

EVALUATION OF SERUM CHROMIUM, COPPER AND LEAD LEVEL AMONG AUTISTIC PATIENTS

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ABSTRACT

Increasing evidence suggests that nutrients and heavy metals increase ROS and thus could lead to neurological defects in autistic patients. Aim of the study was to evaluate serum chromium, copper and lead level among autistic patients. This was a cross-sectional study included 160 subjects, 80 medically assessed and diagnosed as autistic patients, 80 healthy apparent as control group. Serum chromium, copper and lead were measured by using atomic absorption spectroscopy 210-VGP and BMI was estimated. The ratio of autistic male to female is 4:1 fold, independent analyses showed significant decrease in mean chromium and copper level p-value (0.000 and 0.048) respectively, while significant increase in mean lead concentration p-value 0.000 was observed in autistic patients versus control group. Person's correlation analysis analyses showed that serum copper negatively associated with

lead and positively correlated with chromium whereas no correlation noted with other parameters. This study concludes chromium and copper are lower in autistic patients while lead is higher, which may lead to increase ROS and thus neurological damage in autistic patients.

KEYWORDS: Cr, Cu, Lead and Autism.

1. INTRODUCTION

Autism spectrum disorders (ASDs) are a group of neurodevelopment disorders characterized by impaired psychosocial and adaptive skills functioning that has a direct bearing on social

interaction, communication skills, and patterns of activity with symptoms of absence of symbolic play repetitive and stereotyped behavior.^[1,18] ASDs range from 1 to 20 per 1,000 people worldwide.^[2,3] Mitochondrial dysfunction, environmental risk factors, metabolic imbalances and genetic susceptibility all could lead to oxidative stress^[4] which in turn leads to impaired methylation in autism^[6], consequently cell death^[5] and neurological deficits.^[7] It has been suggested that oxidative stress may play a role in the path physiology underlying the behaviors that define autism^[8], first by direct evidence of oxidative injury to lipids, proteins and nucleic acids^[9] second by lower endogenous antioxidant enzymes, antioxidant nutrients and higher organic toxins, heavy metals and toxic free radicals all result in reactive oxygen species (ROS) in autism.^[10]

Copper catalyzes the production of potent hydroxyl radical (OH^\cdot).^[11] Higher total serum copper^[12] and lower ceruloplasmin^[4] are found in groups of autistic children. Copper, especially unbound, is highly pro-oxidant, supplemental copper is rarely needed in autism, and even small doses of copper have been observed to produce negative behavioral effect.^[13] Researchers reported the neurologic toxic effect of lead, in the nervous system of the fetus because it penetrates the incomplete blood brain barrier, the consequent adverse effects, known as behavioral teratology is not limited to the main prenatal brain development processes (e.g., neuronal proliferation and myelination) and extends after birth, with the progressive neuronal development and the volume increase of the brain.^[14]

Chromium is an essential trace element that plays an important role in glucose and cholesterol metabolism.^[15] On the other hand, it is reported that both Cr³ and Cr⁴ have hazardous effects on development of embryonic mice, such as neural tube defects, malformations, and death.^[16,17]

2. MATERIALS AND METHODS

In this cross-sectional study, one hundred and sixty subjects were enrolled, 80 diagnosed as autism patients aged from 3 to 13 years (64 males and 16 females) from different Sudanese psychiatric centers as case and 80 health apparently as control group were included, patients with mental retardation, neuron tube defect and down syndrome were excluded from this study. Random (5ml) veinpuncture blood specimen was withdrawn. Serum was obtained by centrifugation of blood at 3000 rpm for 10 min and stored at -20°C till used.

2.1 Ethical consideration

The study has been approved by the local ethics committee of Al-Neelain University. All parent of participants in the study were given their written informed consent considering the aims of the study, sample and clinical information's were used anonymously.

2.2 Measurement of BMI

Anthropometric data including weight and height were measured thus body mass index (BMI) was defined as weight (Kg) divided by height squared (m^2).

2.3 Principles of chromium copper and lead

Brief according to the manufacture, serum levels of chromium, copper and lead were measured using (atomic absorption spectrophotometer 210-VGP). Principles electron of the atom promoted to higher orbital's (excited state) for a short period of time by absorbing a defined quantity of energy. The amount of energy (wave length) is specific to a particular electron transition in a particular element. The radiation measured by using detector and the absorbance is converted to analyte concentration or mass using Bear lamber low.^[19]

2.4 Estimation of chromium

Serum diluted with deionized water by ratio 1:9 then diluted serum aspirated and absorbance measured at wave length 357.9 nm.

2.5 Estimation of copper

Serum diluted with equal volume then diluted serum aspirated and absorbance measured at wave length 324.8 nm.

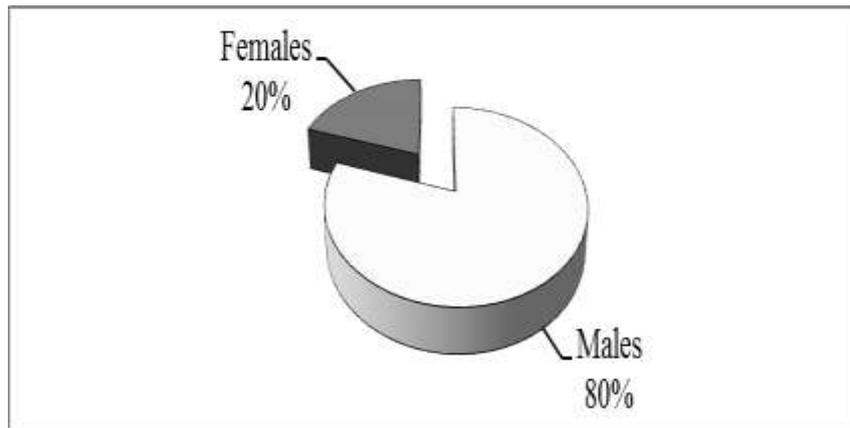
2.6 Estimation of lead

Serum diluted with deionized water by 1:9 then diluted serum aspirated and absorbance measured at wave length 283.3 nm.

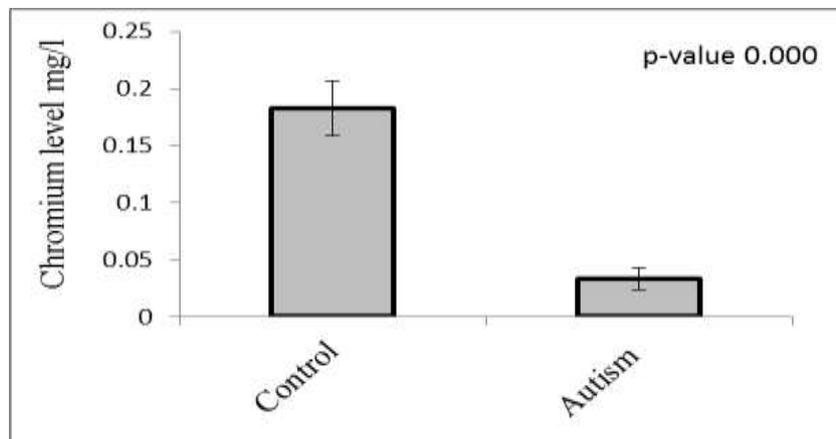
2.7 Statistical analysis

The student's t-test was employed to compare differences between the mean concentration of study parameters and person's correlation for association between study variables. *P*-value 0.05 was considered statistically significant. Data were analyzed by SPSS (Version 16.0; SPSS Inc).

3. RESULTS

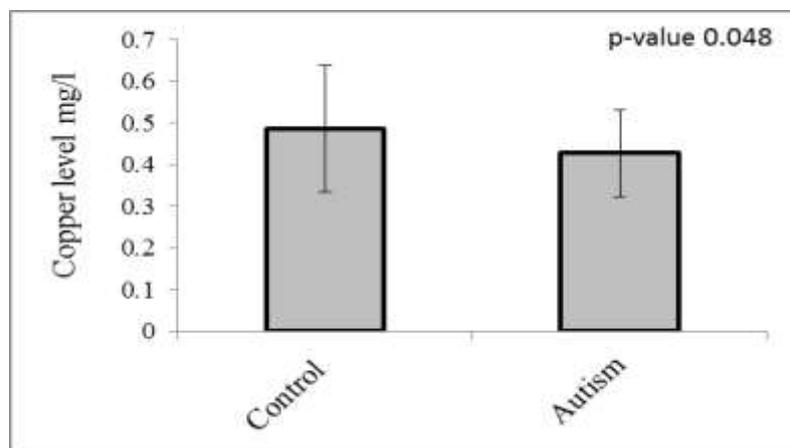


3.1 Frequency of autistic males and females.



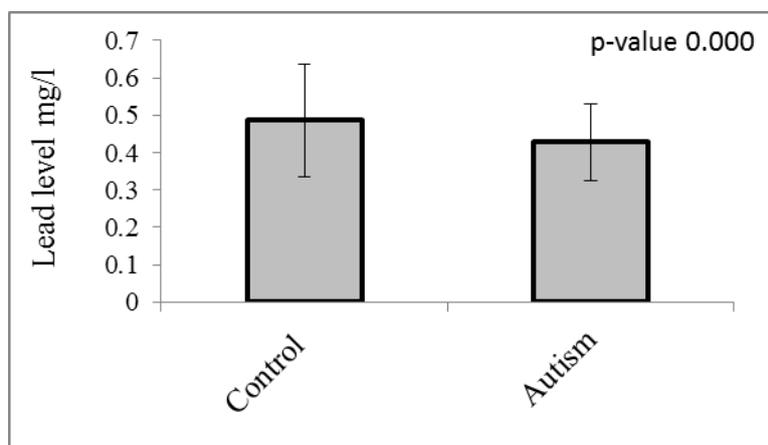
3.2 Mean chromium level among autism and control groups.

Fig. 3.2 Show mean concentration of chromium among autism and control groups, results expressed as Mean \pm SD and significant difference considered as p -value ≤ 0.05 .



3.3 Mean concentration of copper among autism and control groups.

Fig. 3.3 Show mean concentration of copper among autism and control groups, results expressed as Mean±SD and significant difference considered as p -value ≤ 0.05 .



3.4 Mean of lead level among Autism and control groups

Fig. 3.4 Show mean concentration of lead among autism and control groups, results expressed as Mean±SD and significant difference considered as p -value ≤ 0.05 .

3.5 Independent t-test results of males versus females.

Variable	Male	female	p -value
	Mean±SD	Mean±SD	
BMI	18.58±6.13	18.23±5.05	0.832
Copper	0.460± 0.139	0.446±0.110	0.708
Chromium	0.101±0.140	0.141±0.133	0.293
Lead	0.588±0.310	0.545±0.316	0.610

Results expressed as means \pm SD

Significant difference consider as p -value ≤ 0.05

3.6 Correlation between study parameters and variables in autistic patients

	Gender	Age	BMI	Copper	Chromium	Lead
Gender R-value		0.244	-0.018	0.261	0.235	-0.043
P -value		0.129	0.910	0.104	0.145	0.791
Age R-value	0.244		-0.143	-0.129	-0.073	0.233
P -value	0.129		0.379	0.427	0.656	0.168
BMI R-value	-0.018	-0.143		0.147	-0.048	-0.193
P -value	0.910	0.379		0.366	0.769	0.234
COPPER R-value	0.261	-0.129	0.147		0.313*	-0.668**
P -value	0.104	0.427	0.366		0.050	0.000
Chromium R-value	0.235	-0.073	-0.048	0.313*		-0.178
P -value	0.145	0.656	0.769	0.050		0.272
Lead R-value	-0.043	0.223	-0.193	-0.668**	-0.178	
P -value	0.791	0.168	0.234	0.000	0.272	

R indicates positive or negative correlation

P-value indicates strength of correlation.

* Mean significant correlation.

** Mean highly significant correlation.

4. DISCUSSIONS

In fact that, male hormones may amplify the adverse effects of metals thus contribute to the higher prevalence of autism in male, also a researcher suggested that, autism boys generally more susceptible to metals differences than girls.^[21, 22] So from our results the ratio of autism male to female is approximately 4:1 fold in Sudanese population is in agreement with previous study that a 4:1 male-to-female ratio in autism has been widely recognized. There are several experimental evidence links between trace elements, heavy metals and autism, thus cross-sectional hospital base study was aimed to assess serum copper, chromium and lead among autism patients.

Researchers reported that, chromium has hazardous effect on development of embryonic such as neural tube defects, malformations, and death in mice^[15, 16], so our results revealed significant decrease in chromium level in Sudanese autistic patients with *p*-value 0.000, low chromium status in autistic subjects may cause insulin resistance thus impaired glucose tolerance and low HDL consequently lipids metabolism.

A deficiency of copper is known to affect the CNS. Animal studies have revealed the association between copper deficiency and myelination defects^[20], thus the present study observe significant lower in mean copper level of autistic in comparison with control group *p*-value 0.048. In fact that copper has an antioxidant activity thus oxidative stress in autism include lower endogenous nutrients antioxidant for instance xanthine oxidase, production of nitric oxide (NO) and a toxic free radical all result in reactive oxygen species (ROS) in autism^[10], these may exaggerate the cellular damage in autistic patients.

The results of present study provide experimental evidence that, lead significantly increased in autistic patients versus control group with *p*-value 0.000. Our result is in agreement with previous study that, the level of lead concentration in autism patients significant increases.^[29] In fact that, nervous system of the fetus is especially susceptible to lead which may penetrate the incomplete blood brain barrier which known as behavioral teratology is not limited to the

main prenatal brain development processes and extends after birth, with the progressive neuronal development and the volume increase of the brain.^[17]

Person's correlation results showed there was significant positive correlation between copper and chromium level p -value 0.050, thus both chromium and copper deficiency lead to oxidative stress caused by lower endogenous antioxidant enzymes activity and lower antioxidant nutrients.^[10] In addition negative correlation was noted between copper with lead level with p -value 0.000, which indicate increase in heavy metal and decrease endogenous antioxidant enzymes activity consequently result in reactive oxygen species.^[10]

5. CONCLUSIONS

The present study concludes, autism is More common in male than female. Chromium and copper are deficient in Sudanese autistic patients while lead is increase, essential role of chromium copper and as antioxidant factors and destructive effect of lead may exacerbate the complications of ignorance and repetitive effects, thus recommend for monitoring and supplement protocol in Sudanese autistic patients.

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