

RESEARCH PAPER

Evaluation of Serum Vitamin D in Children with Autism Spectrum Disorder

Sharmin Afroz¹, Shelina Begum², Shorifa Shahjadi², Umme, Raihan Siddiqi³, Nusrat Mahruba²

¹Department of Physiology, Mugda Medical College, Dhaka, Bangladesh; ²Department of Physiology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh; ³Department of Physiology, Shaheed Suhrawardy Medical College, Dhaka, Bangladesh

Abstract

Background: Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder that may cause lifelong disability. The aetiology of ASD involves gene-environmental interaction. Vitamin D plays an important role in brain development and maturation.

Objective: This study was aimed to compare serum vitamin D in children with autism spectrum disorder with that of the healthy control.

Methods: This case-control study was conducted in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Blood sample from 50 diagnosed children with ASD and 50 apparently healthy children among 3 to 10 years age group, were tested for serum 25(OH) D. To assess the association independent t test and chi square test were done by using SPSS.

Results: The mean serum vitamin D levels of both the groups were lower than the normal reference value. Again, the mean serum vitamin D was lower in ASD compared to that of control, but the difference was statistically non-significant. Among ASD children, 38.0% had deficient, 42.0% had insufficient and 20.0% had sufficient serum vitamin D. Among healthy children, 36.0% had deficient, 30.0% had insufficient and 34.0% had sufficient serum vitamin D level. However, vitamin D deficiency and insufficiency was not associated with ASD.

Conclusion: It may be concluded that, vitamin D deficiency is prevalent in Bangladesh among both ASD children and apparently healthy control and the mean serum vitamin D was lower in ASD children compared to that of healthy control, but the difference was statistically non-significant. Therefore, for proper growth and development more outdoor activity and adequate dietary intake of vitamin D rich food are recommended to overcome the situation.

Keywords: Autism spectrum disorder, Vitamin D deficiency, Vitamin D insufficiency, Neurodevelopment

Introduction

Autism spectrum disorder (ASD) is a complex neurodevelopmental disorder that may cause lifelong disability. The social and economic impact of autism is devastating. It is characterised by impairments in reciprocal social communication and a tendency to engage in repetitive stereotyped patterns of behaviours, interests and activities. The term "spectrum" is used as the manifestation of the disorder may vary according to severity, developmental level and chronological age.¹ The prevalence of autism has increased in last three decades. Now the global burden of autism is 7.6 per 1000 population or 1 in every 132 persons.² In Bangladesh, the prevalence of

ASD is 0.15 to 0.8%. In rural area, it is 0.075% but in Dhaka city, it is alarmingly high 3%.³⁻⁴

The aetiology of ASD involves interaction between genetic and environmental factors. John J Cannell has suggested that primary environmental trigger for autism might be gestational and early childhood vitamin D deficiency.⁵ Vitamin D is a steroid hormone. About 90% of vitamin D is synthesized photochemically by action of UVB light in skin. Most well-known function of vitamin D is to maintain calcium and phosphate homeostasis. Beside the classic function, vitamin D plays crucial role in health. Vitamin D (calcitriol) exerts its effect via vitamin D receptor (VDR), which is present in most cells of body including CNS. Vitamin D influences brain development including neuronal differentiation, maturation, growth and synthesis of variety of neurotransmitters. It also has role in neuroplasticity and neuroprotection. Vitamin D can regulate expression of more than 200 genes.⁶⁻⁸ It upregulates DNA-repair genes and prevents de-novo

*Correspondence: Dr. Sharmin Afroz, Department of Physiology, Mugda Medical College, Dhaka, Bangladesh.
e-mail: sharminbright@gmail.com
ORCID: 0000-0002-8778-3313

mutations that stabilize the genome and protects cells from oxidative stress and toxic effects.⁹

Vitamin D deficiency is now a global health issue. Latitude, season and skin color, increased indoor preoccupation, air pollution and obesity can modify the photosynthesis of vitamin D.¹⁰

Scientists from different countries reported that, ASD children had significantly lower serum vitamin D levels than healthy children.¹¹⁻¹⁵

A large case control study in Qatar found that the mean value of vitamin D in autism children was much lower than the normal value, and it was significantly lower than that of control children.¹⁵ A cross-sectional study enrolling 96 Chinese children reported that the mean serum 25(OH) D levels were significantly lower in autistic children as compared with normal Children. There was a significant negative relationship between circulating serum 25(OH) D levels and the severity of autism evaluated according to Childhood Autism Rating Scale scores.¹³ In addition, some recent studies reported that vitamin D supplementation could improve the core symptoms of autism in vitamin D deficient ASD children.²⁰⁻²²

Although the above-described studies indicated a possible role of vitamin D deficiency in ASD, other studies could not confirm these positive results. Ugur and Gürkan (2014) in turkey, Molley et al. (2010) in USA and Adams et al. (2011) in Arizona, USA found no significant difference in serum vitamin D level between ASD and healthy control.¹⁶⁻¹⁹

In Bangladesh, because of rapid urbanisation, increased indoor preoccupation, dark skin color, there is high prevalence of vitamin D deficiency in children and woman of reproductive age.²³⁻²⁴ Therefore, this study was aimed to explore serum vitamin D level in children with ASD and to compare these parameters with healthy children.

Materials and Methods

This case-control study was carried out in the Department of Physiology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from March 2018 to February 2019, with prior protocol approval from

Institutional Review Board of BSMMU and National Ethics Review Committee of BMRC. For this purpose, 65 ASD children of both sex (3 to 10 years), diagnosed by pediatric neurologist, were purposively enrolled, after getting informed written consent from the parents of 'Parents Forum of differently abled children, Mohakhali, Dhaka'. Among them, ASD children with any acute illness, malabsorption, Down syndrome, cerebral palsy, epilepsy and renal insufficiency, were excluded. In addition, ASD children who were receiving multivitamins, calcium, vitamin D were also excluded from the study and ultimately 50 ASD children were selected as study group. Furthermore, for comparison, age, BMI and sex matched 50 apparently healthy children were also enrolled as control. All the children enrolled in this study were from middle class socio-economic society. After selection, the parents were requested to report at the Department of Physiology, BSMMU on examination day at 8 am, with their child in fasting condition. Under aseptic precautions, 5ml venous blood of all children was collected and was immediately sent to the laboratory of the Department of Biochemistry and Molecular Biology, BSMMU. The serum 25(OH) D and creatinine were done by CMIA methods by using automated analyzer, Architect plus ci4100. All data were expressed as mean \pm SE and percentage. Statistical analysis was performed by using SPSS. Independent "t" test was done to compare serum 25(OH) D between ASD and control groups and Chi square test was done to observe association of vitamin D deficiency and insufficiency with ASD. The p value ≤ 0.05 was considered as statistical significance.

Result

General characteristics of the ASD children and control were recorded using semi-structured questionnaire (table I).

All the values were almost similar and the differences between the groups were statistically non-significant. The mean serum vitamin D level was lower in ASD (15.54ng/ml) compared to that of control (16.25ng/ml), but the difference was statistically non-significant (table II). However, the mean serum vitamin D levels

Table-I: General characteristics of ASD Children and healthy controls (n=100).

Parameters	ASD (n=50)	Controls (n=50)	t value	p- value
Age (year) ^a	6.16 \pm 0.28	6.04 \pm 0.27	0.128	0.775 ^{ns}
Male: Female ^b	35:1	2.12:1	1.286	0.260 ^{ns}
BMI (Kg/m ²) ^a	15.96 \pm 0.39	16.50 \pm 0.22	-1.075	0.284 ^{ns}

Table-II: Serum 25(OH)D and serum creatinine levels in both groups.

Parameters	ASD (n=50)	Controls (n=50)	t- value	p- value
Serum 25(OH)D (ng/ml)	15.54±0.72 (6-24.5)	16.25±0.76 (7.4-27.5)	-0.674	0.502 ^{ns}
Serum creatinine (mg/dL)	0.45 ± 0.01 (0.28-.60)	0.49 ±0.01 (.31-.64)	-1.890	0.062 ^{ns}

of both the groups were lower than the normal reference value.²⁵

Frequency distribution of subjects in both groups on the basis of vitamin D status were done. Vitamin D status were categorized as deficient (<15ng/ml), insufficient (15-20ng/ml), and sufficient (20ng-100ng/ml).²⁵ Among ASD children, 19 (38%) had deficient, 21 (42%) had insufficient and 10 (20%) had sufficient serum vitamin D. Among control, 18 (36%) had deficient, 15 (30%) had insufficient and 17 (34%) had sufficient serum vitamin D level.

However, the association of vitamin D deficiency and insufficiency was not found with ASD by Chi square test (table III).

Table-III: Association of vitamin D deficiency and insufficiency with ASD

	Serum vitamin D status		Total
	Deficient and insufficient (<20 ng/ml)	Sufficient (20-100 ng/ml)	
ASD	40(80%)	10(20%)	50
Control	33(66%)	17(34%)	50
Total	73	27	100

Discussion

The mean serum vitamin D levels of both the groups were lower than the normal reference value.²⁵ Again, the mean serum vitamin D level was lower in ASD compared to that of control, but the difference was statistically non-significant. This finding was in agreement with the finding of other investigators.¹⁶⁻¹⁹ In a cohort study in USA, Molley et al showed no differences in the concentrations of 25(OH)D between participants with ASD and controls. Moreover, sixty-one percentage of children in the entire cohort had vitamin D deficiency.¹⁶

Another study in Arizona, USA, Adams et al compared children with ASD with non-sibling, neurotypical

controls of similar age, gender and geographical distribution. The investigators found no significant difference in serum vitamin D levels between ASD children and control. Both groups were vitamin D insufficient.¹⁷

Ugur and Gürkan also examined serum 25(OH)D levels of children in Turkey and found no difference between children with ASD and healthy controls (matched with age and gender). Furthermore, they found no correlation between severity of autistic symptoms (ABC and CARS scores) and serum vitamin D levels. In this study, both ASD children and healthy controls had an average lower level of serum 25 (OH)D.¹⁸

On the other hand, many authors found significant lower level of serum vitamin D in ASD children compared to healthy control.^{11-15, 26-28}

In this study, we found major portion of all children were vitamin D deficient and insufficient, which is crucial for their growth and development.

Bangladesh especially Dhaka is densely populated with rapid, unplanned urbanization. As a result, children get less opportunity to spend time in sun light. They are mainly engaged in indoor activity. Due to cultural norms, they use to keep only few portions of body surface bare when stay outside. In addition, people mainly have brown skin and melanin pigment acts as sun block.⁶ Again, Dhaka has a heavily pollutant air.²⁹ The air pollutant absorbs the UVB rays and reduces cutaneous vitamin D synthesis.³⁰ The dietary source of vitamin D is limited and cannot make up the need.

In this study, vitamin D deficiency and insufficiency was observed in 80.0% of ASD children and 66.0% of healthy control. However, no association of vitamin D deficiency and insufficiency with ASD was found. Similar findings were also reported by other investigators.¹⁴ On the other hand, significant association of vitamin D deficiency with ASD was found by other investigators.¹⁵

It is established that, the aetiology of ASD involves gene environment interaction.³¹ Therefore, when

genetically susceptible children expose to vitamin D deficiency in early age, it may act as an environmental trigger for ASD.

In this study, age of the participants was high in relation to neurodevelopment. To be more conclusive similar type of study can be done with younger age group as well as estimation of maternal serum vitamin D can be more helpful.

Conclusion

Vitamin D deficiency is prevalent in Bangladesh among both ASD children and healthy children. The mean serum vitamin D was lower in ASD children compared to that of healthy control, but the difference was statistically non-significant. From this result, we may recommend to increase outdoor activity in order to increase duration of sun exposure and adequate dietary intake of vitamin D rich food.

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Ethical Clearance: IRB of BSMMU; NREC of MMRC

Conflict of interest: We have no conflict of interest.

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