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Study of toxic metal pollution in autistic patients in Thi-Qar Governorate

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ABSTRACT

Background. Autism-spectrum disorders (ASDs) are a group of chronic neurodevelopmental conditions characterized by difficulties in social interaction and communication, as well as rigid thinking and behavior.

Aim of this study. This study aimed to examine the potential impact of trace metals, specifically copper, iron, and zinc, in the development of autism spectrum disease.

Materials and method. A total of 100 blood samples were collected from patients diagnosed with autism, while an additional 100 samples were taken from healthy individuals serving as a control group. The individuals separated into three distinct groups: Group A (control) consisted of one hundred healthy participants aged 3-14 years. Group B consisted of one hundred patients diagnosed with autism, ranging in age from 3 to 14 years old.

Results. The findings demonstrated a substantial elevation in the levels of lead (Pb), selenium (Se), cadmium (Cd), nickel (Ni), and chromium (Cr) in all groups of patients as compared to the control group.

Conclusion. Study the relationship between trace elements and autism. It was observed that the concentration of lead (Pb) and chromium (Cr) was significantly higher in women who did not consume folic acid compared to those who did. On the other hand, the level of nickel (Ni) was significantly lower in women who did not consume folic acid compared to those who did.

Keywords: autism, autism spectrum disorder, trace elements, Cadmium (Cd), Nickel (Ni), Selenium (Se), Chromium (Cr), Lead (Pb)

INTRODUCTION

Autism, also referred to as autism spectrum disorder (ASD), is widely acknowledged as one of the most widespread neurodevelopmental disorders [1]. These issues pertain to communication, social interaction, and conduct. Currently, there is still a significant lack of understanding on the meaning of ASD. Consequently, ASD is frequently perceived in a negative light, with a considerable number of individuals even classifying it as an illness. They frequently exhibit aberrant conduct [2]. Lead (Pb) is a naturally occurring heavy metal element that is not magnetic and is present in the earth's crust. Although Pb is highly dangerous, it has been widely utilized in different industries and consumer products globally because of its malleability and resistance to corrosion [3]. Selenium exerts various biological effects, including the modulation of the arachidonic acid cascade and the promotion of apo A-I expression by influencing PPARγ and NF-κB. Selenium shortage is linked to increased inflammation and enhances the production of seleno-proteins, which play a role in antioxidant defense mechanisms [4]. Cadmium (Cd) is a well-known hazardous metal mostly originating from industrial and agricultural sources [5]. In 2010, the global production of cadmium reached 22,000 tons, whereas the estimated global reserves of this metal are 660,000 tons [6]. Chromium (Cr) exists in two oxidation states: +3 and +6. Cr (+3) is the sole necessary

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trace element that has a significant impact on the metabolism of glucose and cholesterol [7]. Nickel is a resilient, malleable, lustrous transition metal that is widely available in nature. Nickel can exist in various oxidative states ranging from -1 to +4. However, the most common oxidative state in both the environment and biological systems is Ni2+ in the +2-oxidation state [8].

MATERIAL AND METHOD

Sample collection

This study conducted at Autism Center in Nasiriyah, Thi-Qar Governorate from Biochemistry Laboratory in College of Science, at the period between from December 2022 to June 2023. It included (200) cases, (100) control and (110) patients.

TABLE 1. Data of Controls and Patients Groups

Groups	No.	Groups
Controls	100	Controls
Patients	100	Patients

This study comprised a total of 100 male and female volunteers, both control and patients with trace elements, who were between the ages of 3 and 14 and had autism spectrum disorder (ASD). They split into two factions as follows:

Control: The study consisted of one hundred (100) participants who were in good health and ranged in age from 3 to 14 years old.

Autistic patients: The study included a total of one hundred (100) patient volunteers aged between three (3) and fourteen (14) years old.

Collection of Blood Samples

Four milliliter blood samples were collected from both autistic patients and controls. The samples were then left to clot in empty disposable tubes at room temperature. Afterward, the samples were separated using a centrifuge operating at a speed of 3000 revolutions per minute (rpm) for a duration of 10 minutes. The serum samples were isolated and preserved at a temperature of -20ºC for subsequent analysis of biochemical characteristics, unless they were utilized immediately. The flame atomic absorption spectrophotometer was used to test the trace elements Cadmium (Cd), Nickel (Ni), Selenium (Se), Chromium (Cr), and Lead (Pb).

Quantification of Cadmium (Cd) in Serum: Take 0.5 cc of the standards, samples (serum), and quality control specimens and dilute them 4.5 times with distilled water (HPLC). Ensure thorough mixing. A flame atomic absorption spectrophotometer was used to analyze the sample after creating a calibration curve at a wavelength of 288.80 nm (Osselton & Widdop, 2011). The analysis of selenium, nickel, chromium, and lead was conducted using the same methodology.

Digestion of samples

The serum samples underwent digestion by combining 2 mL of concentrated nitric acid and 1 mL of concentrated perchloric acid with 0.5 mL of serum in a Pyrex tube. The mixture samples were subjected to heating at a temperature of 160°C for a duration of 1 hour using an oil bath. Afterward, they were chilled. The volume was augmented to 10 mL by using 0.5 mL of hydrochloric acid.

RESULTS

Table 2 presents the current results of the investigation on the concentration of all heavy metals examined in this study. The concentrations of all heavy metals showed a significant rise ($p < 0.05$) in individuals with autism compared to the control group, as illustrated in figures 1, 2, 3, 4, and 5.

TABLE 2. The concentration of heavy elements in autism patients and control group

Trace elements	Mean ± SD		p. value
	Autism Patients No. 100	Control group No. 100	
Cd	0.086±0.0400	0.005±.0.010	< 0.001**
Se	5.803±1.8270	0.083±0.0110	< 0.001**
Pb	0.203±0.0660	0.033±0.0080	< 0.001**
Ni	0.082±0.0330	0.0005±0.0001	< 0.001**
Cr	0.297±0.0990	0.001±0.0009	< 0.001**

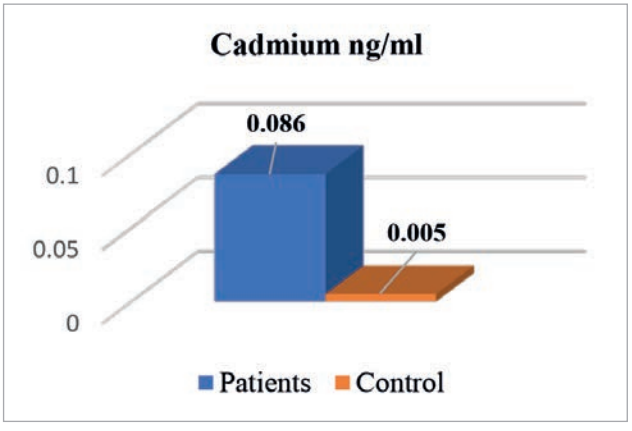

FIGURE 1. Cd level in autism-patients and control group

DISCUSSION

Metals are considered a potential modifiable risk factor in ASD. Women of reproductive age in the United States are commonly exposed to metals in

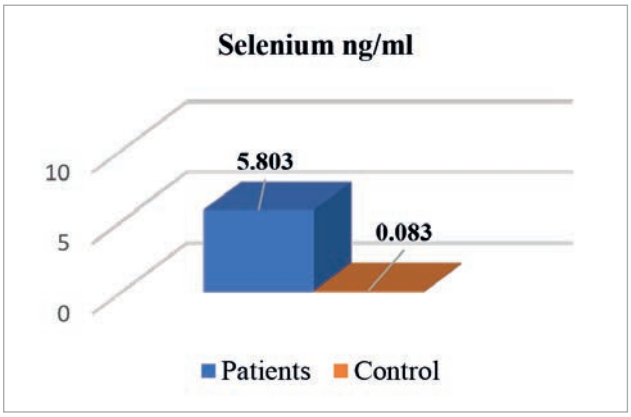

FIGURE 2. Se level in autism-patients and control group

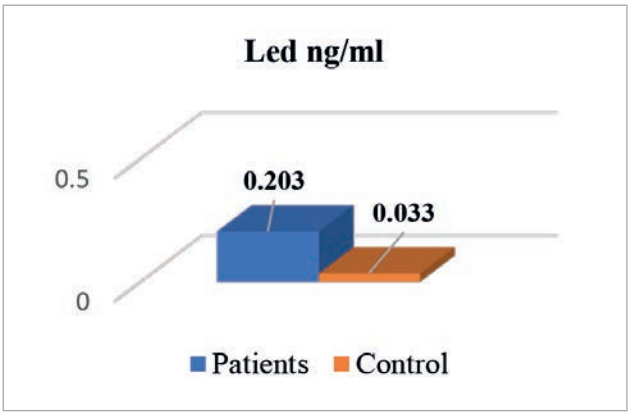

FIGURE 3. Pb level in autism-patients and control group

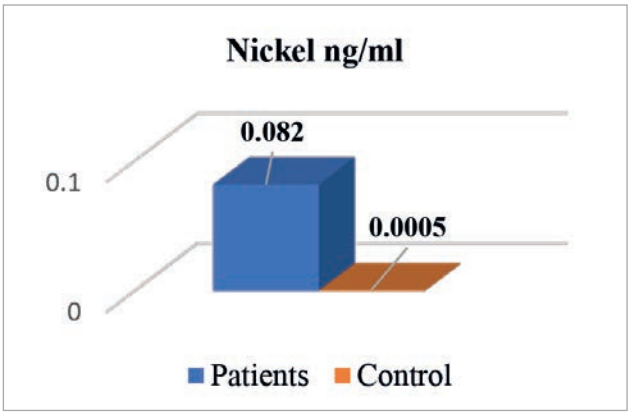

FIGURE 4. Ni level in autism-patients and control group

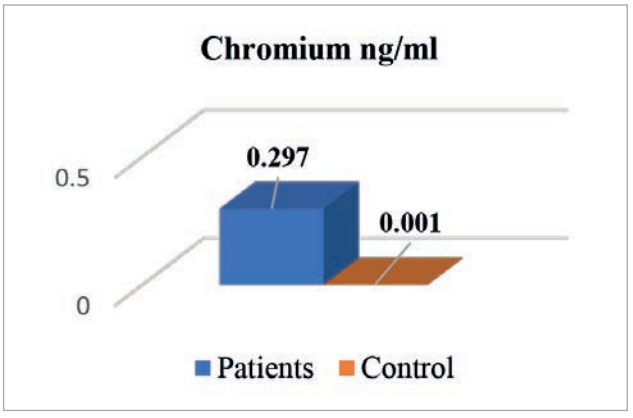

FIGURE 5. Cr level in autism-patients and control group

their surroundings, and pregnant women tend to have greater levels of metal concentrations compared to non-pregnant women [9,10]. Crucial neurodevelopmental processes take place during pregnancy [11], exposure to environmental factors, namely metals, is believed to play a role in the development of autism spectrum disorder (ASD) [12-14]. Children diagnosed with ASD have been found to have elevated blood levels of arsenic compared to control groups [15], mercury [15-17], lead [18-20], and cadmium [21], Have been witnessed. Although these findings show that exposure to metals was detected after the diagnosis of ASD [22]. Furthermore, it has been demonstrated that Cd can trigger an immunological response [23], How often this effect manifests in the brain is unclear. Exposure to potentially harmful substances is one environmental variable that has been linked to an increase in the incidence of autism spectrum disorder [24].

CONCLUSION

It was observed that the concentration of lead (Pb) and chromium (Cr) was significantly higher in women who did not consume folic acid compared to those who did. On the other hand, the level of nickel (Ni) was significantly lower in women who did not consume folic acid compared to those who did.

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REFERENCES

1. Narzisi A, Alonso-Esteban Y, Alcantud-Marín F. Autism and children: diagnosis, functional profiles and intervention. *Children.* 2023 Mar 8;10(3):522. doi: 10.3390/children10030522
2. Khambali M, Nurtasila S. Pendidikan khusus bagi peserta didik disabilitas netra disertai hambatan intelektual.
3. Li MM, Gao ZY, Dong CY, Wu MQ, Yan J, Cao J et al. Contemporary blood lead levels of children aged 0–84 months in China: A national cross-sectional study. *Environ Int.* 2020 Jan 1;134:105288. doi: 10.1016/j.envint.2019.105288
4. Gandhi UH, Kaushal N, Ravindra KC, Hegde S, Nelson SM, Narayan V, Vunta H, Paulson RF, Prabhu KS. Selenoprotein-dependent up-regulation of hematopoietic prostaglandin D2 synthase in macrophages is mediated through the activation of peroxisome proliferator-activated receptor (PPAR) γ. *J Biol Chem.* 2011 Aug 5;286(31):27471-82. doi: 10.1074/jbc.M111.260547
5. Dutta A, Patra A, Jatav HS, Jatav SS, Singh SK, Sathyanarayana E, Verma S, Singh P. Toxicity of cadmium in soil-plant-human continuum and its bioremediation techniques. Soil contamination-Threats and sustainable solutions. 2020 Oct 28;22. doi: 10.5772/intechopen.94307
6. Rodríguez-Barranco M, Lacasaña M, Aguilar-Garduño C, Alguacil J, Gil F, González-Alzaga B. Association of arsenic, cadmium and manganese

exposure with neurodevelopment and behavioural disorders in children: a systematic review and meta-analysis. Sci Total Environ. 2013 Jun 1;454:562-77. doi: 10.1016/j.scitotenv.2013.03.047
7. Broadhurst CL, Domenico P. Clinical studies on chromium picolinate supplementation in diabetes mellitus – a review. Diabetes Technol Ther. 2006 Dec 1;8(6):677-87. doi: 10.1089/dia.2006.8.677
8. Muñoz A, Costa M. Elucidating the mechanisms of nickel compound uptake: a review of particulate and nano-nickel endocytosis and toxicity. Toxicol Appl Pharmacol. 2012 Apr 1;260(1):1-6. doi: 10.1016/j.taap.2011.12.014
9. Watson CV, Lewin M, Ragin-Wilson A, Jones R, Jarrett JM, Wallon K, Ward C, Hilliard N, Irvin-Barnwell E. Characterization of trace elements exposure in pregnant women in the United States, NHANES 1999-2016. *Environ Res.* 2020 Apr 1;183:109208. doi: 10.1016/j.envres.2020.109208
10. Martin EM, Fry RC. Environmental influences on the epigenome: exposure-associated DNA methylation in human populations. *Annu Rev Public Health.* 2018 Apr 1:39:309-33. doi: 10.1146/annurev-publhealth-040617-014629
11. Estes ML, McAllister AK. Maternal immune activation: Implications for neuropsychiatric disorders. *Science.* 2016 Aug 19;353(6301):772-7. doi: 10.1126/science.aag3194
12. Bölte S, Girdler S, Marschik PB. The contribution of environmental exposure to the etiology of autism spectrum disorder. *Cell Mol Life Sci.* 2019 Apr 15;76:1275-97. doi: 10.1007/s00018-018-2988-4
13. Heyer DB, Meredith RM. Environmental toxicology: Sensitive periods of development and neurodevelopmental disorders. *Neurotoxicology.* 2017 Jan 1;58:23-41. doi: 10.1016/j.neuro.2016.10.017
14. Lyall K, Schmidt RJ, Hertz-Picciotto I. Maternal lifestyle and environmental risk factors for autism spectrum disorders. *Int J Epidemiol.* 2014 Apr 1;43(2):443-64. doi: 10.1093/ije/dyt282
15. Ding M, Shi S, Qie S, Li J, Xi X. Association between heavy metals exposure (cadmium, lead, arsenic, mercury) and child autistic disorder: A systematic review and meta-analysis. *Front Pediatr.* 2023 Jul 4:11:1169733. doi: 10.3389/fped.2023.1169733
16. Jafari T, Rostampour N, Fallah AA, Hesami A. The association between mercury levels and autism spectrum disorders: a systematic review and meta-analysis. *J Trace Elem Med Biol.* 2017 Dec:44:289-97. doi: 10.1016/j.jtemb.2017.09.002
17. Jiang Y, Yin X, Xu Q, Tang X, Zhang H, Cao X, Lin J, Wang Y, Yang F, Khan NU, Shen L. SWATH proteomics analysis of placental tissue with intrahepatic cholestasis of pregnancy. *Placenta.* 2023 Jun 1;137:1-3. doi: 10.1016/j.placenta.2023.04.009
18. Rashaid AH, Nusair SD, Alqhazo MT, Adams JB, Abu-Dalo MA, Bashtawi MA. Heavy metals and trace elements in scalp hair samples of children with severe autism spectrum disorder: A case-control study on Jordanian children. *J Trace Elem Med Biol.* 2021 Sep:67:126790. doi: 10.1016/j.jtemb.2021.126790
19. Saghazadeh A, Rezaei N. Systematic review and meta-analysis links autism and toxic metals and highlights the impact of country development status: Higher blood and erythrocyte levels for mercury and lead, and higher hair antimony, cadmium, lead, and mercury. *Prog Neuropsychopharmacol Biol Psychiatry.* 2017 Oct 3;79(Pt B):340-68. doi: 10.1016/j.pnpbp.2017.07.011
20. Zhang J, Li X, Shen L, Khan NU, Zhang X, Chen L, Zhao H, Luo P. Trace elements in children with autism spectrum disorder: a meta-analysis based on case-control studies. *J Trace Elem Med Biol.* 2021 Sep:67:126782. doi: 10.1016/j.jtemb.2021.126782
21. Baj J, Flieger W, Flieger M, Forma A, Sitarz E, Skórzyńska-Dziduszko K, Grochowski C, Maciejewski R, Karakuła-Juchnowicz H. Autism spectrum disorder: Trace elements imbalances and the pathogenesis and severity of autistic symptoms. *Neurosci Biobehav Rev.* 2021 Oct:129:117-32. doi: 10.1016/j.neubiorev.2021.07.029
22. Doherty BT, Romano ME, Gui J, Punshon T, Jackson BP, Karagas MR, Korrick SA. Periconceptional and prenatal exposure to metal mixtures in relation to behavioral development at 3 years of age. *Environ Epidemiol.* 2020 Aug 1;4(4):e0106. doi: 10.1097/EE9.0000000000000106
23. Leffel EK, Wolf C, Poklis A, White Jr KL. Drinking water exposure to cadmium, an environmental contaminant, results in the exacerbation of autoimmune disease in the murine model. *Toxicology.* 2003 Jun 30;188(2-3):233-50. doi: 10.1016/s0300-483x(03)00092-1
24. Błażewicz A, Grabrucker AM. Metal profiles in autism spectrum disorders: A crosstalk between toxic and essential metals. *Int J Mol Sci.* 2022 Dec 24;24(1):308. doi: 10.3390/ijms24010308