Frequency of Hypocalcemia and Hypomagnesemia in Autistic Spectrum Disordered Children of Bangladesh

Shahana Parvin[1], Shorifa Shahzadi[2], Shelina Begum[3], Syeda Nusrat Mahruba[4]

1. Assistant Professor
   Department of Physiology
   Ibrahim Medical College
   Dhaka, Bangladesh
2. Associate Professor
   Department of Physiology
   Bangabandhu Sheikh Mujib Medical University
   Dhaka, Bangladesh
3. Professor
   Department of Physiology
   Bangabandhu Sheikh Mujib Medical University
   Dhaka, Bangladesh
4. Lecturer
   Department of Physiology
   Ibrahim Medical College
   Dhaka, Bangladesh

Correspondence to:
Shahana Parvin
Assistant Professor
Department of Physiology
Ibrahim Medical College
Dhaka, Bangladesh
E-mail: shahanakjsl@gmail.com

Abstract

Background:
Autistic spectrum disorder (ASD) in children is commonly associated with mitochondrial dysfunction and mineral deficiency. Studies have highlighted links between Ca^{2+} and Mg^{2+} deficiency and neuronal excitability, along with connections between iron deficiency and behavioral abnormalities in individuals with ASD.

Objective:
This study was aimed to assess the frequency of hypocalcemia and hypomagnesemia in autistic spectrum-disordered children of Bangladesh.

Methods:
This cross-sectional study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka from March 2014 to January 2015. The study included 100 randomly selected male children, with 50 in a healthy control group (Group A) and 50 diagnosed with autistic spectrum disorder (Group B). Children with ASD were selected from the Parents Forum (DOHS, Mohakhali), while the control group was chosen from schools with typically developing children. Fasting serum levels of various components along with calcium and magnesium were measured, and statistical analysis was conducted using independent sample 't' tests and proportion (Z) tests, with a significance level set at p-value <0.05.

Results:
In this study, out of 50 autistic spectrum disorder cases, the frequencies of hypocalcemia and hypomagnesemia were 74% and 52%, respectively. A comparison with the control group revealed significantly higher frequencies of both hypomagnesemia and hypocalcemia in the ASD group, with p-values <0.001.

Conclusions:
Among most children with autism spectrum disorder in Bangladesh, hypocalcemia and hypomagnesemia are prevalent. These prevalences are significantly higher than those observed in healthy children.

Keywords: Autistic spectrum disorder, Hypocalcemia, Hypomagnesemia

Introduction:

Autism is a neurodevelopmental disorder characterized by altered communication patterns. It is a complex condition involving behavioral, developmental, neuropathological, and sensory abnormalities, typically manifesting within the first three years of life. Subtypes of Autism Spectrum Disorder (ASD) include Asperger syndrome and Pervasive Developmental Disorders.[1] Individuals with ASD often exhibit impairments in social relationships, language and communication deficits, repetitive behaviors, and a narrow range of interests.[2] As per the study conducted by IPNA, BSMMU, and technical support to IPNA by CIPRB, Bangladesh, an estimated 10.5 lac individuals may have ASD in Bangladesh. Studies have explored the association between ASD and various factors, including intracellular calcium levels. Laumonnier et al (2006)[3] observed an increase in intracellular calcium in ASD children compared to controls, while Farsi et al (2013)[4] reported significantly decreased calcium levels in autistic children. Meguid et al (2010)[5] found lower levels of vitamin D and serum calcium in children with ASD, with Ansary et al (2011)[6] reporting decreased serum calcium in about 33.33% of ASD children. Calcium deficiencies in autistic children have been attributed to nutritional factors and exposure

to environmental toxins during early development.[4] Additionally, magnesium deficiency has been associated with neuropsychiatric disorders in autism, including asthenia, tremors, convulsions, irritability, tetanic spasms, muscle cramps, and confusion.[7] Strambi et al[8] (2006) found an association between magnesium deficiency and ASD in a study on 12 autistic boys, showing significantly lower plasma magnesium concentrations in ASD patients compared to controls. Bradstreet et al[9] reported magnesium deficiency in approximately 95% of autistic children, linking it to impaired social interaction and communication failure. Kozielec and Hermelin[10] observed Mg^{2+} deficiency in 33.6% of autistic children. In contrast, Priya and Geetha[11] (2010) noted a significant decrease in serum magnesium in autistic children, while Ansary et al[12] (2011) found no significant changes. Farsi et al[4] (2013) reported higher serum magnesium levels in autistic children. The varying findings highlight the complexity of nutritional factors and their role in ASD, underscoring the need for further research in this area.

Methods:

This was a cross-sectional study that was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka from March 2014 to January 2015. The study included 100 randomly selected male children, with 50 in a healthy control group (Group A) and 50 diagnosed with autistic spectrum disorder (Group B). The protocol was approved by the Institutional Review Board, BSMMU, Dhaka, Bangladesh. The study group comprised autistic children selected from the Parents Forum (DOHS, Mohakhali), while the control group was chosen from schools with typically developing children. In this study, precise inclusion criteria were established to form a homogeneous group, focusing on autistic male children aged 3-8 years with a confirmed diagnosis by a pediatric neurologist. Healthy subjects were included as controls, matched to ASD patients in age, BMI, and sex. Due to the limited number of female cases available, we chose to include only male participants in both the case and control groups to ensure a feasible sample size for the study. Exclusion criteria, such as epilepsy, Turner syndrome, Down syndrome, and medication use, were rigorously applied through history-taking to eliminate potential confounding factors, ensuring internal validity and the clarity of study findings. The diagnosis of autistic spectrum disorder (ASD) was conducted by a pediatric neurologist. Control subjects were carefully selected to match ASD patients in terms of age, BMI, and sex, ensuring a meaningful and comparable comparison between the two groups. Subjects underwent a comprehensive physical examination, with anthropometric measurements recorded for height and weight. Additionally, 5 ml of venous blood was collected from the antecubital vein for biochemical tests, specifically assessing serum levels of magnesium (Mg^{2+}) and calcium (Ca^{2+}). The analyses were performed in the Department of Biochemistry at BSMMU. Statistical analysis, conducted using SPSS for Windows version 16.0, utilized independent sample 't-tests and 'Z' proportion tests as applicable, with a significance level set at p-value<0.05.

Results:

In this study, the mean ±SE age of group A and group B participants were 6.02 ±0.21 and 5.93 ±0.22 years respectively. We did not find any significant correlation between the groups regarding age; the p-value was 0.94. Besides, the mean ±SE BMI of group A and group B participants were 16.90 ±0.73 and 17.25 ±0.14 Kg/m^2 respectively. We did not find any significant correlation between the groups regarding BMI; the p-value was 0.29. (Table-I)

Table-I: Age and BMI of participants

Group A	Group B	p- value
Mean ±SE age in (Year)		
6.02 ±0.21	5.93±0.22	0.94
Mean ±SE BMI (Kg/m2)		
16.90±0.73	17.25 ±0.14	0.29

In this study, the mean ±SE Ca^{++} of group A and group B participants were 9.32 ±0.06 and 8.86 ±0.05 mg/dl respectively. We found a significant correlation between the groups regarding age; the p-value was <0.001. Besides, the mean ±SE Mg^{++} of group A and group B participants were 2.13 ± 0.02 and 1.90 ± 0.03 mg/dl respectively. We found a significant correlation between the groups regarding age; the p-value was <0.001. (Table-II)

Table-II: S. calcium and magnesium levels

Group A	Group B	p-value
Mean ±SD Ca++ (mg/dl)		
9.32 ± .06	8.86±.05	<0.001
Mean ±SD Mg++ (mg/dl)		
2.13 ± .02	1.90±.03	<0.001

In this study, in 50 autistic spectrum disorder cases, the frequency of hypocalcemia and hypomagnesemia were 74% and 52% respectively. In comparing the frequencies of hypocalcemia and hypomagnesemia in both the cases (ASD) and control groups we observed that the frequencies of hypocalcemia and hypomagnesemia were significantly higher in ASD groups and in both the comparison the p-values were <0.001. (Figure-1, 2 & Table-III)
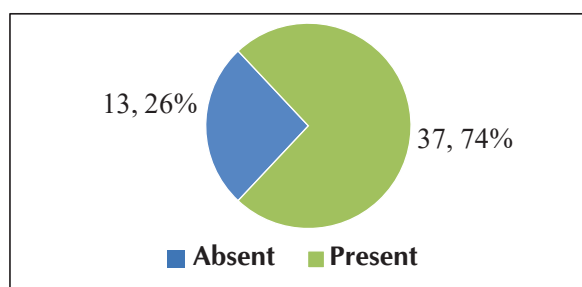

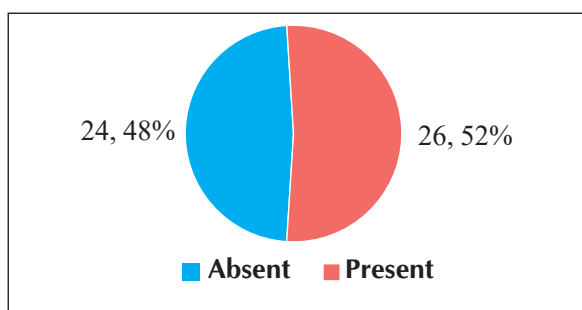**Figure-1: Frequency of hypocalcemia in cases group (ASD)**

Figure-2: Frequency of hypomagnesemia in cases group (ASD)

Table-III: Frequency of hypocalcemia and hypo-magnesemia in two groups

Characteristics	Group-A no.(%)	Group-B no.(%)	p-value
Hypocalcemia	3(6%)	37(74%)	<0.001
Hypomagnesaemia	2(4%)	26(52%)	<0.001

Discussion:

This study aimed to assess the frequency of hypocalcemia and hypomagnesemia in autistic spectrum-disordered children of Bangladesh. Nutritional deficiencies of such children are usually assessed through serum magnesium (Mg2+), calcium (Ca2+), and iron. In this study, a comparison was made with healthy age, height, weight, and BMI-matched male children. The mean values of all biochemical variables in normal children were within physiological limits and consistent with findings reported by other researchers.[13,14] The control and case groups were comparable with no significant differences in age, height, weight, and BMI. Mean values of Mg2+ and Ca2+ were below the normal range. In this study, serum Mg2+ was significantly lower in the study group compared to the control group, consistent with findings observed by Kozielec and Hermelin (1997).[10] In addition, serum Mg2+ levels were found to be abnormally low in 52% of children in the study group and 4% in the control group, and this difference was statistically significant. This finding is consistent with the observations of the same study,[10] which reported that 33.6% of autistic children had Mg2+ deficiency. Moreover, serum Ca2+ levels were significantly lower in the study group compared to the control group, consistent with findings by Meguid et al(2010)[5] and Sun et al(2013)[15]. Additionally, serum Ca2+ levels were found to be abnormally low in 74% of children in the study group and 6% in the control group, with this difference being statistically significant. This observation aligns with the findings of Yasuda et al (2013),[16] who reported that 5.8% of autistic children had Ca2+ deficiency. The findings of this cross-sectional study can be valuable for informing and guiding similar studies in the field of treating children with autism spectrum disorder in Bangladesh.

Limitation:

This study was limited by its single-center design and relatively small sample size. Additionally, the study duration was short. Consequently, the findings may not accurately represent the broader scenario across the entire country.

Conclusion:

The prevalence of hypocalcemia and hypomagnesemia among children with autism spectrum disorder (ASD) in Bangladesh is markedly

elevated, surpassing the rates observed in their healthy counterparts. This finding underscores the importance of recognizing and addressing nutritional imbalances in individuals on the autism spectrum. The increased prevalence of mineral deficiencies identified in this study highlights potential opportunities for targeted interventions and support strategies in the management of ASD. Further research and attention to nutritional aspects could contribute to a more comprehensive understanding of the multifaceted nature of autism in the specific demographic of Bangladesh, potentially informing tailored healthcare approaches. Addressing these nutritional imbalances may offer new insights and avenues for therapeutic interventions aimed at improving the overall well-being of children with ASD in the region.

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