

## Effect of Vitamin A Supplementation on the Severity of Symptoms of Autism Spectrum Disorder: A Single Center Study

REHAM M. ELHOSSINY, M.D.\*; FATMA A. DARWISH, M.Sc.\*; DALIA H. ABDELHAMID, M.D.\*\* and ASMAA W. ABDELAZIZ, M.D.\*

*The Department of Pediatric Medicine\* and Clinical Pathology\*\*, Faculty of Medicine, Ain Shams University*

### Abstract

**Background:** Autism spectrum disorder (ASD) is a widespread neurodevelopmental syndrome which is characterised by communication difficulty. It has steadily increased in prevalence, becoming the most prevalent disorder among psychiatric disabilities. In addition, Vitamin A has a very crucial role in nervous system and brain development. Therefore, Vitamin A deficiency (VAD) can have a tremendous effect on children neurodevelopment and ASD development as a consequence.

**Aim of Study:** To assess the Vitamin A level in the Egyptian ASD children before and after Vitamin A supplementation; as well as its association with ASD symptoms.

**Material and Methods:** This is a two-stage study which the first stage is controlled cross-sectional study, while the second stage is interventional study, clinical trial, open label. We included Children with ASD diagnosed by (DSM-V) criteria, as well as healthy controls.

**Results:** We observed that 33.3% of ASD patients had a family history of similar cases. In addition, we observed a statistical decrease of Vitamin A level in the study group compared to the control group. ASD patients with low Vitamin A level had a mean and SD of  $51.27 \pm 25$ . This was increased significantly after Vitamin A supplementation to be  $81.18 \pm 21.652$ .

**Conclusion and Implications:** However, Vitamin A deficiency is popular in the developing countries including Egypt, yet ASD children had lower Vitamin A levels than normal children. In addition, Vitamin A supplementation seemed to significantly improve autistic symptoms of our patients.

**Key Words:** ASD – Autism – Vitamin A deficiency – VAD.

### Introduction

**AUTISM** spectrum disorder (ASD) refers to a broad group of neurodevelopmental disorders marked by difficulties in social interaction, non-verbal and verbal communication, frequently repetitive actions, and limited interests. Other

prevalent traits include abnormal sensory responses, a tendency for regularity, or strange attachment to routines [1,2].

ASD has steadily increased in prevalence, becoming the most prevalent disorder among psychiatric disabilities. According to The World Health Organization (WHO), the prevalence of ASD in children is approximately 16%; nevertheless, ASD incidence is less than 1% in the overall population worldwide. In addition, in the United States, ASD incidence is estimated to be 1 in every 59 children with the age of 8 years according to the Centers for Disease Control and Prevention (CDC). Yet, in 2016 parent-reported ASD diagnoses in the United States reported a higher incidence of 2.5%. Not only that, but Autism and Developmental Disabilities Monitoring Network (ADDM) observed that ASD incidence was doubled between 2000 to 2002, and 2010 to 2012, respectively [3-6].

There are various hypotheses on what causes autism; it is strongly heritable and thought to be primarily genetic, whereas several genes have been associated and environmental factors may also be involved. ADHD, seizures, and intellectual disability are among the other conditions that the syndrome usually co-occurs with. There are still conflicts of opinion regarding ASD diagnostic criteria and whether there are distinguishable subtypes of autism. moreover, A trend of gradually rising prevalence estimates for autism has resulted from the combination of expanded diagnostic criteria and greater public awareness [7,8].

Although multiple articles proposed that genetic factors play a huge part in the aetiology of ASD, yet the discovery of numerous genetic variants for ASD due to advances in sequencing technology and bioinformatic analysis techniques, only 10-20% of ASD patients currently carry any of these

**Correspondence to:** Dr. Fatma A. Darwish,  
[E-Mail: drfatmaali1992@gmail.com](mailto:drfatmaali1992@gmail.com)

genetic risk factors. In addition, not everyone with genetic risk factors for ASD develops the condition. On the other hand, a different report that assessed the heritability of autism to be 55% emphasized the theory that it is a genetic condition [7,9,10].

Environmental factors were also suggested to be associated with the development of ASD in children according to some studies. They found that deficiency in some essential micronutrients such as Vitamin A, B, and D could contribute to the pathogenesis of ASD [11,12].

Vitamin A is an essential micronutrient which plays a significant role in a complex in the central nervous system (CNS), which is responsible for complicated signalling cascade that regulates gene expression; in addition, it promotes neuronal differentiation and neural tube patterning. Thus, many studies linked Vitamin A deficiency to development of ASD in children [13,14].

### Patients and Methods

#### *Study design:*

This is a two-stage study, in which the First stage is controlled cross-sectional study and the Second stage is interventional study (open label, clinical trial).

#### *Study setting:*

This study was carried out in The Child Psychiatry Clinic, Children hospital, Ain Shams University in November 2021.

#### *Study subjects:*

As regards to Study population, we had two groups. Group I: Patients diagnosed with ASD who are following-up at Child Psychiatry Clinic, Children Hospital, Ain Shams University. And Group II: Healthy normally developed children serving as a control group in November 2021.

*Concerning our Inclusion criteria:* We included Patients of both genders, Patients from 1 year to 8 years old, Children with ASD diagnosed by Diagnostic and Statistical Manual of Mental Disorders (DSM-V) Criteria, healthy normally developed children serving as a control group, and Informed consent from the patients parents.

*While our Exclusion criteria:* We excluded Patients with other developmental disorders or neuro psychiatric disease, chronic illness, congenital malformations and GI disorders. As well as Patients with recent infection, chronic illness, congenital malformations and the use of vitamin or mineral supplements within the last 6 months.

#### *Sample size calculation:*

We analyzed 30 ASD patients who are following-up at Child Psychiatry Clinic, Children hospital, Ain Shams University. and 30 normal ones using the consecutive method. Moreover, we calculated the sample size Using pass 11 program for sample size calculation, at setting power 99%, significance level 0.05 and by reviewing previous studies.

#### *Study duration:*

This study has been held in 6 months.

#### *Study tools:*

##### *History taking:*

We took patients demographics including, Name, Gender, Age, Address, and Family history of similar cases. In addition, Past medical history including, Associated diseases, Medications, and Developmental history. Also, Dietary history was taken to exclude patients with signs of malnutrition.

##### *Clinical examination:*

To evaluate the patient and exclude other developmental disorders or psychiatric diseases or GI disorders. Anthropometric measures: Height, weight, and head circumference. DSM-5 diagnostic criteria (2013): To settle the diagnosis of ASD. Clinical assessment for severity of autism using the Arabic version of the Childhood Autism Rating Scale (CARS). Autism Treatment Evaluation Checklist (ATEC) to document improvement following an intervention by comparing the baseline ATEC scores with the posttreatment ATEC scores [15,16].

##### *Laboratory investigations:*

Venous blood samples (5mL) were collected at room temperature and centrifuged for 20min at 2000-3000rpm. The serum samples were stored at -20 until being processed then they were processed for estimation of retinol concentration using Enzyme-Linked immunosorbent Assay (ELISA) according to the manufacturer instructions. All evaluations and blood collection were conducted again 6 months after Vitamin A Supplementation (VAS) for ASD children. Vitamin A level >200 was considered normal.

##### *Study intervention:*

Regarding the Dose, a single vitamin A supplementation (Vitamin A will be supplemented to those who showed Vitamin A deficiency who were previously assessed in an earlier study) at a dose of 200,000 IU, was given to the ASD patients with vitamin A deficiency. For our Preparation, Oral liquid, oil-based preparation of retinyl palmitate

or retiny 1 acetate. The Possible side effects include irritability, headache, fever, diarrhea, nausea, and vomiting. In addition, participants were followed up for 12 weeks from dose administration with a combination of telephone calls and clinic attendance [17].

*Data management and Statistical analysis:*

Data was analyzed using a statistical package for social science (SPSS 23) software program. Qualitative variables were recorded as frequencies and percentages and were compared using Chi-square test. Quantitative measures were presented as mean and standard deviation and were compared by student *t*-test. Regression analysis and correlation between different variables was performed as indicated. *p*-value <0.05 is significant [18].

*Ethical consideration:*

Ethical approval was taken from Faculty of Medicine, Ethics committee, Ain Shams University. With number MS 320/2021. In addition, informed consent was taken from the care givers of the children. The privacy of participants and confidentiality of the data are maintained. Moreover, the results were collected, tabulated, and statistically analyzed for scientific purposes only.

**Results**

*Study characteristics and patients' demographics:*

We included 60 patients, 30 patients in the study group with Mean age and SD of 5.33 ± 1.729,

and 30 patients in the control group with Mean age and SD of 5.33 ± 1.729. There were 76.7% males and 23.3% females in both groups. All patients demographics, Anthropometric measures and Family history are summarized in (Table 1).

*The Vitamin A level of patients in the study group and control group before Vitamin A supplementation:*

The Vitamin A level in the study group was ranged between 25.80-731, with a mean value of 133.85 ± 163.261, while in the control group it ranged between 47.03-778.90 with a mean value of 207.43 ± 237.234. As shown in (Table 2).

Table (1): Demographics and Clinical characteristics of the participants.

	Study group (n=30)	Control group (n=30)
Age (mean-SD)	5.33±1.729	5.33±1.729
Gender (M:F)	23:7	23:7
Height for age	59.38±25.483	
Weight for age	54.55±23.870	
Headcircumference for age	46.76±23.802	
Age of onset at diagnosis	2.48±0.782	
IQ	59.95±6.353	
Family history of similar cases N (%)	10 (33.3)	
Brother (Autistic: ADHD)	1:1	
Cousin (Autistic: ADHD)	2:3	
Twin (Autistic: ADHD)	2:1	

Table (2): The Vitamin A level of patients in the study group and control group before Vitamin A supplementation.

Vitamin A level	Study group (n=30)		Control group (n=30)		U	P-value
	No.	%	No.	%		
<i>Before Vitamin A supplementation:</i>						
Min.-Max.	25.80-731.20		47.03-778.90		317.00	0.049*
Mean ± S.D	133.85±163.261		207.43±237.234			
Normal level No. (%)	9	30.0	9	30.0	–	1.000
Low level No. (%)	21	70.0	21	70.0		

*Patient's childhood autism rating scale (CARS):*

Patients CARS before vitamin A supplementation ranged between 26-113 with a Mean and SD of 34.97 ± 3.02. As shown in (Table 3).

*Correlation between different patients Demographics and Vitamin A level of patients in the study group:*

There was no statistically significant correlation between Age, Height for age, Weight for age, Head

circumference for age, or Age of onset at diagnosis and Vitamin A level. *p*-value >0.05. As shown in (Table 4).

*Correlation between different patients Demographics and Vitamin A level of patients in the study group:*

There was no statistically significant correlation between Gender and Vitamin A level. *p*-value >0.05. As shown in (Table 5).

*Comparison between The Vitamin A level of patients in the study group before and after Vitamin A supplementation:*

Vitamin A level before supplementation in the 21 patients who had low levels in the study group ranged between (34.06-71.3) with a mean value of  $51.27 \pm 25$ . This level was increased after vitamin A supplementation to be with a mean value of  $81.18 \pm 21.652$ . This shows Significant effect of the Vitamin A supplementation Vitamin A level in the study group.  $p$ -value  $< 0.05$ . As shown in (Table 6).

*The effect of Vitamin A supplementation on patient's ATEC:*

Patients ATEC before vitamin A supplementation ranged between 26-113 with a Mean and SD of  $77.77 \pm 22.236$ . While patients ATEC after Vitamin A supplementation ranged between 31-98 with a Mean and SD of  $72.38 \pm 19.104$ . This shows a Significant effect of the Vitamin A supplementation in ATEC,  $p$ -value  $< 0.05$ . As shown in (Table 7).

Table (3): Patient's childhood autism rating scale (CARS) at baseline.

	Mean $\pm$ SD / N (%)
Initial CARS at diagnosis	34.97 $\pm$ 3.02
<i>CARS C:</i>	
Mild to moderate	22 (73.33%)
Severe	8 (26.67%)

Table (4): Correlation between different patients Demographics and Vitamin A level of patients in the study group.

	Vitamin A level	
	<i>r</i>	<i>p</i>
Age	-0.086	0.651
Height for age	0.208	0.279
Weight for age	0.010	0.960
Head circumference for age	0.116	0.548
Age of onset at diagnosis	0.235	0.211

Table (5): Correlation between different patients Gender and Vitamin A level of patients in the study group.

Vitamin A level	Male (n=23)		Female (n=7)		U	<i>p</i> value
	No.	%	No.	%		
<i>Before Vitamin A supplementation:</i>						
Min.-Max.	47.03-776.00		55.40-778.90		50.00	0.135
Mean $\pm$ S.D	182.23 $\pm$ 221.810		290.20 $\pm$ 284.945			
Normal Level	6	26.1	3	42.9	-	0.640
Low Level	17	73.9	4	57.7		
<i>After Vitamin A supplementation:</i>						
Min.-Max.	38.50-117.70		65.50-107.60		29.00	0.654
Mean $\pm$ S.D	79.88 $\pm$ 22.785		86.70 $\pm$ 17.503			

Table (6): Comparison between patient's vitamin A level before and after Vitamin A supplementation.

Vitamin A level	Before Vitamin A supplementation (n=21)	After Vitamin A supplementation (n=21)	Z	<i>p</i> value
Min.-Max.	34.06-71.3	38.50-117.70	1.651	0.04
Mean $\pm$ S.D	51.27 $\pm$ 25	81.18 $\pm$ 21.652		

\*: Statistically significant at  $p < 0.05$ .

Table (7): Comparison between Before and after Vitamin A supplementation as regard to patient's ATEC.

ATEC	Before Vitamin A supplementation	After Vitamin A supplementation	<i>t</i>	<i>p</i> value
Min.-Max.	26-113	31-98	4.316	$< 0.001$ *
Mean $\pm$ S.D	77.77 $\pm$ 22.236	72.38 $\pm$ 19.104		

## Discussion

ASD has become the most common paediatric disorder in the last ten years, and it is becoming more common worldwide. In America, 1 in 68 children who are 8 years old are reported to have ASD. ASD has steadily increased in prevalence, becoming the most prevalent disorder among psychiatric disabilities. It puts a substantial impact on families and society as a whole [19,20].

Autism spectrum disorder (ASD) is a widespread neurodevelopmental syndrome which is characterised by communication difficulty, stereotyped and repetitive patterns of behaviour, interests, and activities, as well as difficulties in social interaction [21].

Vitamin A is an essential micronutrient whose active metabolite is retinoic acid (RA). Not only it has a very crucial role in nervous system by influencing the growth, proliferation, and differentiation of neurons in the nervous system; as well as, it can have an impact on cognitive function, learning, memory formation, and brain development, but also it is important for digestive, immunological, and serotonin systems [22,23].

Therefore, Vitamin A deficiency (VAD) is very dangerous. Almost 670,000 children under the age of five lose their life each year as a result, about one-third of children under the age of five are thought to be affected by VAD worldwide. It is common in poorer countries, especially among children and women of reproductive age, but is rarely seen in more developed countries [24,25].

Various factors have been contributed to ASD, some studies suggested that genetic factors play a significant role in the aetiology of ASD, yet multiple genetic variants for ASD have been found thanks to breakthroughs in sequencing technology and bioinformatic analysis methods, only 10-20% of ASD patients now carry any of these genetic risk factors. Additionally, not all people with genetic risk factors for ASD acquire the disease [9,26].

In our study, we observed that 33.3% of ASD patients had a family history of similar cases; either brother, cousin, or uncle. Similar, but lower results were reported by Bolton P et al., that Siblings of autistic children may have a 20% increased risk of developing extensive developmental disorder. Yet, lower incidence was reported by Muhle et al., who suggested that only 2% to 8% of ASD patients had genetic predisposition [27,28].

On the contrary, the high heredity concept of autism was challenged by another paper, which

estimated the heritability of autism to be 55% [10].

Thus, other studies linked the development of ASD to environmental factors, they observed that autism pathogenesis is associated with micronutrient deficiency, including vitamin A (VA), vitamin B, and vitamin D (VD). Also, patients with ASD have lower VA levels than normal children or family members [11,12].

So, we assessed the Vitamin A level in the Egyptian ASD children, as well as the effect of Vitamin A supplementation on ASD symptoms improvement.

We observed a statistical decrease of Vitamin A level in the study group compared to the control group with a mean of 133.85, and 207.43, respectively. However, about two-thirds of the patients in both groups had low levels of vitamin A. This could be explained by the recent World Health Organization (WHO) guidelines, which reported that about one-third of children under the age of five are thought to be affected by VAD worldwide. The frequency of VAD is highest in Southeast Asia and Africa, where between 250,000 and 500,000 children in developing nations go blind every year as a result. Thus, they strongly recommended that in areas where vitamin A deficiency is a concern for public health, infants and children between the ages of 6 and 59 months should take high-dose vitamin A supplements. Furthermore, in 2013, 65% of all children worldwide aged 6 to 59 months received two doses of vitamin A, totally preventing them from VAD (80% in the least developed nations) [24,29].

Vitamin A is an essential micronutrient whose active metabolite is retinoic acid (RA). Not only it has a very crucial role in nervous system by influencing the growth, proliferation, and differentiation of neurons in the nervous system; as well as, it can have an impact on cognitive function, learning, memory formation, and brain development, but also it is important for digestive, immunological, and serotonin systems [22,23].

In our study, ASD patients with low Vitamin A level had a mean and SD of  $51.27 \pm 25$ . This was increased significantly after Vitamin A supplementation to be  $81.18 \pm 21.652$  ( $p$ -value  $< 0.05$ ). Göüm et al., also reported similar results; they reported that Vitamin A level in the study groups was elevated significantly from  $54 \pm 17$   $\mu\text{mol/dL}$  at baseline to  $79 \pm 16$   $\mu\text{mol/dL}$  after supplementation ( $p < 0.001$ ) [30].

Nevertheless, 3 cases of the 21 vitamin A deficient patients in our series didn't show a significant elevation of vitamin A level. This could be due to Vitamin A deficiency is associated with disorders associated with malabsorption. Under certain circumstances, serum vitamin A concentrations do not indicate total vitamin A reserves. Because dietary protein, energy, and zinc are needed for the production of retinol binding protein, severe protein-calorie malnutrition may cause serum retinol levels to be unnaturally low (i.e., underestimate vitamin A reserves) (RBP) [31,32].

We used Autism Treatment Evaluation Scale (ATEC) to assess speech/language, communication, Sociability, sensory and cognitive awareness, and physical/health behavior in our study group patients. Patients had a baseline mean score of ATEC of  $77.77 \pm 22.236$ . After vitamin A supplementation, we observed that our intervention significantly improved patients' symptoms. As ATEC after supplementation was with a mean of  $72.38 \pm 19.104$  ( $p$ -value  $< 0.05$ ). Gou. M et al., also reported that all symptoms concerning neurodevelopmental impairment that was reported by parents were significantly improved after Vitamin A supplementation; suggesting that vitamin A supplementation can improve autistic symptoms [30].

In the literature, Vitamin A deficiency was associated with higher odds of stunting, wasting or underweight. However, we found no correlation between different patients Demographics or anthropometric measures, such as Age, Gender, Height for age, Weight for age, Head circumference for age, or Age of onset at diagnosis, ( $p$ -value  $> 0.05$ ) [33,34].

On the contrary, Liu. X et al., established that age, gender, the family structure, and the parents' education levels in different age groups had been associated with children with ASD, the higher rates of VAD were distinguished in ASD indeed. Not only that, but ASD patients with age lower than 6 years have been significantly more associated with Vitamin A deficiency. Additionally, children with lower socioeconomic level were lower than those at average and higher economic status; this could be due to inadequate intake [35].

#### Conclusion:

However, Vitamin A deficiency is popular in the developing countries including Egypt, yet ASD children had lower Vitamin A levels than normal children. In addition, Vitamin A supplementation seemed to significantly improve autistic symptoms of our patients.

#### Limitations:

One limitation of our study that we didn't make a correlation between ASD severity and Vitamin A level in ASD children. In addition, we were unable to deliver two or three doses of Vitamin A supplementation as WHO recommended to ensure optimum outcomes.

#### Recommendation:

Future research should be conducted to investigate the relation between ASD and different patients demographics. Also, two or three doses of Vitamin A supplementation could carry better results regarding autistic symptoms.

#### Funding:

None to declare.

#### Conflict of Interest:

Non to declare.

### References

- 1- ROSEN N.E., LORD C. and VOLKMAR F.R.: "The Diagnosis of Autism: From Kanner to DSM-III to DSM-5 and Beyond," J. Autism Dev. Disord, Vol. 51, No. 12, pp. 4253-4270, Dec., doi: 10.1007/s10803-021-04904-1, 2021.
- 2- DESTEFANO F. and SHIMABUKURO T.T.: "The MMR Vaccine and Autism," Annu. Rev. Virol., Vol. 6, No. 1, pp. 585-600, Sep., doi: 10.1146/annurev-virology-092818-015515, 2019.
- 3- CHAPMAN R. and VEIT W.: "Correction to: The essence of autism: fact or artefact?," Mol. Psychiatry, Vol. 26, No. 11, pp. 7069-7069, Nov. 2021, doi: 10.1038/s41380-021-01057-6.
- 4- XU G., STRATHEARN L., LIU B. and BAO W.: "Prevalence of Autism Spectrum Disorder Among US Children and Adolescents, 2014-2016," JAMA, Vol. 319, No. 1, p. 81, Jan., doi: 10.1001/jama.2017.17812, 2018.
- 5- PALINKAS L.A., MENDON S.J. and HAMILTON A.B.: "Innovations in Mixed Methods Evaluations," Annu Rev Public Health, Vol. 40, No. 1, pp. 423-442, Apr., doi: 10.1146/annurev-publhealth-040218-044215, 2019.
- 6- CDC, "CDC," 2022.
- 7- MANDY W. and LAI M.-C.: "Annual Research Review: The role of the environment in the developmental psychopathology of autism spectrum condition," Journal of Child Psychology and Psychiatry, Vol. 57, No. 3, pp. 271-292, Mar., doi: 10.1111/jcpp.12501, 2016.
- 8- ROBISON J.E.: "My Time with Autism Speaks," in Autistic Community and the Neurodiversity Movement, Singapore: Springer Singapore, pp. 221-232. doi: 10.1007/978-981-13-8437-0\_16, 2020.
- 9- LORD C., ELSABBAGH M., BAIRD G. and VEENSTRA-VANDERWEELE J.: "Autism spectrum disorder," The Lancet, Vol. 392, No. 10146, pp. 508-520, Aug., doi: 10.1016/S0140-6736(18)31129-2, 2018.

- 10- Hallmayer J.: "Genetic Heritability and Shared Environmental Factors Among Twin Pairs With Autism," *Arch Gen Psychiatry*, Vol. 68, No. 11, p. 1095, Nov., doi: 10.1001/archgenpsychiatry.2011.76, 2011.
- 11- SUN C., XIA W., ZHAO Y., LI N., ZHAO D. and WU L.: "Nutritional status survey of children with autism and typically developing children aged 4-6 years in Heilongjiang Province, China," *J. Nutr. Sci.*, Vol. 2, p. e16, Apr., doi: 10.1017/jns.2013.9, 2013.
- 12- TAN M., et al., "Maternal folic acid and micronutrient supplementation is associated with vitamin levels and symptoms in children with autism spectrum disorders," *Reproductive Toxicology*, Vol. 91, pp. 109-115, Jan., doi: 10.1016/j.reprotox.2019.11.009, 2020.
- 13- LI H.-H., YUE X.-J., WANG C.-X., FENG J.-Y., WANG B. and JIA F.-Y.: "Serum Levels of Vitamin A and Vitamin D and Their Association With Symptoms in Children With Attention Deficit Hyperactivity Disorder," *Front Psychiatry*, Vol. 11, Nov., doi: 10.3389/fpsy.2020.599958, 2020.
- 14- WANG N., ZHAO Y. and GAO J.: "Association Between Peripheral Blood Levels of Vitamin A and Autism Spectrum Disorder in Children: A Meta-Analysis," *Front Psychiatry*, Vol. 12, Sep., doi: 10.3389/fpsy.2021.742937, 2021.
- 15- RASHAD M. M., RAZEK G. A. and REFFAT G.: "Validity of the Modified Checklist for Autism in Toddlers (MCHAT): Preliminary Study in Eastern Province of Saudi Arabia," *OALib*, Vol. 02, No. 12, pp. 1-9, doi: 10.4236/oalib.1101951, 2015.
- 16- A.-S.Z. EL-SHEMRY T., "reliability and validity of arabic version of childhood rating scale.," *J. spec edu*, 2002.
- 17- WHO: "WHO Guideline: Vitamin A Supplementation in Infants and Children 6-59 Months of Age. World Health Organization, Geneva," 2020.
- 18- IBM Corp, "IBM SPSS Statistics for Windows, Armonk, NY: IBM Corp," 2015.
- 19- KALUŻNA-CZAPLIN´SKA J., JÓZ´WIK-PRUSKA J., CHIRUMBOLO S. and BJØRKLUND G.: "Tryptophan status in autism spectrum disorder and the influence of supplementation on its level," *Metab Brain Dis.*, Vol. 32, No. 5, pp. 1585-1593, Oct., doi: 10.1007/s11011-017-0045-x, 2017.
- 20- KIRBY A.V., BOYD B.A., WILLIAMS K.L., FALDOWSKI R.A. and BARANEK G.T.: "Sensory and repetitive behaviors among children with autism spectrum disorder at home," *Autism*, Vol. 21, No. 2, pp. 142-154, Feb., doi: 10.1177/1362361316632710, 2017.
- 21- BJØRKLUND G., et al.: "The Role of Vitamins in Autism Spectrum Disorder: What Do We Know?," *Journal of Molecular Neuroscience*, Vol. 67, No. 3, pp. 373-387, Mar., doi: 10.1007/s12031-018-1237-5, 2019.
- 22- MANDY W. and LAI M.-C.: "Annual Research Review: The role of the environment in the developmental psychopathology of autism spectrum condition," *Journal of Child Psychology and Psychiatry*, Vol. 57, No. 3, pp. 271-292, Mar., doi: 10.1111/jcpp.12501, 2016.
- 23- SEALEY L.A., et al.: "Environmental factors in the development of autism spectrum disorders," *Environ Int.*, Vol. 88, pp. 288-298, Mar., doi: 10.1016/j.envint.2015.12.021, 2016.
- 24- World Health Organization (WHO): "World Health Organization, Global prevalence of vitamin A deficiency in populations at risk 1995-2005, WHO global database on vitamin A deficiency".
- 25- BLACK R.E., et al.: "Maternal and child undernutrition: global and regional exposures and health consequences," *The Lancet*, Vol. 371, No. 9608, pp. 243-260, Jan., doi: 10.1016/S0140-6736(07)61690-0, 2008.
- 26- ABRAHAMS B.S. and GESCHWIND D.H.: "Advances in autism genetics: On the threshold of a new neurobiology," *Nat Rev Genet*, Vol. 9, No. 5, pp. 341-355, May, doi: 10.1038/nrg2346, 2008.
- 27- MUHLE R., TRENTACOSTE S.V. and RAPIN I.: "The Genetics of Autism," *Pediatrics*, Vol. 113, No. 5, pp. e472-e486, May, doi: 10.1542/peds.113.5.e472, 2004.
- 28- BOLTON P., et al.: "A Case-Control Family History Study of Autism," *Journal of Child Psychology and Psychiatry*, Vol. 35, No. 5, pp. 877-900, Jul., doi: 10.1111/j.1469-7610.1994.tb02300.x, 1994.
- 29- Unicef, "Vitamin A deficiency," 2023.
- 30- GUO M., et al.: "Vitamin A improves the symptoms of autism spectrum disorders and decreases 5-hydroxytryptamine (5-HT): A pilot study," *Brain Res. Bull.*, Vol. 137, pp. 35-40, Mar., doi: 10.1016/j.brainresbull.2017.11.001, 2018.
- 31- LIN P.: "Ocular Surface Disease Secondary to Vitamin A Deficiency in the Developed World: It Still Exists," *Archives of Ophthalmology*, Vol. 129, No. 6, p. 798, Jun., doi: 10.1001/archophthalmol.2011.126, 2011.
- 32- A.B.B.M. et al., editors. Feingold K.R., "Lipid and Lipoprotein Metabolism," MDText.com, Inc., 2000.
- 33- OLOFIN I., et al.: "Associations of Suboptimal Growth with All-Cause and Cause-Specific Mortality in Children under Five Years: A Pooled Analysis of Ten Prospective Studies," *PLoS One*, Vol. 8, No. 5, p. e64636, May, doi: 10.1371/journal.pone.0064636, 2013.
- 34- SSENTONGO P., et al.: "Association of vitamin A deficiency with early childhood stunting in Uganda: A population-based cross-sectional study," *PLoS One*, Vol. 15, No. 5, p. e0233615, May, doi: 10.1371/journal.pone.0233615, 2020.
- 35- LIU X., et al.: "Correlation between Nutrition and Symptoms: Nutritional Survey of Children with Autism Spectrum Disorder in Chongqing, China," *Nutrients*, Vol. 8, No. 5, p. 294, May, doi: 10.3390/nu8050294, 2016.

## تأثير مكملات فيتامين أ على شدة أعراض اضطراب طيف التوحد : دراسة مركزية واحدة

الخلفية: اضطراب طيف التوحد (ASD) هو متلازمة نمو عصبي واسع الانتشار بصعوبة التواصل. لقد زاد انتشاره بشكل مطرد، ليصبح الاضطراب الأكثر انتشاراً بين الإعاقات النفسية. بالإضافة إلى ذلك، يلعب فيتامين أ دوراً حاسماً للغاية في نمر الجهاز العصبي والدماغ لتلك، يمكن أن يكون لنقص فيتامين أ (VAD) تأثير هائل على النمو العصبي للأطفال وتطور ASD نتيجة لذلك.

الهدف: من هذه الدراسة تقييم مستوى فيتامين أ في الأطفال المصريين الذين يعانون من اضطراب طيف التوحد قبل وبعد تناول مكملات فيتامين أ. وكذلك ارتباطه بأعراض اضطراب طيف التوحد.

المادة والطرق: هذه دراسة من مرحلتين حيث يتم التحكم في المرحلة الأولى عبر دراسة مقطعية، بينما المرحلة الثانية هي الدراسة التداخلية والتجربة السريرية والتسمية المفتوحة. قمنا بتضمين الأطفال المصابين بالتوحد الذين تم تشخيصهم بمعايير (DSM-V)، وكذلك الضوابط الصحية.

النتائج: لاحظنا أن ٣٣.٣٪ من مرضى التوحد لديهم تاريخ عائلي لحالات مماثلة. بالإضافة إلى ذلك، لاحظنا إنخفاضاً إحصائياً في مستوى فيتامين أ في مجموعة الدراسة مقارنة بمجموعة التحكم. كان لدى مرضى ASD الذين يعانون من إنخفاض مستوى فيتامين أ (أ) متوسط و  $SD 51.27 \pm 25$ . وقد زاد هذا بشكل ملحوظ بعد مكملات فيتامين أ (أ) لتصبح  $21.652 \pm 81.18$ .

الخلاصة والتداعيات: ومع ذلك، فإن نقص فيتامين أ (أ) شائع في البلدان النامية بما في ذلك مصر، ولكن لدى أطفال التوحد مستويات أقل من فيتامين أ (أ) من الأطفال العاديين. بالإضافة إلى ذلك، يبدو أن مكملات فيتامين أ (أ) تحسن بشكل كبير أعراض التوحد لمرضانا.