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Magnesium and Calcium status in Autistic Spectrum Disorders (ASD): A case-control study on Bangladeshi children

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Abstract

Background: *The neurodevelopmental anomaly known as an autism spectrum disorder (ASD) is frequently seen in youngsters and is linked to mineral deficiencies and mitochondrial dysfunction. Iron insufficiency is linked to aberrant behaviour, while Mg2+ and Ca2+ deficiencies are linked to neural excitability. Additionally, it has been shown that ASD has a different lipid profile, which may result from mitochondrial malfunction.* ***Objectives:*** *The study was done to determine serum magnesium and calcium in ASD male children.* ***Materials and Methods:*** *This cross-sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka, from March 2014 to January 2015. For this study, 100 male children aged 3-8 years were randomly selected, among which 50 were healthy (control group), and 50 were diagnosed patients with ASD (study group). Independent sample 't-test and proportion (Z) test were used for statistical analysis. P-value <0.05 was accepted as significant.* ***Results:*** *The mean serum magnesium and calcium levels were significantly lower (p<0.001) in cases as compared to controls. Again, the frequency (%) of hypomagnesemia and hypocalcemia were significantly higher in male autistic children.* ***Conclusion:*** *From the results, it may be concluded that there is the presence of hypomagnesemia, hypocalcemia in boys with ASD.*

Keywords: *Autistic spectrum disorder, ASD, hypomagnesemia, hypocalcemia.*

Introduction

According to Manzi et al. (2008) (1), autism is a behaviorally defined syndrome marked by severe social interaction deficits, impairment in verbal and nonverbal communication, and stereotypical patterns of interests and activities. The American Psychiatric Association said behavioral, developmental, neuropathological, and sensory problems are linked to autism (2). Autism is typically diagnosed between the ages of 2 and 10, with the greatest prevalence occurring between the ages of 5 and 8. Autism Spectrum diseases (ASD) are prevalent developmental diseases (3).

Autism is currently a social issue in Bangladesh. About 10.5 million people in Bangladesh may have autism spectrum condition, according to Rahman (2006). Deficits in communication, aberrant social interaction, and limiting or repetitive interests and activities are the three main symptomatic categories of autistic disorders (4).

A strong gender bias exists in autism, with boys diagnosed with the disorder around four times more frequently than girls (5). The increased male-to-female ratio has been noticed, and oxidative stress may play a significant role. Prepubescent girls have an 8-fold higher amount of estrogen than prepubescent boys (6), even though testosterone levels in prepubertal boys and girls are comparable (7). Due to estrogens, super-oxide dismutase (SOD), reduced glutathione, and glutathione peroxidase levels are higher in females. Superoxide dismutase and glutathione peroxidase are two antioxidant enzymes expressing genes more frequently when estrogens are present. Females are less susceptible to oxidative stress than males because their mitochondria produce fewer reactive oxygen species (8).

Environmental and dietary factors significantly impact autism spectrum disorders, which are complex illnesses (9). According to several studies, autistic children had considerably decreased blood levels of certain nutrients such as calcium, magnesium, and iron, which could be caused by dietary deficiencies (9, 10).

Materials and Methods

Type of the study

Case-control study.

Place of the study

Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Shahbag, Dhaka-1000, Bangladesh

Period of the study

From March 2014 to January 2015

Ethical Clearance

Protocol was approved by Institutional Review Board, BSMMU, Shahbag, Dhaka

Sample size

A total of 100 male children aged 3-8 years were enrolled in this study.

Sampling technique

Simple random sampling

Study population

Autistic spectrum disordered children and healthy children were enrolled in this study.

Grouping of the subjects

After selecting the subjects, they were divided into 2 groups:

- Control group (group A): Consist of 50 healthy male children 3-8 years of age.

- Study group (group B): Consist of 50 autistic spectrum disordered male children 3-8 years of age.

Selection and enrollment of study subjects

Subjects were enrolled for this study according to the following selection criteria.

Inclusion criteria

- Autistic male children aged 3-8 years were selected for this study.
- Diagnosis of autistic spectrum disorder (ASD) was done by a pediatric neurologist.
- healthy subjects who were similar to autistic spectrum disorder (ASD) patients in respect of age, height, weight, BMI, and sex were included as a control.

Exclusion criteria

All subjects were screened (by history taking) for conditions like

- Children with epilepsy
- Children with Turner syndrome
- Children with Down syndrome
- Children who take any medication

Site of sample collection

The study group was selected from the Parents Forum (DOHS, Mohakhali) for autistic children and the control group was selected from some schools for normal children.

Study procedure

After the selection of the subject, thorough information was given to their parents about the objective and study procedure. Their parents were encouraged for the voluntary participation of their children. The parents were also allowed the freedom to withdraw their children from the study even after participation whenever they feel like it. When their parents agreed to participate then informed written consent was obtained from their parents. Then the parents of the subject were requested to attend the Department of Physiology of BSMMU, Dhaka on the day of the examination. Detailed personal, medical, family, socioeconomic, occupational, and dietary histories of the children were recorded in a data schedule from their parents. A thorough physical examination of the subjects was done. Anthropometric measurements including height and weight were taken and documented in a data schedule. Then 5 ml of venous blood was collected from the antecubital vein from each subject of both groups for estimation of the biochemical test.

Collection of blood samples

With all aseptic precautions, 5 ml of venous blood was drawn from the antecubital vein by a disposable plastic syringe and was transferred into a dry, clean test tube with a gentle push after removing the needle, to avoid hemolysis. The test tube was kept in a slanting position till the formation of a clot. After centrifuging the clotted blood (at 3000 rpm for 10 minutes) the serum was separated. Then 3 ml of serum was taken from the test tube into an Eppendorf tube and preserved in the refrigerator at - 4˚c in the laboratory. The serum level of magnesium (Mg^{2+}), and calcium (Ca^{2+}) were measured in the laboratory of the Department of Biochemistry, BSMMU.

Data analysis plan

Data were expressed in mean SE and also in percentage. Statistical analysis was done by using SPSS for Windows version 16. Independent sample ‘t-tests and ‘Z’ proportion tests were used as the tests of significance as applicable. $p\text{-value}<0.05$ was accepted as significant.

Results

General characteristics of the subjects:

Among 100 male children enrolled in this study, the mean (±SE) ages were 6.02±0.21 and 5.93±0.27 in groups A and B respectively (Table 1). The mean (±SE) BMI in group A and group B were 16.90±0.73 and 17.25± 0.14 respectively. The age difference between the two groups was not significant (p=0.94). The difference in BMI between the groups was not significant also (p=0.29).

Table 1: Age and BMI in two groups (n=100)

Group	n	Age (Year)	p-value Age	BMI (kg/m^2)	p-value BMI
A	50	6.02± 0.21* (3-8) **	0.94	16.90±0.73* (14-19) **	0.29
B	50	5.93±0.22* (3-8) **		17.25± 0.14* (16-20) **	

***Data are expressed as Mean ± SE.**
****Figures in parentheses indicate ranges.**

Serum levels of the minerals measured:

The serum level of two minerals was measured in the study population. The data are arranged separately in the following segments.

Mean serum Magnesium (Mg2+) level –

The mean (± SE) serum Mg2+ levels were 2.13±0.02 mg/dl and 1.90±0.03 mg/dl in groups A and B respectively (Table 2). In this study, serum Mg2+ levels were significantly lower in the study group in comparison to the control group (p value<0.001) **(Table 2).**

Mean serum calcium (Ca2+) level –

The mean (± SE) serum Ca2+ levels were 9.32±0.06 mg/dl and 8.86±0.05 mg/dl in groups A and B respectively (Table 2). In this study, serum Ca2+ levels were significantly lower in the study group in comparison to the control group (p value< 0.001) **(Table 2).**

Table 2: Serum magnesium (Mg++), and calcium (Ca++) levels in two groups (n = 100)

Group	n	Mg^{++} (mg/dl)	p-value	Ca^{++} (mg/dl)	p-value
			0.000***		0.000***
A	50	2.13 ± .02 (1.9-2.6)		9.32 ± .06 (8.7-10.40)	
B	50	1.90 ± .03 (1.6-2.4)		8.86 ± .05 (8.2-9.2)	

***Data are expressed as Mean ± SE.**
****Figures in parentheses indicate ranges.**

Discussion

The present study was undertaken to observe some biochemical variables in male children with autistic spectrum disorder to evaluate the nutritional deficiency by estimating serum magnesium (Mg2+), and calcium (Ca2+). All these variables were also studied in apparently healthy age, height, weight, and BMI-matched male children for comparison. In this study, the mean values of all the biochemical variables of normal children were within physiological limits and were almost similar to those reported by different investigators (11, 12, 13, 14, 15).

Both the groups (controls and cases) were comparable, as there were no significant differences in the confounding variables such as age, height, weight, and BMI between the two groups. The mean values of Mg2+ and Ca2+ were below the lower limit of the normal range.

Serum Mg2+:

In this present study, serum Mg2+ was significantly lower in the study group than in the of control group. Almost similar findings were observed by Strambi et al. (16); Bradstreet et al. (17) and Adams et al. (18). In addition, serum Mg2+ level was found abnormally low in 52% of children in the study group and 4% of children in the control, which was statistically significant. Similarly, Kozielec and Hermelin (1997) observed that 33.6% of autistic children had Mg2+ deficiency (16, 17, 18, 19).

Serum Ca2+:

In this present study, serum Ca2+ was significantly lower in the study group than in the control group. Almost similar findings were observed by Yasuda et al., Meguid et al., and Sun et al. (20, 21, 22).

In addition, serum Ca2+ level was found abnormally low in 74% of children in the study group and 6% of children in the control, which was statistically significant. Similarly, Yasuda et al. (20) observed that 5.8% of autistic children had Ca2+ deficiency.

Conclusion

Based on the findings of this study, it is possible to assume that boys with autism spectrum disorder have low levels of magnesium and calcium.

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