## The nutritional and some metabolic markers of autistic children

Heba said Abdelhaliem,Hanady Gaber Sheha, EmanElsayed Habib Clinical nutrition Dep, NNI.Egypt

## Abstract

Autism is a neurological disorder of behavior and the disability to socialize. Autism disorders (ASD) affect more the percent of children who are not apparent in the behavior before the age of three years. Genetics have a major role in the etiology of autism, in conjunction with the early environmental factors of growth. Epidemiological studies indicated that the environmental factors are focused on the physiological and behavioral effects of dietary change but has not examined the effect of exclusion diets. The present study aimed at comparing dietary regimens and habits of children with autistic disorder, compared with apparently healthy children. A total of 20 children with autistic disorder and 20 healthy male children apparently normally developing of similar age (8-10y) from (Menoufia Governorate) were enrolled in the study. The study measurements included: anthropometric measurements, nutritional value of their diet, biomarkers of vitamin and minerals status in plasma, plasma glutathione, and biomarkers of energy production. The results showed that weight and BMI were significantly high in children with autistic disorder compared with healthy controls ( $p \le 0.05$ ). Energy, Carbohydrates, total fats, Cholesterol, VitA, E and K intake were significantly high in autistic children compared to healthy controls. The autism children significantly had high level in blood of Vit. A, total Vit E, and Vit K while the control group significantly higher level of total Carotenes(beta carotene and other carotenes, in blood), Vit B6, Folic Acid, Vit B12, Vit C and total Choline. Children with autism had significantly elevated oxidative stress, as indicated by increased GSH / GSSG ratio. The study concluded that regular screening for children with ASD is necessary to be in control.

Keywords: Children, autism, anthropometric measurement, BMI

## Introduction

Autism is a neurodevelopmental disability characterized by lack of social and emotional reciprocity, limited verbal and non verbal language skills and the presence of stereotyped and repetitive behaviors. The prevalence of autism has been increasing in the last several decades and autism is now thought to be a relatively common neurodevelopmental disorder with estimates of 1 case per 110 individuals (*Bandini et al., 2010, Emond et al., 2015*).

The incidence and prevalence of autism have dramatically increased over the last 20 years. It is more prevalent in males, with a male: female sex ratio in the range 2:1 to 3:1. Genetics has a key role in the etiology of autism, in conjunction with developmentally early environmental factors Epidemiologic studies indicated that environmental factors such as toxic exposures, teratogens, perinatal insults, and prenatal infections such as rubella and cytomegalovirus account for few cases *(Hedigeret al., 2008 and Herndon et al., 2019).* 

Patients with ASD may also suffer from leaky gut syndrome, which is caused by inflammation of the intestinal mucosa and abnormal bacterial overgrowth leading to a disorder of bowel motility. A fundamental relationship between gut micro biome, diet and ASD has been recently suggested . Such an extensive array of symptoms in the digestive tract in patients with ASD, strongly suggests the need for introducing nutritional therapy in addition to routine treatment. Suitable diet can lead to relief of symptoms, both digestive and metabolic as well as psychological ones. Unfortunately, very few physicians and nutritionists can monitor the diet and nutrition of ASD patients *(Institute of Medicine, 2019).* About 25% of children with ASD have at least one chronic gastrointestinal (GI) tract symptom. Also, GI issues may affect absorption of vitamins/minerals. Diet quality can relieve GI symptoms such as abdominal pain, constipation, diarrhea, gastrointestinal reflux. Scientific research has indicated that pathogenesis of autism may have a beginning already in fetal life. Some dietician's tasks are to properly assess the nutritional status of mothers before and during pregnancy, thereby allowing changes in nutrition to be made wherever necessary so that metabolic indicators are improved *(Ledford&Gast, 2006 and Riten&Missaro, 2020).* 

The purpose of this study is to investigate the nutritional, metabolic, and anthropometric and some biochemical status of children with autism compared to control children of similar age and gender.

## Children and methods

#### Children

Twenty male children aged 8–10 years with autistic disorder and twenty normal matched for age, sex and economic status normally developed children were enrolled as controls who visited the children outpatients' clinic at, Menof city Menoufia Government, Egypt, were enrolled in this study.

#### Methods

#### Anthropometric measurements and dietary data collection

Informed consents were read, fully comprehended and signed by tutoring parents of the recruited children. The diagnosis autistic disorder was accomplished using three psychometric questionnaires. The assessment of the nutritional status and anthropometric assessment included weight, height, and BMI for age (*WHO, 2009*). Experienced dietitian collected food frequency questionnaire from parents for all participants. The parents of each child were requested to provide food diary of their children for three days. A detailed description of all food and beverages consumed were recorded. Individual food intake was calculated and analyzed using Computer Aided Nutritional Analysis Program, of the National Nutrition Institute, Cairo, Egypt(*food composition Table 2006*). The Recommended Dietary Allowance (RDA) for micronutrients were calculated using Food and Agriculture Organization (*FAO/WHO, 2002*).

#### **Biochemical measurements**

Morning blood samples (10 ml) were collected after an overnight fast (12 hours) and collecting urine samples. All study data (questionnaires and laboratory samples) were assigned a coordinating subject code. All laboratory samples were delivered blinded to for analysis (Autism or Control). Vitamins were measured in the blood compartment (serum, plasma, or RBC). Fat-soluble vitamins (A, D, E, K) are primarily concentrated in serum. For water-soluble vitamins (*O'Byrne SM and Blaner WS* **2013)**, some are primarily in the plasma (like vitamin C), whereas others are significantly present in both

serum and RBC, so whole blood was used. Essential minerals were measured in RBC, serum, and whole blood. In most cases, serum reflects an average of the last several days, RBC reflects an average of the last several months, and whole blood is an average of both. Serum Na, K, Mg, Ca, P, Fe were analyzed using commercial assays (*Burtis and Ashwood ,1999*). Whole blood samples were collected in a potassium EDTN trace metal free, to get packed red blood cells. Other blood samples were collected in tubes with no EDTN to get serum Blood samples were spun for 10 minutes in centrifuge tubes at 3000 rpm. Glutathione (GSH and GSSG) were measured by *Michelet et al.,(1995*). Serum Ferritin, ATP, and NADH, NADPH were estimated by *Gorman et al., (2007) and Klemm et al. (1997).* 

#### Statistical methods:

Statistical analysis was performed using Microsoft Excel 2010 in an ANOVA assay. Data was expressed as mean  $\pm$  SD and statistical differences between groups were conducted for significance using the unpaired Student's t-test. Statistical significant difference was considered at p  $\leq$  0.05. Pearson's correlation analysis was used to examine the correlation between the dietary intake of some micronutrients and vitamins and their levels in serum (*Snedecor and Cochran, 1982*), *SPSS (2000*).

## Results and discussion

#### Demographic and anthropometric parameters of the studied autistic and healthy children

Demographic and anthropometric parameters are summarized in Table (1). Results showed that the average age of children in both groups were 8.9 years. Both paternal and maternal ages were higher in the autism group than normal group. From the same table, it could be noticed that weight and BMI were significantly higher in children with autistic disorder compared with healthy controls ( $p \le 0.05$ ) although, the heights were nearly similar. Previous research reported mixed results concerning height, weight and BMI in children with ASD (*Zimmer et al., 2012*).

Parameters	ASD ( <i>n</i> = 20)	Control ( $n = 20$ )		
Age(y)	$8.9 \pm 0.72^{a}$	8.9 ± 0.52 <sup>a</sup>		
Paternal age(y)	$38 \pm 5.42^{a}$	30.8 ± 5.85 <sup>b</sup>		
Maternal age(y)	$32 \pm 5.20^{a}$	28.5 ± 3.21 <sup>b</sup>		
Height (cm)	$123.7 \pm 7.06^{a}$	123. 8 ± 9.18 <sup>a</sup>		
Weight(kg)	$39 \pm 0.6^{a}$	$30 \pm 0.4^{b}$		
BMI	25.36± 0.9 <sup>ª</sup>	19.5 ± 0.7 <sup>b</sup>		

Table (1) Demographic and anthropometric parameters of the autistic and healthy controls

Data are means  $\pm$  (SD). Values with different letters are significantly different.  $P \le 0.05$ 

#### Socioeconomic status of the studied autistic and healthy children

**Table (2)** showed that the highest percentage of autistic children was found among families of low economic status (60%) while the control group was found in both low and medium economic status (50% each). As regard to educational level of mothers and fathers for autistic children, it was found 75 and 70% pre-university respectively while the parents of healthy children was reported 70% for the mothers and 95% for the fathers had university level. The percentages of breastfeeding of autistic children and control group were 85% and 60% respectively .ForPsychiatry Family History, the highest percentage have no Psychiatry Family History in both groups. Consanguinity Degree showed that 55% of autistic children had the first Consanguinity Degree while 85% in healthy children have no Consanguinity.

Table (2)				
Socioeconomic status of studied autistic and healthy children				
Parameters	ASD (n = 20)		Control (n = 20)	
	Number	%	Number	%
Familymonthly income				
Low (< 2000 LE)	12	60	10	50
Medium(2000-5000 LE)	8	40	10	50
High (>5000 LE)	0	0	0	0
Mother Education				
University	5	25	14	70
Pre-University	15	75	6	30
Father education				
University	6	30	19	95
Pre-University	14	70	1	5
Delivery Feeding				
Breast Feeding	17	85	12	60
Bottle Feeding	3	15	4	20
Mix Feeding	0	0	4	20
PsychiatryFamily History				
Yes	2	10	0	0
No	18	90	20	100
Consanguinity Degree	11	55	2	10
First	4	20	1	5
Second	3	15	0	0
Third	2	10	17	85
No Consanguinity				
<b>U</b>				
	1	1	1	1

#### Problems of studied autistic and healthy children

Nutritional and other problems of studied autistic and healthy children were presented in table (3). The highest percentage in autistic children had diarrhea, Sleep problems, eats too much, hyperactive, destructive, shouts/screams and repetitive movements. For healthy group, the high percentage had limited diet while the high percentage had no nutritional or other problems. Sensory integration dysfunction may also play a role in problematic eating behaviors. **Bennettoet al. (2007)** found that children with ASD have problems correctly identifying taste and olfactory sensations suggesting that over or under responsiveness to sensory stimuli may also contribute to the high prevalence of feeding difficulties among their population. This is an area that requires further investigation. Children who are selective eaters are often referred to feeding programs which involve multidisciplinary teams including physicians, psychologists, occupational therapists and speech therapists. **Ledford and Gast (2006)** found that most of the literature on the effectiveness of these interventions is in the form of case reports (n < 7) groups. **Laud et al. (2009)** found that intensive

feeding interventions lasting an average of 47 days decreased problematic eating behaviors in 46 autistic children for 3 years follow-up with 29 of the participants who had eating problems were either stabilized or they had been discharged from therapy or continued to improve.

	ASD (n = 20)		Control (n = 20)	
Parameters	Number	%	Number	%
Diarrhea	11	55	3	15
Constipation	9	45	2	10
Sleep problems	18	90	1	5
eats too much	17	85	3	15
special diet	3	15	17	85
Hyperactive	16	80	1	5
Destructive	13	65	1	5
shouts/screams	19	95	1	5
repetitive movements	14	70	0	0

 Table (3)

 Problems of studied autistic and healthy children

# The average intake of energy and different macronutrients by the studied autistic and healthy controls

Data in table (4) presented the average intake of energy and different macronutrients for three days of both children groups. Dietary intakes by children with autistic disorder and healthy children did not show any significant difference between the two groups regarding intake of Proteins, Vit. B6, D, andPanthothenic acid. Children with autistic disorder had significantly lower intake of fibers, Folic acid, Niacin, Vit. C, Riboflavin, Vit B12 and all minerals (iron, Calcium, Zinc, Iodine, Phosphorus and Fluoride ) compared with the control children . On the other hand, Energy, Carbohydrates, total fats, Cholesterol, Vit A, E and Vit. K intakes were significantly higher in autistic children compared with the healthy controls. The results were found similar to previously published reports of certain micronutrient deficiencies in children with autism. Poor calcium intake has been consistently reported in studies of nutrient intake of children with autism (Laud et al., 2009). The risk of inadequate intake of Vitamin D found in this study had also been previously reported by (Lindsay et al., 2016). This data was attributed to the fact that many parents of children with autism limit or completely eliminate dairy food from their child's diet as part of an advice of gluten and casein free diet. Furthermore, data from Hediger et al. (2008) suggest that children with autism have poorer bone density than age matched typically developing control group. Lower calcium intake may be partially responsible for the low intake of vita D.

In this study, the group with autism had greater average intake of magnesium than the control group. *Johnson et al. (2008)* also found higher average intake of magnesium by preschool aged children with autism and concluded that children with autism were less likely to be at risk for magnesium deficiency than controls. Foods high in magnesium include green vegetables, cashews, almonds, and whole unrefined grains *(Gerrioret al. 2014)*. While there is no tolerable upper limit for magnesium from food sources, the tolerable upper limit for magnesium intake from non-food sources is

110 mg for children less than 8 years old and 350 mg for children greater than 8 years old. A cautionary note should be given to parents that dietary intake alone is often sufficient, and that non-food sources should not exceed the tolerable upper limit. Children on supplementation should be monitored closely for side effects, which include diarrhea, hypotension, and decreased reflexes *(Institute of Medicine 2011)*. Also some children with autism are using high fat supplements, and commercial preparations can contain high Vitamin A. Caution should be given to parents using high fat in dietary intake should be assessed carefully to assure that children are at risk for vitamin A toxicity. Foods that contain Vitamin A include sweet potatoes, high fat foods and eggs *(Gerrioret al., 2014)*. The symptoms of vitamin A toxicity include headache, seizures, vomiting, abdominal pain, eczema, skin erythema, conjunctivitis, and musculoskeletal tenderness. Chronic Vitamin A toxicity has also been associated with premature epiphyseal closure and may be associated with osteoporosis *(Udall and Greene, 2016)*.

#### Table 4 :

## The average intake of energy and different macronutrients of the studied autistic and healthy children

Nutrients	ASD (n = 20)	Control (n = 20)
	Macronutrients	
Energy (Kcal/d)	1998.70 ± 10.02 <sup>a</sup>	1925.11 ± 6.08 <sup>b</sup>
Carbohydrates (g/d)	274.82± 4.87 <sup>a</sup>	264.70± 5.99 <sup>b</sup>
Total fats (g/d)	78.62± 6.76 <sup>a</sup>	64.17± 6.67 <sup>b</sup>
Proteins (g/d)	74.95± 3.98 <sup>a</sup>	72.19± 4.97 <sup>a</sup>
Cholesterol (mg/d)	263.93 ± 2.07 <sup>a</sup>	216.65 ± 9.34 <sup>b</sup>
Fiber (g/d)	10.64 ± 1.09 <sup>b</sup>	15.09± 2.34 <sup>ª</sup>
	Vitamins	
Vit. A (mcg/d)	886.53 ± 11.04 <sup>a</sup>	799.06± 6.61 <sup>b</sup>
Vit. D (mcg/d)	2.99± 0.09 <sup>a</sup>	2.76± 0.91 <sup>a</sup>
Vit. E (mg/d)	8.34± 0.76 <sup>a</sup>	6,73± 1.04 <sup>b</sup>
Vit K (mcg/d)	104.23± 10.23 <sup>a</sup>	93.45 ± 6.33 <sup>b</sup>
Vit B12 (mcg/d)	4.81 ± 0.88 <sup>b</sup>	$5.43 \pm 0.56^{a}$
Riboflavin(mg/d)	1.64± 0.36 <sup>b</sup>	1.75 ± 0.44 <sup>a</sup>
Folic acid (mcg/d)	181.68 ± 3.05 <sup>b</sup>	194.84 ± 5.67 <sup>a</sup>
Niacin (mg/d)	28.09 ± 7.98 <sup>b</sup>	31.38± 2.44 <sup>ª</sup>
Vit. B6 (mg/d)	1.83± 0.43 <sup>a</sup>	1.88 ± 0.03 <sup>a</sup>
Panthothenic acid (mg/d)	$4.63 \pm 0.09^{a}$	$4.78 \pm 0.07^{a}$
Vit. C (mg/d)	32.21±2.03 <sup>b</sup>	81.49± 4.92 <sup>ª</sup>
	Minerals	
Calcium (mg/d)	783.23 ± 10.65 <sup>b</sup>	863.43 ± 10.32 <sup>a</sup>
Iron (mg/d)	9.92 ± 0.03 <sup>b</sup>	12.29 ± 1.03 <sup>a</sup>
Zinc (mg/d)	6.57 ± 1.02 <sup>b</sup>	8.98 ± 1.02 <sup>a</sup>
lodine (mcg/d)	77.43 ± 9.03 <sup>b</sup>	84.67 ± 7.88 <sup>a</sup>
Phosphorus (mg/d)	822.31 ± 3.85 <sup>b</sup>	894.36 ± 14.02 <sup>a</sup>
Fluoride (mcg/d)	186.13± 8.66 <sup>b</sup>	224.77 ± 11.03 <sup>a</sup>
Magnesium (mg/d)	314.89 ± 9.67 <sup>a</sup>	289.83± 18.06 <sup>b</sup>

Data are means  $\pm$  (SD). Values with different letters are significantly different. at P≤0.05

Frequency of food intake of studied autistic and healthy children Cases with autistic disorder had a significantly higher intake of cereals, potatoes and snacks than healthy controls. On the other hand, healthy controls had a significantly higher intake of fresh vegetables, fruits, meat, fish, egg and dairy foods. As expected, children with autism had poorer food variety scores compared to matched control. Overall, healthy children had a wider range of food choices than children with autism. Some children with autism appeared to be as flexible in their food choices as typical children, while others were much more limited and seemed to restrict their intake. This finding is similar to previously published data. *Emond et al. (2010)* determined that food variety was limited even prior to the diagnosis of autism in children as young as 15 months. *Bandiniet al. (2010)* found that autistic children had a more "limited food choice" compared to controls. Others have reported similar results *(Williams et al., 2015)*.

Frequency of food group intake of studied autistic children and healthy children				
E a d anom	Frequency (per week)			
Food group	ASD (n = 20)	Control (n = 20)		
Cereals and potatoes	5.0± 1.03 a	3.5± 0.53 b		
Fruit and vegetables	2.5± 0.88 b	7.5± 1.13 a		
Meat, fish and egg	2.0± 0.03 b	4.0± 0.54 a		
(calcium enriched) Dairy foods	2.0± 0.77 b	5.5± 0.32 a		
Snacks	7.5± 1.03 a	3.0± 1.02 b		

 Table 5

 Frequency of food group intake of studied autistic children and healthy children

Data are means ± (SD). Values with different letters are significantly different. at P≤0.05

#### Percent of children eating daily meals

Table 6 shows higher Percentage of control children who eat any of the three daily meals. 43.4 % control children versus 34.6 ASD for breakfast, 84.3 % control children versus 41.5 ASD and 22.4 % control children versus12.5 %ASD.

reitent of children eating daily means			
Meal habits	Frequency		
	ASD (n = 20) %	Control (n = 20) %	
Breakfast	34.65	93.4	
Lunch	41.54	84.34	
Dinner	12.5	22.45	

Table 6	
Percent of children eating daily meal	ls

#### Blood levels of vitamins in the studied autistic and healthy children

The table shows that Vita A, E and Vita K are higher in the ASD children than the control while other vitamins are lesser than the control. This reflect the amount and frequency of what they eat. This finding is comparable to that **of Hyman et al. (2018)**. However **Lindsay et al. (2006)** concluded that, in general, the mean intakes for macronutrients, vitamins and minerals exceeded the references ranges, Another study found that the majority of children with ASD did not in general meet references ranges of the vitamins (**Ho et al. 2017**).

Vitamins	ASD (n = 20)	Control (n = 20)	Reference range
Vit. A (plasma) µg/100 ml	70.3± 10.7 a	54.9± 12.88 b	39-71
Total Carotenes(beta carotene and other carotenes, in plasma) µg/100 ml	110±15.98 b	178±5.3 a	111-251
Vit B6 (as P5P in RBC)µg/l	7.9±1.6 b	15.2±5.3 a	8-21
Folic Acid (serum)µg/l	11.7 b±2.2	20.7±6.1 a	12-28
Vit B12(plasma) µg/l	399± 235 b	676±21.5 a	327-938
Vit C(plasma)mg/100 ml	0.57±0.01 b	1.33±0.46 a	0.75-1.85
Vit D3(25-hydroxy in plasma)µg/l	12.9±2.4 b	30.6±8.4 a	19-44
Total Vit E (serum)mg/100 ml	1.58±0.08 a	0.90±0.32 b	0.6-1.4
Vit K (plasma)ng/l	394± 15.8 a	295±18.9 b	129-530
Total Choline(RBC)mg/l	263± 10.4 b	310± 15.1 a	260-362

 Table (7)

 Blood levels of vitamins in the studied autistic and healthy children

Data are means ± (SD). Values with different letters are significantly different. at P≤0.05

#### The minerals in blood of the studied autistic and healthy children .

Table (8) presented the average levels of some minerals as measured in blood of the studied autistic and healthychildren. The autism children had high significantly level of Serum magnesium and Serum Sodium all other tested minerals were significantly higher in the control group than the autistic group. The present study showed that children with autistic disorder exhibited low intake of Ca compared with the healthy controls. Other studies have also found that children with autistic disorder have significantly lower amounts of blood Ca (*Meguid et al., 2015*). This is consistent with a previous study of the dietary patterns of children with ASD in Egypt. The low blood Ca level in autistic children confirmed a previous study that correlated the low Ca serum values in children with ASD with unhealthy teeth and nerve disease (*Meguid et al., 2015*).

The trace element Zn is crucial for cognitive development, healthy neurological function, and heavy metal detoxification (*Böckermanet al., 2015*). In the present study, a difference for Zn intake was observed among children with autistic disorder and healthy controls (table 4. Previous studies

similar to this study have shown that ASD children had low blood Zn level compared to healthy controls and children had neurological disorders (*Crăciunet al., 2016*).

Herndon et al. (2009) found a high prevalence of Fe deficiency in children with ASD. The present study showed that Fe intake and serum Fe level were significantly lower in children with autistic disorder compared to healthy controls. This may be due to associated food selectivity, which is commonly seen in ASD children (*Bilgiçet al., 20108*).

Significantly high Mg intake and high level of serum Mg was noted in the studied autistic children compared to healthy controls. These results agreed with (*Strambi et al., 2006*) who reported significantly high levels of Mg in the blood of ASD children (*Al-Farsi et al., 2013*).

		,	
Minerals	ASD (n = 20)	Control (n= 20)	Reference range
Calcium-Serum(total) mg/dl	5.6±0.5 b	9.6±0.45 a	9.25-9.9
Iron-Serum µg/dl	53± 3.4 b	98± 3.5 a	42-130
Serum Ferritin µg/l	23.1±2.2 b	46.9± 2.7 a	17-63
Magnesium-Serum mg/dl	11.95±0.14 a	8.03±0.15	8-16
Sodium-Serum mEq/l	0.38±0.02 a	0.30±0.01	0.15-0.30
Zinc-RBCaµg/g	5.2±1.21 b	8.9±1.4 a	6.8-10.8
Phosphorus-Serummg/dL	74.6± 5.5 b	79.6±3.5 a	73-83.5
Potassium-Serum mEq/L	124.1±8.3 b	194.2± 9.78 a	186-236

 Table (8)

 Blood levels of some minerals in the studied autistic and healthy children

Data are means ± (SD). Values with different letters are significantly different. at P≤0.05

#### The metabolic markers in the studied autistic and healthy children

Glutathione is the primary anti-oxidant in the body, the average levels of metabolic markers in the studied autistic and healthy children was summarized in table (9). Children with autism had significantly elevated oxidative stress, as indicated by increased GSSG/GSH ratio, and increased plasma nitrotyrosine. GSSG is reduced to GSH by glutathione reductase, which requires NADPH. NADPH levels were substantially higher in children with autism, which would explain why they also had a decreased GSH/GSSG ratio *[Geieret al., 2019]*. The higher level of total choline in the children with autism is interesting, and may suggest an impairment in conversion of choline to acetylcholine. The finding of decreased plasma ATP, NADH, and NADPH, but normal levels of their precursor (vitamin B3- niacin) may suggest an impairment in the formation of NADH from niacin. The clinical significance of decreased levels of ATP in the plasma is unclear, since most ATP is intracellular. Impaired transport of ATP throughout the body is suggested. ATP may be related to decreased muscle tone and decreased endurance commonly observed in children with autism. NADH is mainly involved in catabolic reactions (energy metabolism and mitochondrial function) whereas NADPH is involved in

anabolic reactions (antioxidation and reductive biosynthesis) [Belenkyet al., 2017]. Decreased plasma ATP and NADH may also relate to impaired mitochondrial function, which has been reported in some children with autism [Oliveira et al., 2015 and Correiaet al., 2016].

The average levels of metabolic markers in the studied autistic and healthy children				
Metabolic Markers	ASD (n = 20)	Control(n=20)	Reference range	
Reduced plasma glutathione (GSH) nmol/ml	3.23± 0.48	4.09±0.79	3.1-5.1	
Oxidized glutathione (GSSG) nmol/ml	0.247±0.13	0.362±0.10	0.22-0.52	
ATP (plasma) nmol/l	20.5± 4.2	15.5±4.8	13-21	
NADH (RBC) nmol/ml	23.3± 4.1	16.7± 4.3	16-25	
NADPH (RBC) nmol/ml	30.6±6.1	24.9±8.5	20-40	
CoQ10 (plasma) µg/ml	0.55± 0.15	0.60± 0.16	0.4-0.8	

 Table (9)

 The average levels of metabolic markers in the studied autistic and healthy children

#### Conclusion

Nutritional inadequacies were observed in children with autistic disorder and they also exhibited more abnormalities in meal pattern than healthy children .Therefore, the nutritional status of children with ASD should regularly be screened for nutrient adequacy to reduce these deficiencies by dietary means or by administering appropriate vitamin and mineral supplements.

## References

Bandini, L. G.; Anderson, S. E.; Curtin, C.; Cermak, S.; Evans, E. W. and Scampini, R. (2010): Food selectivity in children with autism spectrum disorders and typically developing children. Journal of Pediatrics, 157: 259–264.

Belenky, P.; Bogan, K.L. and Brenner, C.(2017): NAD+ metabolism in health and disease. Trends Biochem. Sci., 32 (1): 12-9.

Bennetto, L.; Kuschner, E. S.and Hyman, S. L. (2007):

Olfaction and taste processing in autism. Biological Psychiatry, 62: 1015–1021.

Böckerman, P.; Bryson, A.; Viinikainen, J.; Viikari, J. ;Lehtimäki, T. and Vuori, E. (2015): The serum copper/zinc ratio in childhood and educational attainment: a population-based study. J Public Health (Oxf).

#### Burtis CA, Ashwood ER (1999):

Tietz Textbook of Clinical Chemistry. Philadelphia: W.B. Saunders Company, 3

#### Correia, C.; Coutinho, A.M.; Diogo, L. and Grazina, M.(2016):

Brief report: High frequency of biochemical markers for mitochondrial dysfunction in autism: no association with the mitochondrial aspartate/glutamate carrier SLC25A12 gene. J. Autism Dev. Disord., 36 (8): 1137-40.

Crăciun, E.C.; Bjørklund, G.; Tinkov, A.A.; Urbina, M.A.; Skalny, A.V.; Rad, F. and Dronca, E. (2016):

Evaluation of whole blood zinc and copper levels in children with autism spectrum disorder. Metab. Brain Dis., 31:887–890.

#### Emond, A.; Emmett, P.; Steer, C. and Golding, J. (2015):

Feeding symptoms, dietary patterns, and growth in young children with autism spectrum disorders. Pediatrics, 126: e337–e342.

#### FAO/WHO (2002) :

Human vitamin and mineral requirements: report of a joint FAO/WHO expert consultation Bangkok, Thailand. Food and Agriculture Organization of the United Nations, Rome.

#### Geier, D.A.; Kern, J.K.; Garver, C.R.; Adams, J.B. and Audhya, T. (2009):

A prospective study of transsulfuration biomarkers in autistic disorders. Neurochem. Res., 34 (2): 386-93.

#### Gerrior, S.,;Bente, L. and Hiza, H. (2014):

*Nutrient Content of the U.S. Food Supply, 1909-2000.* (Home Economics Research Report No. 56). US Department of Agriculture, Center for Nutrition Policy and Promotion.

Gorman, M.W.; Feigl, E.O. and Buffington, C.W.(2007):

Human plasma ATP concentration. Clin. Chem., 53 (2): 318-25.

Hediger, M. L.; England, L. J.; Molloy, C. A. ;Yu, K. F., Manning-Courtney, P., and Mills, J. L. (2008):

Reduced bone cortical thickness in boys with autism or autism spectrum disorder. *Journal of Autism and Developmental Disability, 38*: 848–856.

Herndon, A. C.; DiGuiseppi, C.; Johnson, S.; Leiferman, J. and Reynolds, A. (2019):

Does nutritional intake differ between children with autism spectrum disorders and children with typical development? Journal of Autism and Developmental Disorders, 39: 212–222.

#### Ho, H. H.; Eaves, L. C. and Peabody, D. (2017):

Nutrient intake and obesity in children with autism. *Focus on Autism and Other Developmental Disabilities*, *12*: 187–193.

Hyman, S. L.; Stewart, P. A.; Schmidt, B.; Cain, U.; Lemcke, N. and Foley, J. T.(2018): Nutrient intake from food in children with autism. *Pediatrics*, *130*(Suppl 2): S145–S153.

#### Institute of Medicine (2019) :

Dietary reference intakes: Applications in dietary assessment. Washington, DC: National Academy Press.

Johnson, C. R.; Handen, B. L.; Mayer-Costa, M., and Sacco, K. (2008):

Eating habits and dietary status in young children with autism. *Journal of Developmental and Physical Disabilities*, 20: 437–448.

#### Klemm, A.; Klemm, A.and Steiner, T. (1997):

Determination, purification, and characterization of alpha-NADH and alpha-NADPH. Methods Enzymol., 280: 171-86.

#### Laud, R. B.; Girolami, P. A., Boscoe, J. H., andGulotta, C. S. (2009) .:

Treatment outcomes for severe feeding problems in children with autism spectrum disorder. *Behavior Modification*, 33:520–536.

Ledford, J. R., andGast, D. L. (2006):

Feeding problems in children with autism spectrum disorders: A review. Focus on Autism and Other Developmental Disabilities, 21: 153–166.

#### Lindsay, R. L.; Arnold, L. E.; Aman, M. G.; Vitiello, B.; Posey, D. J. and McDougle, C. J. (2016):

Dietary status and impact of risperidone on nutritional balance in children with autism: a pilot study. *Journal of Intellectual and Developmental Disability*, 31: 204–209.

#### Meguid, N.A.; Hashish, A.F. and Anwar, M. (2010):

Reduced serum levels of 25-hydroxy and 1,25-dihydroxy vitamin D in Egyptian children with autism. J. Altern. Complement Med., 16:641–645.

#### Michelet, F.; Gueguen, R.; Leroy, P.; Wellman, M.; Nicolas, A. and Siest ,G. (1995): Blood and plasma glutathione measured in healthy subjects by HPLC: relation to sex, aging,

biological variables, and life habits. Clin.Chem. ,41 (10): 1509-17.

#### Oliveira, G.; Diogo, L.; Grazina, M. and Garcia, P. (2015):

Mitochondrial dysfunction in autism spectrum disorders: a population-based study. Dev. Med. Child Neurol., 47 (3): 185-9.O'Byrne SM, Blaner WS. Retinol and retinyl esters: biochemistry and physiology. J Lipid Res. 2013;54:1731–43.

#### Riten, D. J. and Missaro, T. (2020):

Perspectives on the nutritional ecology of children with Autism. Journal of Autism and Developmental Disability, 16: 133–143.

#### Schopler, E.; Reichler, R.J. and Rochen-Renner, B. (1998):

The childhood autism rating scale (CARS). Western Psychological Services, Los Angeles

Siu, A.L.; Bibbins-Domingo, K.; Grossman, D.C.; Baumann, L.C.; Davidson, K.W.; Ebell, M.; García, F.A. and Gillman, M. (2016):

Screening for autism Spectrum disorder in young children: US preventive services task force recommendation statement. JAMA, 315:691–696.

#### Snedecor, C.W. and Cochran, W.C.(1982):

Statistical methods (7th ed), The Stae University Press American, Iowa .

#### SPSS(2000):

Statistical package for the social sciences, version 14.0. Chicago, IL: SPSS Inc.

Strambi, M.; Longini, M.; Hayek, J. Berni, S.; Macucci, F. and Scalacci E. (2006) :

Magnesium profile in autism. Biol. Trace Elem. Res., 109:97–104.

#### Udall, J. N.; Jr., F. and Greene, H. L. (2016):

Vitamin update. *Pediatrics in* Review, 13, 185–194.

#### WHO, World Health Organization (2008):

Training course on child growth assessment, WHO child growth standards. B: measuring a child's growth. World Health Organization, Geneva.

#### WHO, World Health Organization (2009):

WHO Anthro for personal computers, version 3.01: Software for assessing growth and development of the world's children. World Health Organization, Geneva.

#### Williams, K.; Gibbins, B. G. and Schreck, K. A. (2015):

Comparing selective eaters with and without developmental disabilities. *Journal of Developmental and Physical Disabilities*, 17:299–309.

## Zimmer, M. H.; Hart, L. C.; Manning-Courtney, P.; Murray, D. S.;Bing, N. M. and Summer, S. (2012):

Food variety as a predictor of nutritional status among children with autism. Journal of Autism and Developmental Disorders, 42: 549–556.

## بعض المؤشرات التغذوية والأيضية للأطفال المصابين بالتوحد

هبه سعيد عبد الحليم وهنادي جابر شيحه و ايمان السيد حبيب

قسم التغذيه الاكلينييه , المعهد القومي للتغذيه

## الملخص العربي

التوحد هو اضطراب عصبي في السلوك وإعاقة للتواصل الاجتماعي. تؤثر اضطرابات التوحد (ASD) بشكل أكبر على نسبة الأطفال الذين لايظهرون في السلوك قبل سن ثلاث سنوات. تلعب الوراثة دورًا رئيسيًا في مسببات التوحد،جنبًا إلى جنب مع العوامل البيئية المبكرة للنمو. أشارت الدراسات الوبائية إلى أن العوامل البيئية تركز على التأثيرات الفسيولوجية والسلوكية لتغيير النظام الغذائي ولكنها لم تدرس تأثير حمية الاستبعاد على المدخول الغذائي. هدفت الدراسة الحالية إلى مقارنة النظم الغذائية والعادات للأطفال الذين يبدو أنهم يتمتعون بصحة جيدة ، مقارنة بالأطفال المصابين باضطراب التوحد. تضمنت قياسات الدراسة: القياسات البشرية،القيمة الغذائية لنظامهم الغذائي،المؤشرات الحيوية لحالة الفيتامينات والمعادن في البلازما،الجلوتاثيون في البلازما ، والمؤشرات الحيوية لإنتاج الطاقة. تمت الدراسه على 20 طفلًا مصابًا باضطراب التوحد و 20 طفلًا ذكورًا يتمتعون بصحة جيدة (8-10 سنوات) من محافظة المنوفية. أظهرت النتائج أن الوزن ومؤشر كتلة الجسم كانا مرتفعين بشكل معنوي عند الأطفال المصابين باضطراب التوحد مقارنة بالضوابط الأصحاء (p 0.05). الطاقة، الكربوهيدرات ، الدهون الكلية ، الكوليسترول ، فيتامينA ،فيتامين BوفيتامينK. كان المدخول مرتفعًا بشكل ملحوظ فيا لأطفال المصابين بالتوحد مقارنة بالضوابط الصحية. كان لدى الأطفال المصابين بالتوحد مستوى مرتفع في الدم من فيتامين. أ،إجمالي فيتامين هـ ، وفيتامين ك بينما كانت المجموعة الضابطة ذات مستوى مرتفع بشكل ملحوظ من إجمالي الكاروتين (بيتا كاروتين والكاروتينات الأخرى في الدم) ،فيتامينب 6 ،حمض الفوليك ، فيتامين ب 12 ،فيتامين ج،والكولين الكلي. يعاني الأطفال المصابون بالتوحد من ارتفاع ملحوظ في الإجهاد التأكسدي ، كما يتضح من زيادة نسبةGSSG / GSH (الجلوتاثيون هو مضاد الأكسدة الأساسي في الجسم) ،يجب فحص الحالة التغذوية للأطفال المصابين بالتوحد بانتظام للتأكد من كفاية العناصر الغذائية لتقليل أوجه النقص هذه عن طريق الوسائل الغذائية أو عن طريق إعطاء مكملات الفيتامينات والمعادن المناسبة. الكلمات المفتاحية : الأطفال،التوحد ، معامل كتله الجسم،القياسات البشرية