



Serum Levels of 25-Hydroxyvitamin D in Children with Autism

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Abstract: Autism spectrum disorder (ASD) is a neurodevelopment disorder characterized by impairment in socio-communicative functioning and by limited interests and repetitive and stereotypic behaviors. Vitamin D has a unique role in brain homeostasis, embryogenesis and neurodevelopment, immunological modulation, antioxidation, antiapoptosis, neural differentiation and gene regulation. Recently, it has been reported that Children with ASD have significantly lower serum levels of 25-hydroxy vitamin D than healthy children. **Objectives:** This study is to evaluate serum 25-hydroxy vitamin D levels in children with autism and to evaluate the relationship between vitamin D deficiency and the severity of autism. **Methods:** Comparing serum levels of 25-hydroxy vitamin D in 50 children diagnosed with Autism, with CARS score >30, and 30 control children. **Conclusion:** Serum levels of 25-hydroxy vitamin D in the autistic children were significantly lower than that of the control group. The mean 25-OHD levels in patients with severe autism were significantly lower than those in patients with mild/moderate autism. Serum 25-hydroxy vitamin D had significant negative correlations with Childhood Autism Rating Scale (CARS).

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1. Introduction

Autism spectrum disorder (ASD) is a neurodevelopment disorder characterized by impairment in socio-communicative functioning and by limited interests and repetitive and stereotypic behaviors ⁽¹⁾. Vitamin D has a unique role in brain homeostasis, embryogenesis and neurodevelopment, immunological modulation (including the brain's immune system), antioxidation, antiapoptosis, neural differentiation and gene regulation ⁽²⁾. Children with ASD had significantly lower serum levels of 25-hydroxy vitamin D than healthy children. Therefore vitamin D deficiency during pregnancy and early childhood may be an environmental trigger for ASD ⁽³⁾

Aim of the Work

This study is to evaluate serum 25-hydroxy vitamin D levels in children with autism and to evaluate the relationship between vitamin D deficiency and the severity of autism.

2. Subjects and Methods

This study was carried out in the Neuropsychiatry outpatient clinic Pediatric Department, Tanta University Hospital. Fifty children diagnosed as autism, with age range (3-15) years were included.

Diagnosis of autism was based on the criteria for the diagnosis of autism that are set out in the Diagnostic and Statistical Manual of Mental Disorders

DSM-V (Fifth Edition) ⁽⁴⁾.

The initial Childhood Autism Rating Scale (CARS) score for these children was ≥ 30 . Children with a CARS score ≥ 30 were considered to have autism ⁽⁵⁾.

Thirty healthy control children with the same age and sex were served as a control group.

All children included in the study didn't receive any medication for at least 2 month before the study.

Duration of the Study:

12 months from January 2018 to January 2019.

Inclusion criteria:

Children diagnosed as autism with CARS score ≥ 30 .

Exclusion criteria:

1- Children who had a history and clinical features of Fragile X-disorder.

2- Children with tuberous sclerosis and phenylketonuria.

3- Children with renal, hepatic or metabolic diseases.

4- Children with epilepsy or other severe neurological disorder that may affect the plasma levels of vitamin D.

Methods of the study:

All children included in the study were subjected to the following:

1- Full history taking:

This included personal, family, birth history, early developmental, dietetic history and history of recurrent infections.

2- Complete physical examination:

Including complete neurological examination for all children.

3- Mental status examination:

Including the evaluation of social interaction, language and communicative functions.

4- Childhood Autism Rating Scale (CARS):

CARS was applied for children with autism to assess its severity, for a diagnosis of autism.

5- Hearing test:

Including Auditory Brain Stem Response (ABR) for children with autism.

6- Electroencephalography (EEG) was done for autistic children.

7- Brain Magnetic Resonance Imaging (MRI)

MRI was done for autistic children to exclude children with structural lesion or tuberous sclerosis.

8- Estimation of Serum levels of 25-hydroxyvitamin D:

Serum levels of 25 (OH) vitamin D were estimated in children with autism and the control children by using the ELFA technique (Enzyme linked fluorescent assay).

Statistical method

The analysis was calculated by SPSS version 25. The quantitative variables were described by mean, standard deviation and Linear Correlation Coefficient.

3. Results

In this study, patients were assessed by measuring serum 25- hydroxyvitamin D level and comparing them with the control group.

Correlation between serum vitamin D level and CARS score in autistic children was also done.

The data of the patients were statistically analyzed and the results were summarized and tabulated in the following tables and figures.

Table (1) and figure (1) show age distribution among the studied groups. Both groups are of the same age, age range of autistic children (50 children) was from 3 to 15 years and the mean was (7.87 ± 3.44) , age range in control group (30 children) was from 3 to 15 years and the mean was (7.25 ± 3.32)

Table (1): Age distribution among the studied groups

Age (years)	Case (n=50)	Control (n=30)
Range	3 - 15	3 - 15
Mean \pm SD	7.87 ± 3.44	7.25 ± 3.32
Median	7.25	10.00

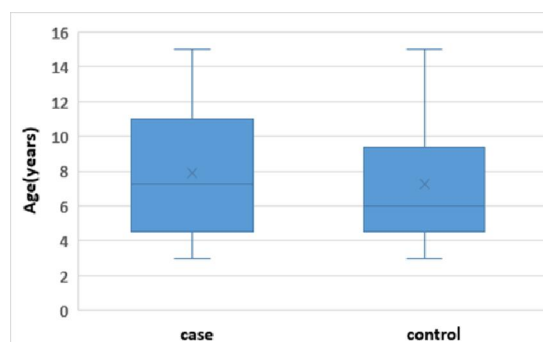


Fig. 1: Age distribution among the studied groups

Table (2) show sex distribution among the studied groups. Autistic children were 50 children (31 males and 19 females) while control group included 30 children (16 males and 14 females).

Table (2): Sex distribution among the studied groups

Sex	case (n=50)	Control (n=30)
Male	31 (62 %)	16 (53.3%)
Female	19 (38%)	14 (46.7%)

Table (3) shows childhood Autism Rating scale (CARS) score of the studied autistic children, which ranged from 35 to 57 (mean 43.52 ± 7.68).

Table (3): The initial Childhood Autism Rating Scale (CARS) score of autism among the studied patients

(CARS) score of autism	Cases of autism (n=50)
Range	35 - 57
Mean \pm SD	43.52 ± 7.68
Median	41.50

Table (4) and figure (2) show comparison between serum 25- hydroxy vitamin D level in the autistic children and the control group.

The mean serum vitamin D level in autistic children was (13.93 ± 4.62) , this level was significantly lower than that of the control group, in

which the mean serum vitamin D level was (37.74 ± 10.41) with (p value 0.001).

Table (4): Serum Vit D (ng/ml) level among the studied groups

Vit D (ng/ml) level	Cases of autism (n=50)	Control (n=30)
Range	7.9 – 24.00	30.31 – 62.90
Mean ± SD	13.93 + 4.62	37.74 + 10.41
Median	12.35	34.25
t test (p value)	13.64 (0.001)*	

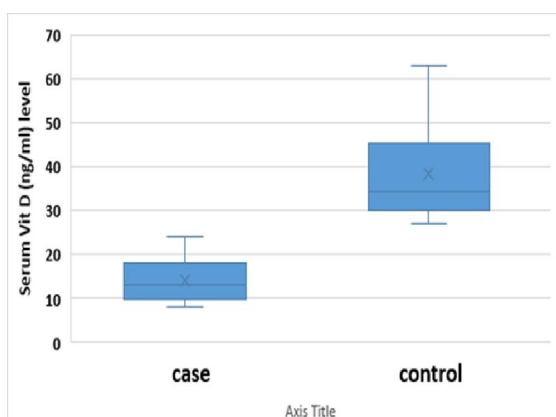


Fig (2): Serum Vit D (ng/ml) level among the studied groups

Table (5) and figure (3) show negative correlation between serum 25-hydroxy vitamin D level and CARS score among the autistic children. The higher CARS score is associated with more significant decrease in serum 25-hydroxy vitamin D level.

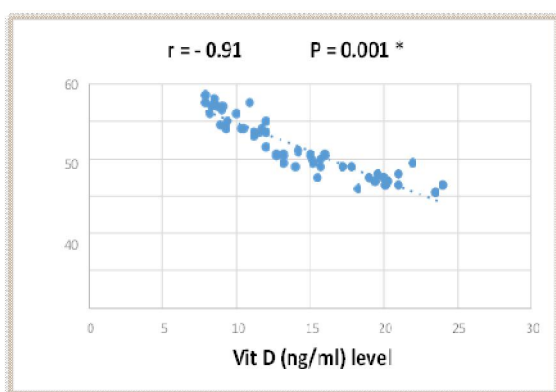


Fig (3): correlation between the Serum 25 OH Vit D (ng/ml) level with CARS score of autism among autism cases

Table (5): correlation between the Serum 25OH Vit D (ng/ml) level with CARS score of autism among autism cases

	Serum Vit D (ng/ml) level	
	r	P
(CARS) score of autism	-0.91	0.001 *

4. Discussion

This study was carried out to evaluate serum 25-hydroxy vitamin D levels in children with autism and to evaluate the relationship between vitamin D deficiency and the severity of autism.

The classical function of Vitamin D, which involves mineral balance and skeletal maintenance, has been known for many years. With the discovery of vitamin D receptors in various tissues, several other biological functions of vitamin D are increasingly recognized and its role in many human diseases like cancer, diabetes, hypertension, cardiovascular, and autoimmune and dermatological diseases is being extensively explored⁽⁶⁾.

One important yet little known of the numerous functions of vitamin is the regulation of nervous system development and function. The neuroprotective effect of vitamin D is associated with its influence on neurotrophin production and release, neuromediator synthesis, intracellular calcium homeostasis, and prevention of oxidative damage to nervous tissue. Clinical studies suggest that vitamin D deficiency may lead to an increased risk of disease of the central nervous system (CNS), particularly Autism, schizophrenia and multiple sclerosis⁽⁷⁾.

In the present study, serum level of 25 hydroxy vitamin D was measured in 50 autistic children.

Vitamin D level in the autistic children was significantly lower than that of the control group.

The mean 25-OHD levels in patients with severe autism were significantly lower than those in patients with mild/moderate autism. Serum 25-hydroxy vitamin D had significant negative correlations with Childhood Autism Rating Scale (CARS).

The results of this study agree with **meguid N.A., et al 2010⁽⁸⁾** who measured circulating levels of both forms of vitamin D (25(OH)D and 1,25(OH)2D) and serum calcium for seventy (70) children with autism diagnosed according to the DSM-IV criteria of the American Psychiatric Association with mean age ± SD (5.3 ± 2.8 years). Children with autism had significantly lower 25(OH) D and 1, 25(OH) 2D as well as lower calcium serum values than the controls.

Also this study agrees with **Mustafa G. A., et al, 2012⁽⁹⁾** who measured serum levels of 25-hydroxy vitamin D and anti-MAG (anti-myelin-associated glycoprotein) auto-antibodies in 50 autistic children, aged between 5 and 12 years, and 30 healthy-matched children. Autistic children had significantly lower

serum levels of 25-hydroxy vitamin D than healthy children with 40% and 48% being vitamin D deficient and insufficient, respectively. Serum 25-hydroxy vitamin D had significant negative correlations with Childhood Autism Rating Scale.

Also this study agree with **Saad K., et al, 2016**⁽¹⁰⁾ who performed a case-controlled cross-sectional analysis conducted on 122 autistic children, to assess their vitamin D status compared to controls and the relationship between vitamin D deficiency and the severity of autism. Fifty-seven percent of the patients had vitamin D deficiency, and 30% had vitamin D insufficiency. Serum 25-OHD levels had significant negative correlations with Childhood Autism Rating Scale (CARS) scores.

Also this study agree with **Bener A., et al, 2014**⁽²⁾ who performed Case-control study Of the total number of 508 children (254 of autism and 254 of healthy children, The mean age in years for autism versus control children was 5.51 ± 1.58 versus 5.76 ± 1.56). The mean value of Vitamin D in autism children was much lower than the normal value, and there was a significant difference found in the mean values of Vitamin D between autism and control children.

Also this study agree with **Tostes M. H., et al, 2012.**⁽¹¹⁾ who measured the circulating levels of 25-hydroxyvitamin D (25-OHD) in pediatric patients with autism and in typically developing controls. Serum levels of 25-OHD were lower in children with autism when compared to healthy control children.

Also this study agree with **Du L. et al, 2015**⁽¹²⁾ who measured serum levels of 25-hydroxyvitamin D levels in 117 children with newly diagnosed ASD and 109 healthy controls. Serum level of 25- hydroxy vitamin D in children with ASD was significantly lower than that in healthy controls.

Also this study agree with **Neumeyer A., M., et al, 2013**⁽¹³⁾ who had measured serum 25 hydroxy vitamin D level in boys with Autism Spectrum Disorders. 18 boys with ASD and 19 controls (8–14 years old) were included in the study. Serum 25(OH) vitamin D levels were significantly lower in autistic children than that in control group.

Also the results of this study agree with **Gong Z., L., et al, 2014**⁽¹⁴⁾ who performed a cross-sectional study on 96 Chinese children (48 confirmed ASD cases and 48 age-matched and sex- matched controls). The results indicated that the mean serum 25(OH) D levels were significantly lower in autistic children as compared with normal cases. 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.

On the other hand, the results of this study were contradictory to the results obtained by **Hashenzadeh et al. (2015)**⁽¹⁵⁾ who found no significant difference in

serum 25(OH)D concentrations between children with ASD aged 3–12 years ($n = 13$), and age and sex matched typically developing children ($n = 14$) but This study had the smallest sample size, a limited statistical power to detect differences among groups.

Also the results of this study were contradictory to the result obtained by **Adams et al. (2011)**⁽¹⁶⁾ who measured 25(OH) vitamin D level in 55 children aged 5-16 years with Autistic Spectrum Disorder and 44 healthy children of similar age, gender and geographical distribution served as a control group. The results showed that vitamin D levels were within published reference ranges in the autistic group.

Conclusion

Vitamin D level in the autistic children was significantly lower than that of the control group.

The mean 25-OHD levels in patients with severe autism were significantly lower than those in patients with mild/moderate autism. Serum 25-hydroxy vitamin D had significant negative correlations with Childhood Autism Rating Scale (CARS).

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