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Research Article

Altered Blood Levels of certain heavy metals in Iraqi autistic children

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Abstract

Autism is a developmental condition that affects people all their lives and is usually identified in children. It is accompanied by several physiologic and homeostatic changes including. The aim of this work was to evaluate the blood concentration of certain heavy metals (Nickel, Chromium, Manganese, and Zinc) in children with autism. Blood samples were collected from 40 normal children and 40 autistic ones and the blood concentrations of these metals were assessed. Our findings showed significant differences between control group and autism cases assessment of some heavy metals in children with autism. Serum samples taken from children with autism and control showed a significant difference in the levels of these heavy metals, with children with autism having significantly higher levels of nickel and chromium and significantly lower concentrations of manganese and zinc.

1. Introduction

A developmental illness that typically manifests in children, autism spectrum disorders (ASD) impact individuals throughout their lives. ASD is categorized as a "spectrum" condition since it encompasses a variety of developmental defects with corresponding characteristics that differ in severity. According to APA [1], ASD has been linked to restricted and repetitive patterns of behavior, social relatedness impairments (such as failure to form healthy peer relationships), and verbal and nonverbal communication impairments (such as delayed or nonexistent spoken language). According to [2], ASDs are a group of neurodevelopmental disorders that include Rett's disorder, autism, Asperger's syndrome, childhood disintegrative disorder, and Pervasive Developmental Disorder, Not Otherwise Specified (PDD-NOS). Boys are almost 4.5 times as likely than girls to have ASD. Early infancy is when the condition first manifests, and most of the time it has a chronic course with symptoms that last into adulthood [3].

According to another study [4], estimated prevalence of ASD increased from 2011 to 2014 as a result of adjustments in the National Health Interview Survey (NHIS) questions regarding developmental impairments. A group of neurodevelopmental disorders known as autism spectrum disorders (ASDs) are typically perinatal in nature and can be identified in early childhood when symptoms are most severe [5, 6]. The exact cause of ASDs is unknown, however a variety of theories point to a genetic and environmental interaction. Genetic variations involved in ASDs that are passed down from parents to affected individuals are thought to account for around 40% of the risk of ASDs [7].

The majority of heavy metals are non-essential hazardous substances that are extensively found in the environment. Chronic exposure to low concentrations of heavy metals has raised concerns about public health in many nations. Despite significant drops in blood levels of

heavy metals like Pb and Cd and advancements in public health regulations. A growing body of research indicates a connection between exposure to heavy metals like lead (Pb) and memory impairment. Furthermore, research has shown that as bone heavy metal concentrations, such as Pb concentrations, rise over time as a measure of cumulative exposure, the degree of performance impairment also increases [8]. Furthermore, lower Mini Mental Status Exam scores are linked to higher Pb content in bone [9]. One of the main risk factors for developmental neurotoxicity is thought to be exposure to heavy metals [10, 11].

Children with ASD have blood levels of lead and mercury correlated with differential expression of many genes [12, 13]. Due to a genetically lowered capacity to eliminate mercury, high blood levels of mercury during different developmental stages have been linked to immunological, neurological, and behavioral problems that are strikingly similar to those observed in autism [14, 15]. Due to the extensive environmental contamination of heavy metals, it is difficult to avoid persistent exposure to metals, which suggests that a combination of genetic and environmental factors, particularly exposure to metals, may play a significant role in the etiology of ASDs. While lead, cadmium, arsenic, and aluminum have all been linked to autism, the evidence that mercury is the primary causative factor is stronger [16, 17]. According to research on the connection between toxic metal load in the body and autistic symptoms, there is a strong positive correlation between the relative levels of toxic metal burden and the severity of autism [18]. These findings are further supported by the finding that nearly all autistic patients show clinical improvement after chelation therapy to remove heavy metals from the body [19].

2. Material and Methods

2.1. Case and Control group

80 children were included in this study; 40 normal children and 40 autistic children. Venous blood samples (about 3 ml each) were obtained from both groups by expert laboratory technicians and with the permission of the local directorate of health. Samples were then kept into tubes containing EDTA for the purpose of heavy metal analysis.

2.2. Place and time of study

The study was conducted at several health institutions and learning centers in different Iraqi cities including Najaf, Babylon, Karbala, Baghdad, Diwaniya and Muthanna. It was carried out during the period (October 2020-December 2022).

2.3. Consent and ethical approval

A written consent was obtained from parents and an ethical approval was obtained from the university of Alkafeel/College of Pharmacy.

2.4. Statistical analysis

Data presenting and analysis were performed using GraphPad Prism 9.3.1/USA. Each figure compares between normal and autistic children and shows metal measured the measuring unit. The level of significance was evaluated using t-test and those differences with p value less than 0.05 was considered d significantly different.

3. Results

3.1. Characterization of participants according to the age

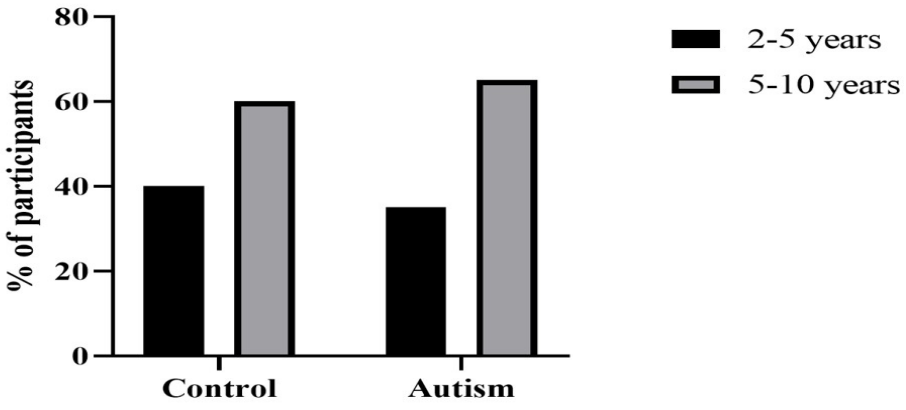

Figure 1: Characterization of participants according to the age

Out of 40 normal individuals, 16 participants (40%) aged 2-5 years while the remaining 24 individuals (60%). Out of 40 children with autism, there were 14 individuals (35%) with age 2-5 years while the remaining 26 (65%) were with age 5-10 years Figure 1.

3.2. Characterization of participants according to the gender

Out of 40 normal individuals, 22 (55%) were males and 18 (45%) were females. On the other hand, out of 40 children with autism, there were 28 individuals (70%) males while the remaining 12 (30%) were females Figure 2.

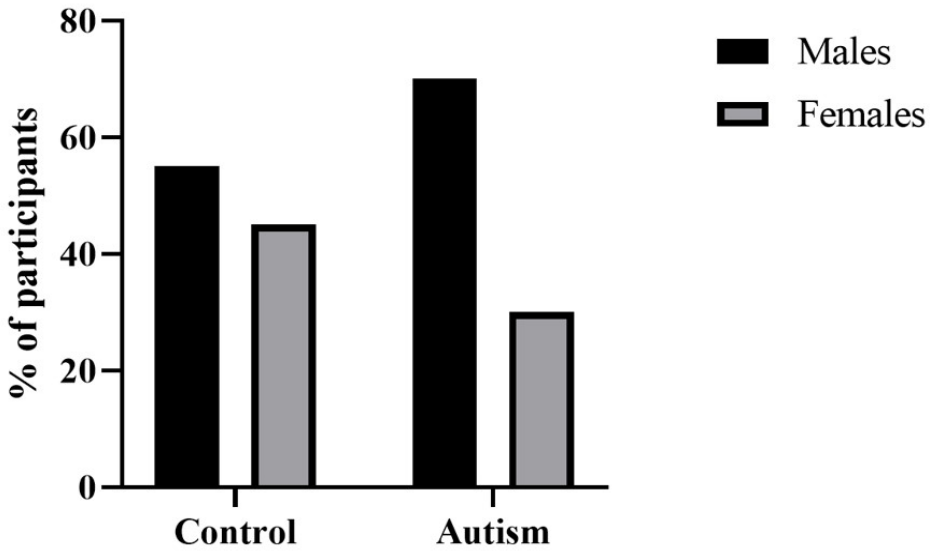

Figure 2: Characterization of participants according to the gender

3.3. Heavy Metals in blood of autistic children

Our findings showed a significant difference between control and children with autism ($P < 0.05$) in terms of all heavy metal elements (mean ± SEM). The concentration of Nickel in serum control was 0.321 ± 0.01 μg/l while its concentration in serum from autistic children reached 1.59 ± 0.21 μg/l as shown in Figure 3. The concentration of chromium was 0.097 ± 0.002 μg/l in control while in children with autistic its concentration was 0.78 ± 0.001 μg/l as shown in Figure 4. The manganese concentration in the serum of control was 10.32 ± 0.1 μg/l whereas its concentration in of case with autistic children was 0.4 ± 0.006 μg/l as shown in Figure 5. The concentration of zinc in serum samples obtained from control individuals 74.4 ± 12.76 μg/l while with the control it was 175.6 ± 13.3 μg/l Figure 6.

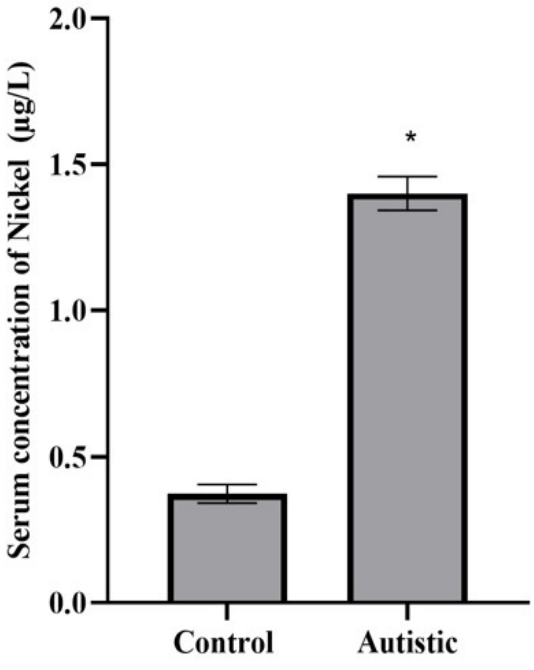

Figure 3: Serum concentration of Nickel in normal and autistic children. Data presented as mean ± SEM, n=40, * $p > 0.05$ compared to control, t-test

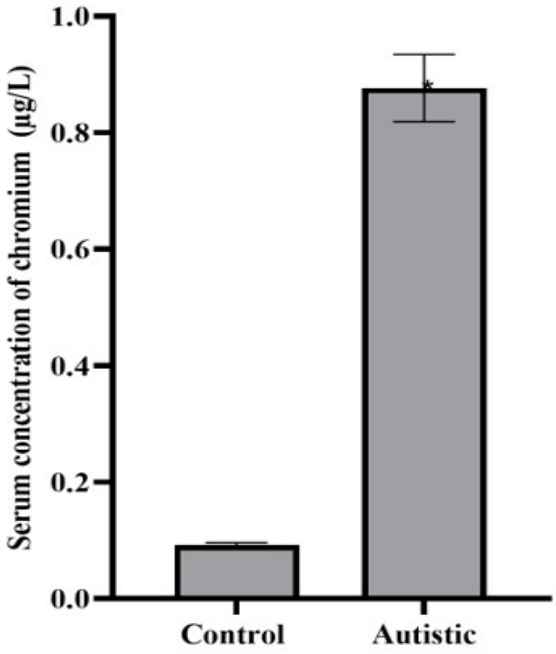

Figure 4: Serum chromium concentrations in autistic children. Data are expressed as mean ± SEM, n = 40. $p > 0.05$ versus control (t-test)

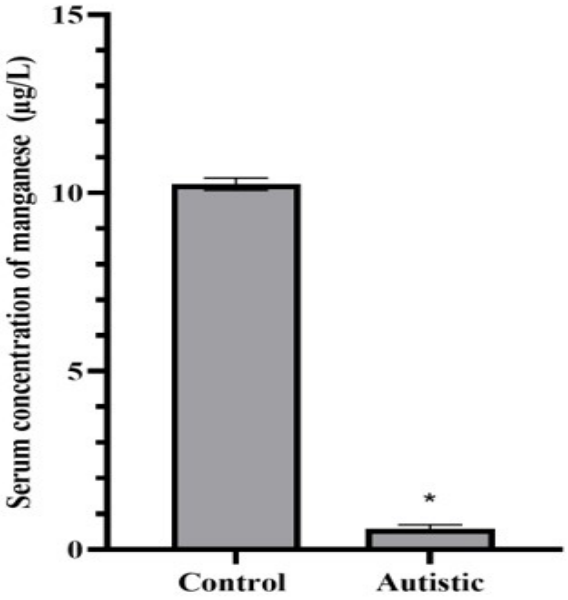

Figure 5: Serum manganese concentrations in autistic children. Data are expressed as mean ± SEM, n = 40. $p > 0.05$ versus control (t-test).

4. Discussion

In this investigation, the serum levels of particular heavy metals in children with autism were compared to those of healthy controls. The results showed notable differences between the groups: Nickel and chromium concentrations were higher in autistic children, but manganese and zinc levels were significantly lower.

Increased exposure, improved gastrointestinal absorption, and/or decreased fecal clearance can all contribute to elevated blood levels of hazardous metals. This happens because the majority of harmful metals attach to glutathione and are often eliminated in the bile before passing out of the body through the stool [20]. Significantly higher blood concentrations of dangerous metals, especially tungsten and thallium, were the most obvious difference between the autism group and the control group. A higher body burden is indicated by elevated blood levels of hazardous metals. According to this, some autistic children may have a higher burden of toxic metals because of increased intestinal absorption brought on by increased gut permeability, increased exposure to the environment, or compromised detoxification processes like decreased glutathione levels and altered gut microbiota from frequent oral antibiotic use. Furthermore, genetic factors probably

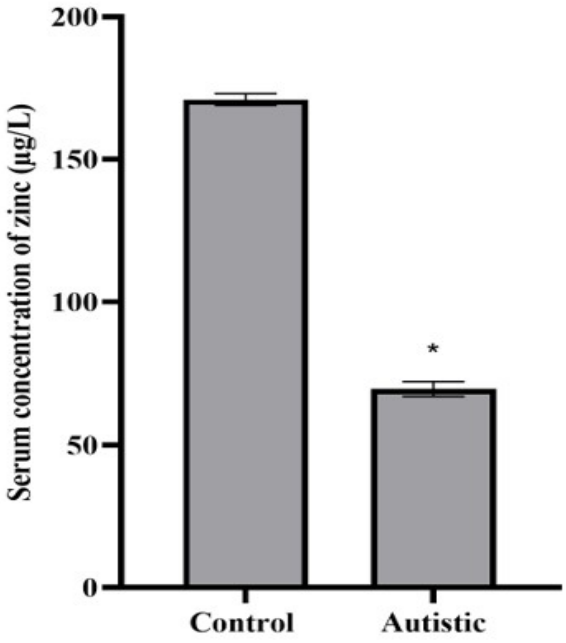

Figure 6: Serum zinc concentrations in autistic children. Data are expressed as mean ± SEM, n = 40. $p > 0.05$ versus control (t-test)

contribute to heightened vulnerability to these metals' detrimental effects [21]. Measurements of lower plasma reduced glutathione (-21%, $p < 0.0001$) in this same group [22] and in earlier investigations by (James et al., 2009) are in line with research showing that hazardous metal levels are higher in the autistic population. Reduced glutathione levels are predicted to lead to a higher body load of hazardous metals because glutathione binds to these metals and facilitates their elimination through bile. Additionally, the higher levels seen in children with autism might also be partially explained by the fact that they use oral antibiotics more frequently.

The capacity to excrete mercury is nearly completely lost when antibiotics are used (Kern et al., 2007). The fundamental reason appears to be that methylmercury, which is easily taken, can be changed into inorganic mercury, which is poorly absorbed and so mostly eliminated, by typical gut anaerobes. On the other hand, some strains of Escherichia coli convert inorganic mercury into methylmercury, completing the reverse reaction [23].

The higher levels of dangerous metals in the autistic group are also consistent with increased oxidative stress, as seen by higher levels of plasma nitro tyrosine and the ratio of oxidized glutathione (GSSG) to reduced glutathione. Increased amounts of toxic metals are likely to lower glutathione levels and exacerbate oxidative stress [22]. While none of the patients in the Saudi Arabian kingdom had high quantities of arsenic and cadmium, the results of the current investigation supported a prior study that found these two elements were significantly more prevalent [24].

The study found that people with an ASD diagnosis had significantly higher levels of the dangerous metals zinc and chromium in their hair and nail samples when compared to neurotypical controls. The surge was significantly more severe for those with poor functioning than for those with moderate to high functioning. Additionally, the findings of Elsheshtawy et al. 's study were similar [25]. ICP-AES was used to measure the plasma concentration of 13 metals (Al, As, Ca, Cd, Co, Cr, Cu, Fe, Mn, Ni, Pb, Si, Zn) in blood samples from autistic children and healthy controls. The results showed that the plasma levels of Zn, Ca, Fe, As, Ni, Cd, and Si were significantly higher in the autistic children.

5. Conclusions

The concentration of some heavy metals such as Nickel and chromium increase in blood of autistic patients while the concentration of Manganese and Zinc decrease in blood of autistic patients when compared with control.

Article Information

Disclaimer (Artificial Intelligence): The author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc.), and text-to-image generators have been used during writing or editing of manuscripts.

Competing Interests: Authors have declared that no competing interests exist.

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