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Serum Sodium Status in Children with Autism Spectrum Disorder

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Abstract

***Background**: Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder that may cause lifelong disability. Nutritional factor is related to the development and progression of autism spectrum disorder. The aim of the study was to assess minerals and trace elements play important role in brain development. Assess of serum sodium status in children with autism spectrum disorder. **Method**: This case control observational study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1st January 2022 to 31st December 2022. For this study, a total number of sixty (60) children age ranged 5-10 years both male and female were included and divided into two groups. Cases were consisted of thirty (30) diagnosed ASD children and controls were consisted of from thirty (30) healthy children. Then the parents were requested to attend the Department of Biochemistry and Molecular Biology in Bangladesh Medical University(BMU) for collection of blood sample in scheduled dates.Serum sodium level was estimated in children of both groups. Statistical -analysis was done by using Statistical Package of Social Science (SPSS) for windows version 22. Unpaired "t" test was done to compare the data as applicable. p value d" 0.05 was considered as level of significance. **Results:** In this study, serum sodium level was lower in children with ASD than that of healthy children, but the level was statistically non-significant. **Conclusion:** Serum sodium level was lower in children with ASD.*

Inroduction:

Autism spectrum disorder (ASD) is a neuro-developmental disorder of global concern. It is characterized by persistent deficits in social communication and social interaction across multiple contexts, including deficits in social reciprocity, nonverbal communicative behaviors used for social interaction, and skills in developing, maintaining and understanding relationships, and the presence of restricted and repetitive behavior, interests, or activities. The term "spectrum" is used as the manifestation of the disorder may vary according to severity, developmental level and chronological age. ASD includes autism, pervasive developmental disorder not otherwise specified (PDD-NOS) and Asperger's disorder.[1] Autism was first described by Leo Kanner.[2]

For the first time, the burden of ASDs has been estimated for the Global Burden of Disease Study with 52 millions of cases of ASDs equating to a prevalence of 7.6 per 1000 or one in 132 persons.[3] Now the global prevalence of ASD has reached 100 per 10,000 people, on average according to global survey published in 2022 .[4]In Bangladesh, the prevalence of ASD is 0.15 to 0.8%. In rural area, it is 0.075% but in Dhaka city, it is alarmingly high 3%.[5,6] The disease is seen four times more frequently in males than females hence the male to female ratio is 4:1.[7,8] It is well recognized that boys outnumber girls with the disorder and girls

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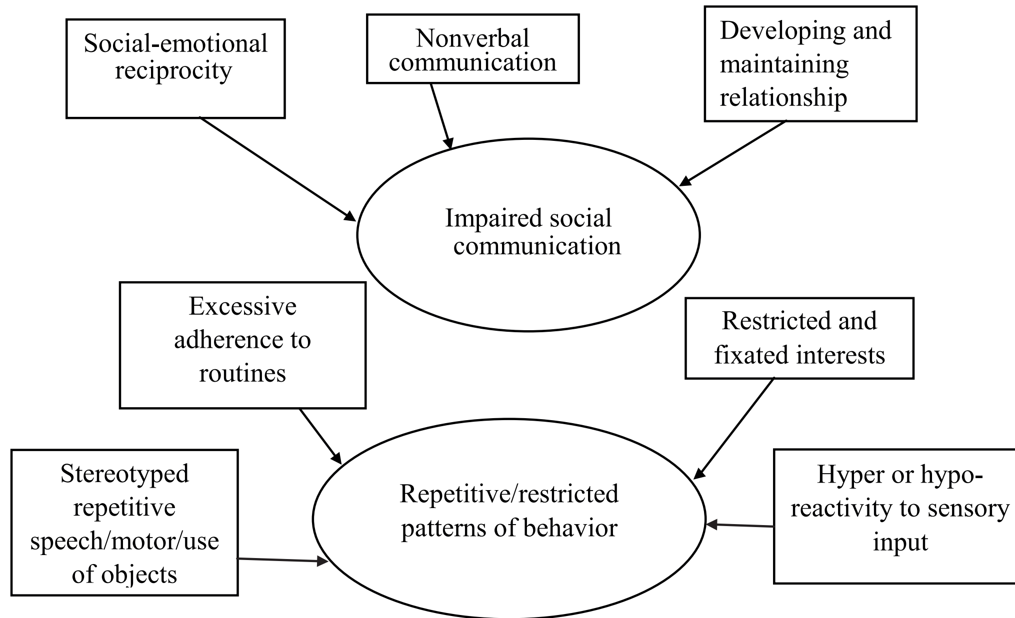
with a diagnosis of ASD tend to have lower IQ, more cognitive impairment and fewer repetitive stereotyped behaviors.[8]

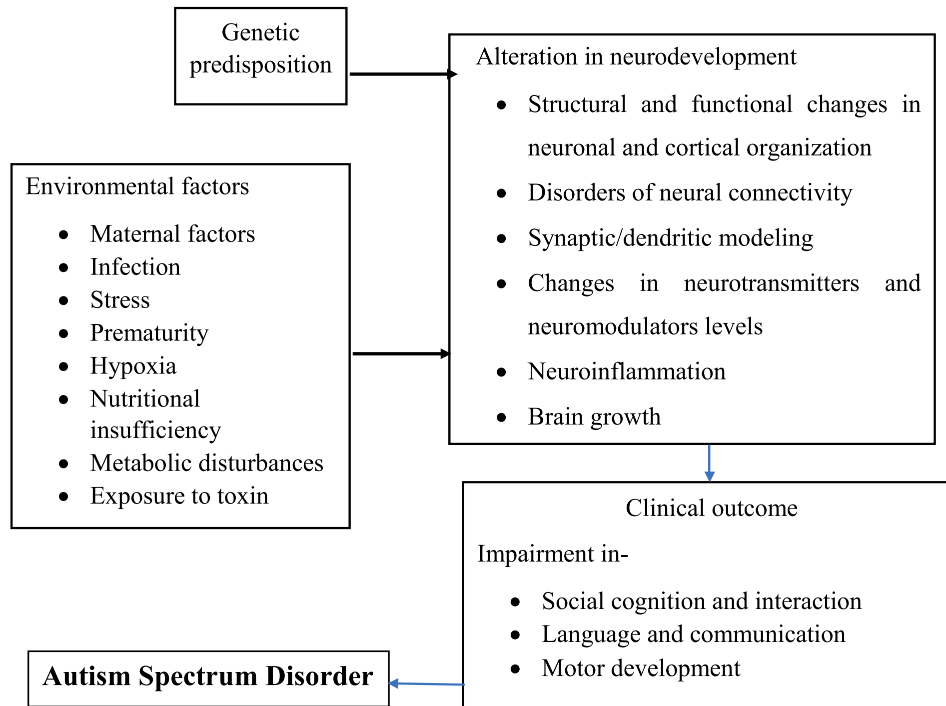
ASD is a disorder of prenatal and postnatal brain development. Generally initial sign symptoms of ASD are typically noticeable in the early development period (prior to age of three years) such as age of first smile, response to their names, pointing to objects and ability to play with peers.[9]By the age of three all typical symptoms such as impaired social reciprocity, poor communication skills and restricted repetitive behavior, affecting three major domains are observed.[10] In South-East Asia most ASD children were diagnosed between 3 and 6 years .[11] Along with the comorbidity such as epilepsy, bowel disorder, intellectual disability and type-I diabetes, the social and economic impact of autism is devastating .[12] The two domains in Diagnostic and Statistical Manual of Mental Disorders (DSM-5) are as follows:[8]



Though causes of autism remain unclear but it is established that, etiology of ASD involves gene environment interaction. ASD is a multifactorial disorder that influenced by genetic, environmental and immunological factors as well as increased vulnerability to oxidative stress.[13]It wasconfirmed thatthere is 90% complex inheritance and genetic heterogenicity.[7]

ASD is a neurodevelopmental disorder (NDD) with multiple genetic risk factors and gene-environment interactions.[14] In addition, micronutrients and trace elements as an environmental factor in the pathogenesis of ASD.[15] The environmental factors are poorly understood. Evidences indicate that prenatal environmental risk factors such as advanced parental age, obstetric complications, maternal infections, stress during pregnancy, and postnatal risk factors such as nutritional deficiency, metabolic imbalance may be associated with ASD.[8] ASD have feeding difficulties and refuse more foods compared to neurotypical peers .[16] Children with ASD have definite food preferences and idiosyncrasies and abnormalities in meal patterns and nutritional inadequacies.[17]Dietary inadequacy ,unique and selective eating patterns are common in autistic children.[18] ASD children exhibited several abnormalities in eating behavior in our country.[19]

Micronutrients are necessary for neuro-development and adequate supply of these nutrients in pregnancy and lactation period has a vital role in brain development .[20] Impairment of micronutrients may lead to nervous system impairment related to pathogenesis of ASD .[21] Nutritional deficiency is related to severity of autistic symptoms and significantly correlated with core behavior of autism .[22,23]Alteration of minerals and trace elements related to increased number of biomarkers related to neuroinflammation.[24]



Sodium is the major cation in ECF and plays a central role in maintaining the Na^{+}-K^{+}ATPase pump in this compartment .[26] Sodium helps to control blood pressure and regulates muscle contraction and neural communication. Muscles and nerves require electrical current, which is generated by controlling the flow of electrically charged molecules like positively charged sodium, to function properly and by this, muscle contraction and neural communication is maintained .[27] Sodium maintains fluid and acid base balance. It has a vital role in maintaining resting membrane potential, producing action potential and absorption of nutrients.Hyponatremia is the most common electrolyte abnormality encountered in children.[28] Children with autistic disorder are chronically hyponatremic due to different reasons. Vasopressin causes dilutional hyponatremia and, diarrhea and vomiting deplete sodium directly in these children .[29]

Low blood sodium level is incorporated in the pathophysiology of ASD. Conditions such as diarrhoea and dietary abnormalities are common in ASD children that causes low serum sodium level in ASD. It has been postulated that hyponatremia in ASD is due to high concentration of water-conserving arginine vasopressin (AVP) .[30] Again, depletion of taurine (TAU), the inhibitory neurotransmitter that suppresses vasopressin, causes elevated level of vassopresin, is also responsible for hyponatremia in ASD.[31]Arginine vasopressin appears chronically elevated in children with ASD because of high androgens, recurring gastrointestinal inflammation, hypoglycemia and stress.[32]Vasopressin causes dilutional hyponatremia and, diarrhea and vomiting deplete sodium directly in these children.[29]

Vasopressin conserves water at the kidneys, diluting sodium concentration in blood and ECF (dilutional hyponatremia) and, diarrhea and vomiting deplete sodium directly in these children.[29] Hyponatremia drives water into astrocytes inducing compensatory release of taurine, glutamine (GLN) and their water and also reduces sodium gradients that transport taurine and glutamine into the brain.[33]The depletion of brain glutamineby hyponatremia which is also important because, glutamine is a prominent fuel in brain neurons, astrocytes, endothelial cells and the intestines, especially during hypoglycemia and prevents entry of ammonia in neurons.[29] Swollen astrocytes compressing brain capillaries and causes

low brain blood flow in autistic disorder .[34]Previously, it was believed that high sodium levels generate hypertonic milieu that stimulates macrophages to release proinflammatory cytokines.

With the prevalence estimated 25% to 68% of wide range of maladaptive behaviors including irritability are commonly encountered in ASD. The causes of irritability in autistic children are often multifactorial, ASD itself, hypersensitivity to environmental triggers that is related to micronutrients defficiency, communication difficulties and excessive rigidity.[35] Irritability, confusion, headache and lethargy are common early neurological symptoms of low sodium levels in ASD. Hyponatremic encephalopathy is the severe effect of hyponatremia in autistic children. Possible mechanisms of low sodium level in autism spectrum disorder are related to dietary factors and gastrointestinal issues leading to inadequate nutrition, hormonal influence (vasopressin), neurotransmitter (glutamine) disruptionand sodium channel dysfunction.[36]

Methods:

This case control observational study was carried out in the Department of Physiology, Sir Salimullah Medical College (SSMC), Dhaka from 1st January 2022 to 31st December 2022. The ethical permission was taken from the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College (SSMC), Dhaka. For this study, a total number of sixty (60) children age ranged from 5-10 years both male and female were included. They were divided into two groups. Cases were consisted of thirty (30) diagnosed ASD children and controls were consisted of thirty (30) healthy children. The ASD children were selected from Sishu Bikash Kendro, Sir Salimullah Medical College and Mitford Hospital, Dhaka and Brain Gym Bangladesh, Adabor, Dhaka. Whereas, healthy children were selected from personal contact from Dhaka city. After proper counseling, the aim, objectives, risk, benefits and procedure of the study were explained in details to the guardians of the participants. Theywere encouraged for voluntary participation.They had been allowed to withdraw themselves even after participation from the study whenever they like. Only positive respondents were recruited as research participants. The ethical permissionwas taken from the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College (SSMC), Dhaka. Informed written consent was taken from guardians of the participants. Before collection of blood, detailed prenatal history, antenatal history, birth history, history of infancy and dietary history were taken and thorough physical examination of all the participants was done anddata were collected in a standard pre-fixed questionnaire. Then the parents were requested to attend the Department of Biochemistry and Molecular Biology in BSMMU forcollection of blood sample in scheduled dates. Blood was collected from each participant of both case and control groups for estimation ofserum levels of sodium. Serum sodium levels was estimated by ion selective electrodes technique (ISE) electrolyte auto analyzer method, by using A-LYTE Integrated Multisensor Technology (IMT).With all aseptic precautions, 5 ml venous blood was drawn from the ante-cubital vein by a sterile disposable syringe from each participant for estimation of serum sodiumin the Department of Biochemistry and Molecular Biology in Bangabondhu Sheikh Mujib Medical University (BSMMU). Data were expressed as mean ± SD (Standard Deviation). The statistical analysis was done by using Statistical Package of Social Science (SPSS) for windows version 22. Unpaired "t" test was done to compare the data as applicable. p value ≤0.05 was considered as level of significance.

Results:

General characteristics of the ASD children and control are shown in Table I. BMI of all the subjects were within reference range. All the children of both groups were age and BMI matched. Here, the mean serum sodium level was lower but not significantly different in ASD children compared to healthy controls (Table II). However, all the values of serum sodium were within normal reference range in children of both groups. In addition, lower serum sodium level in ASD children than that of healthy controls was shown in Figure I.

Table I. General characteristics age and body mass index (BMI) in both ASD and healthy controls (N=60)

Variables	ASD (n=30)	Control (n=30)	p-value
Age (Years)	7.38 ± 1.94 (5-10)	7.83 ± 1.76 (5-10)	0.67
BMI $(kg/m)^2$	15.82 ± 1.81 (12.85-21.27)	16.16 ± 1.79 (13.14-21.27)	0.467

Data are expressed as mean (±SD). For statistical analysis unpaired "t" test was performed to compare between two groups. p-value d"0.05 was accepted for level of significance. Figure in parentheses indicate ranges. ASD= Children with autism spectrum disorder; Control= Healthy children; N= Total number of children; n=number of children in each group.

Table II. *Mean serum sodium level in both ASD and control (N=60)*

Parameter	ASD (n=30)	Control (n=30)	p-value
Sodium (mmol/L)	137.27 ± 2.00 (134 - 141)	138.2 ± 1.83 (135-143)	0.064

Data are expressed as mean (±SD). For statistical analysis unpaired "t" test was performed to compare between two groups. p-value ≤0.05 was accepted for level of significance. Figure in parentheses indicate ranges. ASD= Children with autism spectrum disorder; Control= Healthy children; N= Total number of children; n=number of children in each group.

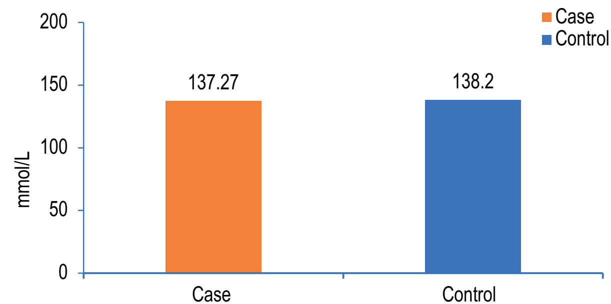


Figure-1: Mean serum sodium level of the children in both case (ASD) and control (N=60)
Case: Children with autism spectrum disorder (ASD) **Control:** Healthy children
N = Total number of study children

Discussion:

The present study was undertaken to observe serum levels of sodium status in children with autism spectrum disorder.For this study, a total number of sixty (60) children age ranged from 5 to 10 years of both male and female were enrolled. Among them there were thirty (30) diagnosed ASD children (case) and their serum levels of sodium were measured. All these variables were also studied in thirty (30) healthy control subjects for comparison. In this study the age of all the subjects of both groups (case and control) were from 5 to 10 years and BMI of two groups (case and control) were almost similar and no significant difference was present between two groups. So, both groups were age and BMI matched. Pulse rate, systolic blood pressure (SBP) and diastolic blood pressure (DBP) were also measured in both groups and the values of all children were within normal reference range.ASD have feeding difficulties and refuse more foods compared to neurotypical peers .[16] ASD children exhibited several abnormalities in eating behavior in our country.[19]Impairment of micronutrients may lead to nervous system impairment related to pathogenesis of ASD.[21] Nutritional deficiency is related to severity of autistic symptoms and significantly correlated with core behavior of autism .[22,23] Therefore their regular diet may fail to meet the demand of sodium.

In the study, it was reported that the mean serum sodium level was lower in children with ASD than that of healthy control but the difference was not statistically significant. This finding was in agreement with the finding of other investigators of different countries (El-Ansary et al., 2009; El-Ansary, Bacha and Al-Ayadhi, 2011; Skalny et al., 2016).Whereas, some other investigators (Meguid et al., 2017; Sojar et al., 2019) found significantly ($p<0.001$) lower level of serum sodium in

childrenwith ASD compared to healthy control. The researchers observed that this might be due to nutritional inadequacies exhibited by abnormalities in meal patterns in ASD children.On the contrary, Adams et al. (2011), observed serum sodium level was higher in childrenwith ASD than that of healthy controlwhich was not statistically significant. The researchers suggested that this may be due to adequate dietary intake of micronutrient.However, Al Hadad, Ramadan and Othman (2022), Erturk E.,Isik U. and Aktepe E.(2023) showed that serum sodium level was almost similar in children with ASD and healthy children which is similar to the present study.Irritability, confusion, headache and lethargy are common early neurological symptoms of low sodium levels in ASD. Hyponatremic encephalopathy is the severe effect of hyponatremia in autistic children. Possible mechanisms of low sodium level in autism spectrum disorder are related to dietary factors and gastrointestinal issues leading to inadequate nutrition, hormonal influence (vasopressin), neurotransmitter (glutamine) disruption and sodium channel dysfunction.[36] However, in our study, the lowered sodium may be associated with inadequate dietary intake of foods, which is evident from their dietary history.

Conclusion:

From this study, it may be concluded autism spectrum disorder was associated with lower sodium level. The concept that blood sodium level influences the progression of autism is novel. Therefore, we may recommend adequate dietary intake of sodium rich foods for children with ASD. Supplement of thisnutritional element may be used for reduction of severity of symptoms in autistic children.

Limitations:

No severity score of ASD children was done and correlation of parameters with ASD score was not done.Subjects were collected only from urban area.Age of the participants were high in relation to neurodevelopment.Follow up study after supplementation of sodium in ASD children was not done.

Data Availability:

The datasets analysed during the current study are not publicly available due to the continuation of analyses but are available from the corresponding author on reasonable request.

Conflict of interest: The authors of this study have no conflict of interest.

Funding:

This research received no external funding.

Ethical consideration:

The study was approved by the Ethical Review Committee of Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh. Informed consent was obtained from each participant or caregivers of the patients.

Author Contributions:

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; had agreed on the journal to which the article had been submitted; and agreed to be account able for all aspects of the work.

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References

1. American Psychiatric Association, Diagnostic and Statistical Manual of Mental Disorders (DSM-5^{TM}): American Psychiatric Pub, 5th edition; 2015. Available at: https://cdn.websiteeditor.net/30f11123991548a0af708722d458e476/files/upload/DSM%2520V.pdf
2. WeintraubK. Autism Counts. Macmillan publishers Limited, Nature 2011; 479(1): 22-24.
3. Baxter AJ,Brugha TS, Erskine HE, Scheurer RW, Vos T and Scott JG. The Epidemiology and Global Burden of Autism Spectrum Disorder. Physiological Medicine 2015; 45(1):601-613. doi:10.117 /SD03329171400172X
4. Zeidan J, Fombonne E, Scorah J et al; Global Prevalence of autism: A systematic review update. Autism Research 2022; 15: 778-790.
5. Akhter S, Hussain AHME, Shefa J, Kundu GK, Rahman F and Biswas A. Prevalence of Autism Spectrum Disorder (SD) among the children aged 18-36 months in a rural community of Bangladesh:A cross sectional study [version 1; referees: 1approved, 2 approved with reservations].Non Communicable

Disease Control (NCDC), Directorate General of Health Services, Dhaka-1206, Bangladesh. F 1000 Research 2018; 7(424): 1-14. doi: 10.12688/11000research. 13563. 1

6. Hossain MD, Ahmed HU, Uddin MMJ et al; Autism Spectrum Disorder (ASD) in South Asia: A Systematic Review. BMC Psychiatry 2017;17(281): 1-7. doi: 10.1186/ s12888-017-1440-x

7. Alsagob, M., Colak, D. and Kaya, N. Genetics of Autism Spectrum Disorder: An update on Copy Number Variations Leading to Autism in the Next Era. King Faisal Specialist Hospital and Research Centre, Riyadh, Saudi Arabia. Discovery Medicine2015;19(106): 367-379.

8. Courteur AL and Szatmari P. Autism Spectrum Disorder. In: Thapar, A. et al. (2015), Rutter's Child and Adolescent Psychiatry. 6th edition.United Kingdom. Jhon Wily & Sons. Ltd.;2015Chapter 15; p. 665-682.

9. Ping HJ, Shan CUIS, Yu HAN, Picciotto IRVAH, Hong QL and Xin Z. Prevalence and Early Signs of Autism Spectrum Disorder (ASD) Among 18-36 Month Old Children in Tanjania of China. Biomed Environ Sci 2014; 27(6): 453-461. doi: 10.3967/bes2014.008

10. Bloom ED, Lord C, Zwaigenbaum L et al; The Development Neurology of Autism Spectrum Disorder. JNEUROSCI Georg 2006; 26: 6897-6906.

11. Kalra V, Seth R and Sapra S.Autism-Experiences in a Tertiary Care Hospital. Indian Journal of Pediatrics2005;72:27-230.Availableat: https:// pubmed.ncbi.nih.gov

12. Kohane IS, McMurry A, Weber G et al; The Co-Morbidity Burden of Children and Young Adults with Autism Spectrum Disorders. Center for Biomedical Informatives, Harvard Medical School, USA 2012; 7(4): 1-7. doi: 10.1371/journal.pone.0033224

13. Keller8 F and Persico AM. The Neurobiological Concept of Autism. Molecular Neurobiology 2003; 28: 1-22. DOI: 10.1385/MN:28:1:1

14. Pietropaolo S, Crusio WE and Feldon J. Gene-Environment Interactions in Neurodevelopment Disorders. Neural Plasticity2017; 1-2. http://dx.doi.org/ 10.1155/2017/9272804

15. Baj J, Fleiger W, Fleiger M et al; Autism Spectrum Disorder: Trace elements imbalances and the pathogenesis and severity of autistic symptoms. Neuroscience and Behavioral Reviews 2021; 129(1): 117-132. https://doi.org/10.1016/j.neubiorev.2021.07.029

16. Malhi P, Venkatesh L, Bharti B and Singhi P. Feeding Problems and Nutrient Intake in Children with and without Autism: A Comparative Study. Indian J Pediatr2017; 84(4): 283-288. DOI: 10.1007/s12098-016-2285-x

17. Shearer TR, Larson K, Neuschwander J and Gedney B. Minerals in the Hair and Nutrient Intake of Autistic Children. Journal of Autism and Developmental Disorders 1982; 12(1): 25-34. Available at: https:// pubmed.ncbi.nlm.nih.gov/6896512/

18. Graf-Myles J, Farmer C, Thurm A et al; Dietary Adequacy of Children with Autism Compared to Controls and Impact of Restricted Diet. J Dev BehavPediatr,2013; 34(7): 1-12. doi: 10.1097/ DBP.0b013e3182a00d17

19. Shefa, J., Islam, K. and Rahaman, M.F.U. Nutrient level & its effect on cognition among ASD children in Bangladesh: A cross-sectional study. MOJ Public Health 2018; 7(6): 266-272. Available at: https:// medcraveonline.com

20. Gonzalez HF and Visentin S. Micronutrients and Neurodevelopment: An Update. Arch Argent Pediatr 2016; 114(6): 570-575. Available at: https:// www.researchgate.net./publication/311928957

21. Yasuda H and Tsutsui T. Estimation of autistic children by metallomics analysis. Scientific Reports 2013; 3(1199): 1-7. https://doi.org/10.1038/srep01199

22. Adams JB, Audhya T, Means SM et al; Nutritional and metabolic status of children with autism vs. neurotypical children, and the association with autism severity Nutrition & Metabolism 2011; 3(34): 1-32. Available at: http://www.nutritionandmetabolism.com/content /8/1/ 34

23. Zhao G, Liu S, Gan X et al; Analysis of Whole Blood and Urine Trace Elements in Children with Autism Spectrum Disorders and Autistic Behaviors. Biological Trace Elements Research 2022.https://doi.org/10.1007/ s12011-022-03197-4

24. Skalny AV,Simashkova NV, Skalnaya AA et al; Trace Element Levels are Associated with Neuro-inflammatory Markers in Children with Autism Spectrum Disorder. Journal of Trace Elements in Medicine and Biology 2018. JTEMB-26132. http:// dx.doi.org/10.1016/j.jtemb.2018.04.0319

25. Pardo CA and Eberhart CG. The Neurobiology of Autism. International Society of Neurobiology. Brain Pathology 2007; 17: 434-447.DOI: 10.1111/j.1750-3639.2007.00102.x

26. Scott MG, LeGrys VA and Hood JL. Electrolytes and Blood Gases. In: Rifai, N., Horvath, A.R. and Wittwer, C.T. Tietz Fundamental Clinical Chemistry and Molecular Diagnostics. 7th Edition. India: Reed Elsevier Private Limited. 2015;Chapter 28, p. 807-810.

27. Cloe A. The Action of Sodium in the Human Body. Healthy Eating/Nutrition/Sodium. 2018 December 7. www.healthyeating.sfgate.com

28. Moritz ML. and Ayush JC. New Aspects in the Pathogenesis, Prevention, and Treatment of Hyponatremic Encephalopathy in Children.Pediatr Nephrol 2009; 25: 1225-1238. doi: 10.1007/s00467-009-1323-6

29. Good, P. Do Salt Cravings in Children with Autistic Disorders Reveal Low Blood Sodium Depleting Brain

Taurine and Glutamine? Medical Hypotheses 2011; 77: 1015-1021. doi: 10.1016/j.mehy.2011.08.038

30. Momeni N, Nordstorm BM, Horstmann V, Avarseji H and Sivberg BV. Alteration of Prolyl Endopeptidase Activity in the Plasma of Children withAutism Spectrum Disorder.BMC Psychiatry 2005; 5(27): 1-6. doi: 10.1186/1417-244X-5-27

31. Hussy N, Bres V, Rochette M et al; Osmoregulation of Vasopressin Secretion via Activation of Neurohypophysical Nerve Terminals Glycine Receptors by Gilal Taurine. The Journal of Neuroscience 2001; 21(18): 7110-7116.

32. Neville KA, Verge CF, O'Meara W and Walker JL. High Antidiuretic Hormone Levels and Hyponatremia in Children With Gastroenteritis. Department of Endocrinology & Emergency Department, Pediatrics 2005;116(6): 1401-1407. DOI: 10.1542/peds.2004-2376

33. Massieu L, Montiel L, Robles G and Quesada O. Brain Amino Acid During Hyponatremia In Vivo: Clinical Observations and Experimental Studies. Neurochemical Research 2004;29(1): 73-81.Available at:https://www.researchgate.net/publication/8592505

34. Aschner M, Allen JW, Kimelberg HK, Lopachin RM and Streit WJ. Glial Cells in Neurotoxicity Development. Annu. Rev. Pharmacol. Toxicol.1999; 39(1): 151-173. Available at: www.annualreviews.org.

35. Ooi A, Banno B, McFee K, and Friedlander R. Evaluating and managing irritability and aggression in children and adolescents with autism spectrum disorder : An algorithm. BCMJ 2023; 65(8): 291-322.

36. Erturk E, Isik U and Aktepe E. Analysis of blood sodium level in autism spectrum disorder. Int J Dev Disabil 2023, Apr10;70(8):1520-1523. Doi:10.1080/20473869.2023.2197309

37. El-Ansary A, Al-Daihan S, Al-Dbass A and Al-Ayadhi L. Measurement of Selected Ions Related to Oxidative Stress and Energy Metabolism in Saudi Autistic Children. Clinical Biochemistry 2009;43(1): 63-70. doi: 10.1016/j.clinbiochem.2009.09.008

38. El-Ansary A, Bacha AGB and Al-Ayadhi L.Y. Proinflammatory and Proapoptotic Markers in Relation to Mono and Di-cations in Plasma of Autistic Patients from Saudi Arabia. Journal of Neuroinflammation 20118(142): 2-Available at: http://www.jneuroinflammation.com/content/8/1/142

39. Skalny AV, Simashkova NV, Klyushnik TP et al; Assessment of serum trace elements and electrolytes in children with childhood and atypical autism. Journal of Trace elements in Medicine and Biology 2016.http://dx.doi.org/10.1016/j.jtemb.2016.09.009

40. Sojar SH, Goldner JSV, Krishnamoorthy K, Murphy SA, Masiakos PT and Kling JE. A 17-Year-Old Boy with High-Functioning Autism, Gastrointestinal Illness, and Seizures. Pediatrics 2019; 143(1): 1-9.DOI: https://doi.org/10.1542/peds.2017-3964

41. Al Hadad AA, Ramadan AN and Othman AAA. Study of trace elements and electrolytes in autism spectrum disorder in an Egyptian children sample. Faculty of Medicine, Menoutia University 2022; 35: 116-119. doi: 10.4103/mmj.mmj_348_20

42. Meguid NA, Anwar M, Bjorkland G et al; Dietary Adequacy of Egyptian Children withAutism Spectrum Disorder Compared to Healthy Developing Children. Metab Brain Dis2017; 32: 607-615. DOI: 10.1007/s11011-016-9948-1.