows improved social skills. Also, increases in socio-emotional and socio-cognitive abilities correlate with brain change[38.]

Conclusion:

Once thought, Autism has no cure; however, early interventions can reduce complications. Study findings indicate that proper and initial intervention services can significantly progress a child's development. Autism is a spectrum disease; its symptoms vary from person to person. Most of the time, they possess difficulties in social communication and repetitive behaviors. If caught, early difficulties can be treated with relatively simple measures, including diet and lifestyle changes, early evaluations, and therapy. Since it has no cure, multiple treatment therapies can reduce symptoms and disorders. It supports them in gaining new skills and making the most of their strengths. Also, study findings show strong gut-brain connection links in autism-related behaviors. In contrast, probiotics display potential in correcting gut-related disorders and are also springy satisfactory results in treating autistic behavior-related symptoms. Probiotics appear to be a vital dietary factor and a potentially unexpected result-free therapy that can be proposed to treat GIS and ASD symptoms.

References:

1. What is autism spectrum disorder? [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2020 [cited 2021Oct19]. Available from: https://www.cdc.gov/ncbddd/autism/facts.html
2. Data & Statistics on Autism Spectrum Disorder [Internet]. Centers for Disease Control and Prevention. Centers for Disease Control and Prevention; 2020 [cited 2021Oct19]. Available from: https://www.cdc.gov/ncbddd/autism/data.html
3. Shuchona Foundation [Internet]. Shuchona.org. [cited 2021 Oct 19]. Available from: https://www.shuchona.org/autism-spectrum-disorder-asd
4. Wright J, Spectrum. The real reasons autism rates are up in the U.s. Scientific American [Internet]. 2017 Mar 3 [cited 2021 Oct 19]; Available from: https://www. scientific american.com/article/the-real-reasons-autism-rates-are-up-in-the-u-s/
5. Autism Doctor NYC [Internet]. Kellmancenter.com. [cited 2021 Oct 20]. Available from: https://www. kellmancenter. com/autism.html?gclid=CjwKCAjw2P-KBhBy EiwADBYWCuq KDJWgjwB7O AS0ccmxd GSGucc4Pq041 wtxo9Qowmha DBNKNFtFKRoCA3 QQAvD_Bwe
6. CDC. Signs and symptoms of autism spectrum disorders [Internet]. Cdc.gov. 2021 [cited 2021 Oct 20]. Available from: https://www.cdc.gov/ncbddd/autism/signs.html
7. CDC. Screening and diagnosis of autism spectrum disorder [Internet]. Cdc.gov. 2020 [cited 2021 Oct 20]. Available from: https://www.cdc.gov/ncbddd/autism/screening.html
8. Herculano-Houzel S. The human brain in numbers: a linearly scaled-up primate brain. Front Hum Neurosci. 2009;3:31
9. Mayer EA. Gut feelings: the emerging biology of gut-brain communication. Nat Rev Neurosci. 2011;12(8):453–66.
10. Breit S, Kupferberg A, Rogler G, Hasler G. Vagus nerve as modulator of the brain–gut axis in psychiatric and inflammatory disorders. Front Psychiatry. 2018;9:44.
11. Sahar T, Shalev AY, Porges SW. Vagal modulation of responses to mental challenge in posttraumatic stress disorder. Biol Psychiatry. 2001;49(7):637–43.

12. Appleton J. The gut-brain axis: Influence of Microbiota on mood and mental health. Integr Med (Encinitas). 2018;17(4):28–32.

13. RMIT University. Research confirms gut-brain connection in autism. Science Daily [Internet]. 2019 May 30 [cited 2021 Oct 21]; Available from: https://www.sciencedaily.com/releases/2019/05/190530101143.htm

14. Pandika M. Autism's gut-brain connection. National geographic [Internet]. 2014 Nov 14 [cited 2021 Oct 21]; Available from: https://www.nationalgeographic.com/science/article/141114-autism-gut-brain-probiotic-research-biology-medicine-bacteria

15. Autism Spectrum Disorder [Internet]. Patient Library. 2021 [cited 2021Oct25]. Available from: https://www.geneticsupport.org/child-development/autism-spectrum-disorder/?https://www.geneticsupport.org/child-development/&gclid=

16. van De Sande MMH, van Buul VJ, Brouns FJPH. Autism and nutrition: the role of the gut-brain axis. Nutr Res Rev. 2014;27(2):199–214.

17. Karimi P, Kamali E, Mousavi SM, Karahmadi M. Environmental factors influencing the risk of autism. J Res Med Sci. 2017;22(1):27.

18. Gardener H, Spiegelman D, Buka SL. Prenatal risk factors for autism: comprehensive meta-analysis. Br J Psychiatry. 2009;195(1):7–14.

19. Bauer AZ, Kriebel D. Prenatal and perinatal analgesic exposure and autism: An ecological link. *Environ Health.* 2013;12:41.

20. Lee LC, Harrington RA, Louie BB, Newschaffer CJ. Children with autism: Quality of life and parental concerns. *J Autism Dev Disord.* 2008;38:1147–60.

21. University of Missouri-Columbia. (2008, February 29). Financial Struggles Plague Families Of Children With Autism. *ScienceDaily*. Retrieved May 22, 2021 from www.sciencedaily.com/releases/2008/02/080229105843.htm Financial Struggles Plague Families Of Children With Autism — ScienceDaily

22. Food and Agriculture Organization& World Health Organization (2001) Health and Nutritional Properties of Probiotics in Food Including Powder Milk with Live Lactic Acid Bacteria. Report of a Joint FAO/WHO Expert Consultation. Geneva: WHO.

23. Santocchi E, Guiducci L, Prosperi M, Calderoni S, Gaggini M, Apicella F, et al. Effects of probiotic supplementation on gastrointestinal, sensory and core symptoms in autism spectrum disorders: A randomized controlled trial. Front Psychiatry. 2020;11:550593.

24. Abdellatif B, McVeigh C, Bendriss G, Chaari A. The promising role of probiotics in managing the altered gut in autism spectrum disorders. Int J Mol Sci. 2020;21(11):4159.

25. Eltokhi A., Janmaat I.E., Genedi M., Haarman B.C.M., Sommer I.E.C. Dysregulation of synaptic pruning as a possible link between intestinal microbiota dysbiosis and neuropsychiatric disorders. *J. Neurosci. Res.* 2020 doi: 10.1002/jnr.24616.

26. Shultz S.R., MacFabe D.F., Ossenkopp K.P., Scratch S., Whelan J., Taylor R., Cain D.P. Intracerebroventricular injection of propionic acid, an enteric bacterial metabolic end-product, impairs social behavior in the rat: Implications for an animal model of autism. *Neuropharmacology.* 2008;54:901–911. doi: 10.1016/j.neuropharm.2008.01.013.

27. Mangiola F., Ianiro G., Franceschi F., Fagiuoli S., Gasbarrini G., Gasbarrini A. Gut microbiota in autism and mood disorders. *World J. Gastroenterol.* 2016;22:361–368. doi: 10.3748/wjg.v22.i1.361.

28. Pandey K.R., Naik S.R., Vakil B.V. Probiotics, prebiotics and synbiotics—A review. *J. Food Sci. Technol.* 2015;52:7577–7587. doi: 10.1007/s13197-015-1921-1.

29. Bingham, M (2003) Functional foods: dietary intervention strategies in autistic spectrum disorders. In *Food Science and Technology Bulletin^{TM}: Functional Foods*, vol. 1, pp. 4-1–4-11 [Bingham, M, editor]. Reading: IFIS Publishing.Google Scholar

30. Roza SJ, van Batenburg-Eddes T, Steegers EA, Jaddoe VW, Mackenbach JP, Hofman A, et al. Maternal folic acid supplement use in early pregnancy and child behavioural problems: The Generation R Study. *Br J Nutr.* 2010;103:445–52. 31.

31. Roth C, Magnus P, Schjølberg S, Stoltenberg C, Surén P, McKeague IW, et al. Folic acid supplements in pregnancy and severe language delay in children. *JAMA.* 2011;306:1566–73.

32. Julvez J, Fortuny J, Mendez M, Torrent M, Ribas-Fitó N, Sunyer J. Maternal use of folic acid supplements during pregnancy and four-year-old neurodevelopment in a population-based birth cohort. *Paediatr Perinat Epidemiol.* 2009;23:199–206.

33. Schlotz W, Jones A, Phillips DI, Gale CR, Robinson SM, Godfrey KM. Lower maternal folate status in early pregnancy is associated with childhood hyperactivity and peer problems in offspring. *J Child Psychol Psychiatry.* 2010;51:594–602.

34. Schmidt RJ, Tancredi DJ, Ozonoff S, Hansen RL, Hartiala J, Allayee H, et al. Maternal periconceptional folic acid

intake and risk of autism spectrum disorders and developmental delay in the CHARGE (CHildhood Autism Risks from Genetics and Environment) case-control study. *Am J Clin Nutr.* 2012;96:80–9.

35. DeVilbiss EA, Lee BK. Brief report: trends in US National autism awareness from 2004 to 2014: the impact of national autism awareness month. *J Autism Dev Disord.* 2014;44:3271–3273.

36. Wallace S, Fein D, Rosanoff M, Dawson G, Hossain S, Brennan L, et al. A global public health strategy for autism spectrum disorders. *Autism Res.* 2012;5:211–217.

37. Shih A, Rosanoff M, Wallace S, Dawson G. Autism Speaks Global Autism Public Health Initiative: Bridging gaps in autism awareness, research, and services around the world. *Beijing Da Xue Xue Bao.* 2009;18(41):389–391.

38. Center for BrainHealth. Social awareness increases demonstrate brain changing in adults with autism: Research shows virtual learning platform enhances neural health and social cognition in high-functioning adults on the spectrum. Science Daily [Internet]. 2018 Mar 28 [cited 2021 Oct 29]; Available from: https://www.sciencedaily.com/releases/2018/03/180328130733.htm

39. Ghozy, S., Tran, L., Naveed, S., Quynh, T., Helmy Zayan, A., Waqas, A., Sayed, A., Karimzadeh, S., Hirayama, K. and Huy, N., 2022. Association of breastfeeding status with risk of autism spectrum disorder: A systematic review, dose-response analysis and meta-analysis.