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The Frequency of Iron Deficiency, Hypercholesterolemia, and Hypertriglyceridemia in Autistic Spectrum Disordered Children of Bangladesh

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Abstract
Background: *Autistic Spectrum Disorder (ASD) is a complex neurodevelopmental condition marked by challenges in social interaction, communication, and repetitive behaviors. Recent research points to metabolic and nutritional issues in children with ASD, such as iron deficiency, hypercholesterolemia, and hypertriglyceridemia. This study aimed to assess the frequency of iron deficiency, hypercholesterolemia, and hypertriglyceridemia in autistic spectrum-disordered children of Bangladesh.* ***Methods:*** *In a cross-sectional study conducted at Bangabandhu Sheikh Mujib Medical University from March 2014 to January 2015, 100 male children participated: 50 healthy controls (Group A) and 50 diagnosed with autism spectrum disorder (Group B). Fasting serum levels of various components, including calcium and magnesium, were measured. Statistical analyses, such as independent sample t-tests and proportion (Z) tests, were performed, with significance set at P-value <0.05.* ***Results:*** *In Group A (Control group), none of the participants had iron deficiency, 4% had hypomagnesemia, and 6% had hypocalcemia. In contrast, Group B (ASD cases) showed markedly higher rates: 20% had iron deficiency, 52% had hypomagnesemia, and 74% had hypocalcemia. The frequency of iron deficiency, hypomagnesemia, and hypocalcemia differed significantly between Groups A and B. These differences were statistically significant (p<0.05).* ***Conclusion:*** *In Bangladesh, almost one-fifth of male children with autistic spectrum disorder experience iron deficiency, while half of them is affected by hypomagnesemia, and three-fourths suffer from hypocalcemia. These rates are markedly higher compared to their healthy counterparts.*

Keywords: *Iron deficiency, Hypercholesterolemia, Hypertriglyceridemia, Autistic spectrum disorder, Children*

I. INTRODUCTION

Autism is a behaviorally defined syndrome marked by significant deficits in social interaction, communication challenges, and repetitive behaviors [1]. According to the American Psychiatric Association, autism is linked with various behavioral, developmental, neuropathological, and sensory abnormalities [2]. Typically diagnosed between ages 2 to 10, with peak prevalence between 5 to 8 years, autism is part of a group of common developmental disorders known as autism spectrum disorders (ASD) [3]. Autism was first described in 1943 by Kanner, who noted that autistic children experience profound loneliness and excessive shame from early in life [4]. In Bangladesh, autism is a significant social issue, with about 10.5 lakh individuals potentially affected. The core symptoms of autism include deficits in communication, abnormal social interaction, and restrictive or repetitive interests and behaviors [5]. It is a metabolic disorder that impacts the CNS and its function [6]. Various metabolic defects associated with autism include mitochondrial dysfunctions, phenylketonuria, creatine deficiency, and inborn errors in cholesterol biosynthesis [1]. Mitochondrial dysfunction is a significant factor in autistic spectrum disorders, with a recent study indicating that 80% of children with ASD may have this issue [7]. The number of mitochondria in a cell correlates with the cell's energy needs, with high numbers found in the skeletal muscle, gastrointestinal system, and brain. A study reported increased triglyceride and cholesterol levels in ASD, possibly due to inhibited mitochondrial fatty acid oxidation [8]. Dziobek et al. [9] found significantly elevated levels of triglycerides, LDL, and total cholesterol, and lower levels of HDL in 22 autistic children compared to controls. In ASD, increased serum cholesterol levels are attributed to heightened activity of the rate-limiting enzyme for cholesterol synthesis, HMG-CoA reductase [10]. Cholesterol plays a crucial role in neuroactive steroid production and the growth of myelin membranes, essential for nerve fiber insulation and normal brain development during embryonic and fetal stages [11]. On the other hand, oxidative stress in ASD leads to the generation of reactive oxygen species (ROS) through lipid peroxidation [12], compounded by reduced activities of antioxidant enzymes like superoxide dismutase [13], glutathione peroxidase, and catalase. Bradstreet et al. [14] reported that magnesium deficiency affects about 95% of autistic children, impairing social interaction and communication. Magnesium inhibits the excitatory neurotransmitter acetylcholine, which triggers muscle contraction [15], and also acts as a natural calcium channel blocker. Calcium is crucial for skeletal and smooth muscle contraction, and magnesium deficiency can lead to elevated intracellular calcium levels, potentially causing muscle cramps and hypertension. On the other hand, El-Ansary et al. [16] found that changes in magnesium levels were insignificant in autistic children. Meguid et al. [17] reported significantly lower levels of both forms of vitamin D and serum calcium in children with ASD. Vitamin D deficiency impairs calcium absorption, leading to calcium deficiency in ASD. In autism, low plasma Ca^{2+} and high brain Ca^{2+} levels can lead to oxidative stress [18], as mitochondrial oxygen radicals are stimulated by increased intracellular calcium ions. In a study by Latif, Heinz, and Cook [19], it was suggested that approximately 52% of autistic children were iron deficient, which could contribute to learning and behavioral impairments. This iron deficiency in autistic children is likely due to selective food intake and abnormal eating habits. Iron is crucial for the development and function of the brain, particularly during its early stages of development [20]. The objective of this study was to assess the frequency of iron deficiency, hypercholesterolemia, and hypertriglyceridemia in autistic spectrum-disordered children of Bangladesh.

II. METHODOLOGY

This cross-sectional study was conducted at Bangabandhu Sheikh Mujib Medical University in Dhaka from March 2014 to January 2015. The study enrolled 100 male children, divided into two groups: 50 healthy controls (Group A) and 50 diagnosed with autistic spectrum disorder (Group B). Approval from the Institutional Review Board was obtained. Children with autism were recruited from the Parents Forum (DOHS, Mohakhali), while controls were selected from schools. Inclusion criteria ensured that autistic males aged 3-8 years were included with a confirmed diagnosis, while healthy controls were matched for age, height, weight, BMI, and sex. Exclusion criteria were applied to minimize confounding factors. The diagnosis was performed by a pediatric neurologist, with physical examinations and venous blood samples analyzed for magnesium and calcium levels. Statistical analysis utilized SPSS 16.0, with a significance set at $P<0.05$.

III. RESULT

In this study, the average (±SE) ages were 6.02±0.21 and 5.93±0.27 years in Group A and Group B, respectively, ranging from 3 to 8 years. The mean (±SE) BMI values were 16.90±0.73 and 17.25±0.14 in Group A and Group B, respectively. Both groups, healthy controls and those with autism were matched for BMI, as the values were similar and statistically non-significant in their differences. The mean (± SE) serum iron levels were 90.00 ± 2.67 µg/dl in group A and 77.40 ± 5.43 µg/dl in group B. Serum iron levels were significantly lower in group B compared to group A ($p < 0.01$). On the other hand, the mean (± SE) serum magnesium (Mg^{2+}) levels were 2.13 ± 0.02 mg/dl in group A and 1.90 ± 0.03 mg/dl in group B. Serum Mg^{2+} levels were significantly lower in group B compared to group A ($p < 0.001$). Besides, the mean (± SE) serum calcium (Ca^{2+}) levels were 9.32 ± 0.06 mg/dl in group A and 8.86 ± 0.05 mg/dl in group B. Serum Ca^{2+} levels were significantly lower in group B compared to group A ($p < 0.001$). The frequency of iron deficiency, hypomagnesemia, and hypocalcemia differed significantly between Groups A and B. In Group A, none of the participants had iron deficiency, 4% had hypomagnesemia, and 6% had hypocalcemia. In contrast, Group B showed markedly higher rates: 20% had iron deficiency, 52% had hypomagnesemia, and 74% had hypocalcemia. These differences were statistically significant with p-values of less than 0.01 for iron deficiency, and less than 0.001 for both hypomagnesemia and hypocalcemia, indicating a notable disparity in the prevalence of these conditions between the two groups.

Table 1: Age and BMI distribution (N=100)

Group A (n=50)	Group B (n=50)	P-value
Mean ±SE age in (Year)		
6.02 ±0.21	16.90 ±0.73	0.94
Mean ±SE BMI (Kg/m^2)		
5.93 ±0.22	17.25 ±0.14	0.29

Table 2: Serum magnesium (Mg^{++}), calcium (Ca^{++}) and iron levels in two groups

Groups	Mg^{++} (mg/dl)	Ca^{++} (mg/dl)	Iron (µg/dl)
A	2.13 ± .02	9.32 ± .06	90 ± 2.67
B	1.90 ± .03	8.86 ± .05	77.40 ± 5.43
p-value	<0.001	<0.001	0.01

Figure 1: Mean serum Iron in two groups

Figure 2: Mean serum magnesium (Mg^{++}) in two groups

Figure 3: Mean serum calcium (Ca^{++}) in two groups

Table 3: Frequency of hypomagnesemia, hypocalcemia, and iron deficiency in two groups

Parameter	Group A		Group B		p-value
	n	%	n	%	
Iron deficiency	0	0%	10	20%	< 0.01
HPM	2	4%	26	52%	< 0.001
Hypocalcemia	3	6%	37	74%	< 0.001

HPM: Hypomagnesaemia

Figure 4: Frequency of hypomagnesemia, hypocalcemia, and iron deficiency in two groups

IV. DISCUSSION

This observational study aimed to evaluate how often iron deficiency, hypercholesterolemia, and hypertriglyceridemia occur in children with autism spectrum disorder in Bangladesh. In this study, the mean values of all biochemical variables in the control group were within physiological norms and were consistent with findings from previous studies [21,22]. Both the control and case groups were comparable, showing no significant differences in age, height, weight, and BMI. However, the mean values of Mg^{2+} and Ca^{2+} were noted to be below the lower limit of the normal range. In this study, the study group exhibited significantly lower serum iron levels compared to the control group. Similar findings have been reported in previous studies [23,24]. Specifically, abnormally low serum iron levels were found in 52% of children in the study group and only 4% of children in the control group. Furthermore, iron deficiency was reported in 84% of ASD children by Konofal et al. (2008) [24]. In this study, serum magnesium (Mg^{2+}) levels were found to be significantly lower in the study group compared to the control group. Similar findings have been reported in previous studies by Bradstreet et al. (2010) [14], and Adams et al. (2011) [25]. Specifically, abnormally low serum Mg^{2+} levels were detected in 52% of children in the study group compared to 4% in the control group, a statistically significant difference. In this study, serum calcium (Ca^{2+}) levels were found to be significantly lower in the study group compared to the control group. Similar findings have been reported in previous studies by Yasuda et al. (2013) [26], and Meguid et al. (2010) [27]. Specifically, abnormally low serum Ca^{2+} levels were detected in 74% of children in the study group compared to 6% in the control group, which was statistically significant. Additionally, Yasuda et al. (2013) [26] reported that 5.8% of autistic children exhibited Ca^{2+} deficiency. The results obtained from this current study may provide valuable insights and serve as a foundation for future research in similar areas.

Limitation of the study:

The study is constrained by its single-center approach and a limited sample size. Moreover, the research was conducted over a short duration, which may restrict the applicability of findings. Therefore, caution should be exercised when applying these results to the broader socio-cultural context of the country.

V. CONCLUSION

In Bangladesh, nearly one-fifth of male children diagnosed with autistic spectrum disorder experience iron deficiency, with half of them affected by hypomagnesemia, and three-fourths suffering from hypocalcemia. These rates are notably higher compared to their healthy counterparts. These findings underscore the importance of comprehensive nutritional assessments and management strategies tailored specifically for children with autism spectrum disorder to address these significant mineral deficiencies. Early detection and intervention could potentially mitigate adverse health outcomes associated with these deficiencies, emphasizing the need for targeted healthcare approaches for children with ASD in Bangladesh.

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