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Abstract:

Autism is a neuro developmental condition of unknown etiology which is usually diagnosed in the first 3 years of life. Several studies have linked with reduced intake of some nutrients with autism and autism spectrum disorders.

To identify nutritional risk factors that predispose to autism among preschool and school children living in Al-Madinah Al-Monawarah.

Thirty children with autism/autism spectrum disorders (AU/ASD), 2-12 years old and thirty six matched control children were compared as regards BMI and food intake, using 24 hour recall and food frequency questionnaire.

Children with AU/ASD consumed similar amount of energy, protein and many other nutrients, many of which were below the international recommendations for children at the same age group, both consumed significantly less omega-3 and iron than the control group.

Children with ASD like the children in KSA consumed less than the recommended amount of certain nutrients from food.

Autistic children suffer from more reduced intake of omeg-3 and iron, with limited intake of many food varieties could be linked to autism in susceptible children.

Key word: Autism, neuro, children, nutrients, food frequency, recommended amount.

Introduction:

Autism is a neuro developmental condition which is usually diagnosed in the first 3 years of life. The essential features of autistic disorder are the presence of markedly abnormal or impaired development in social interaction and communication and a markedly restricted repertoire of activity and interests. Manifestations of the disorder vary greatly depending on the developmental level and chronological age of the individual **(DMS V. DC., 2013).**

Genetic factors seem to be important in the etiology of autism. However, genetics alone cannot explain the increase in autism cases (87.0%) between 1990 -2000. This leaves nutrients and toxins interacting with these genetic weaknesses as the most likely candidates as causal factors for Autism. Several nutrients deficiencies have been incriminated of causing autism including omega -3 fatty acids, vitamin D, folic acid and vitamin B_{12} **(Weber and Newmark, 2007; Bertoglio, 2010; Altbäcker 2014 and Patrick & Ames 2014).**

The important historical observation about autism it was unknown in ancient culture. It was first described in 1943. Prevalence estimates had increased in the last 2 decades and range from 0.7 per 10, 000 population to 72.6 per 10, 000 with a mean of 20.6 per 10, 000. The mean male: female ratio is 4.2:1 **(Cristina, 2013).**

In the Arab world, the prevalence ranges from 1.4 cases per 10,000 children in Oman, 4.3 per 10, 000 Bahraini population, to 29 per 10,000 children in the United Arab Emirates. While these rates are lower than those of the developed world, which are 39 per 10,000 for autism and 77 per 10,000 for all forms of ASD, it does not necessarily mean the condition is less prevalent in the Arab world. In Saudi Arabia, autism affects six out of every 1000 individuals (60/10. 000) **(Al-Farsi, 2011; Al-Ansari and Ahmed, 2013; Eapen, 2011; Fido and Al Saad, 2013; Autism and Saudi Arabia, 3013).**

Research hypothesis:

We hypothesize that insufficiency of some nutrients in genetically predisposed children may be a risk factor in the etiology of autism spectrum disorders.

Objective:

To identify nutritional risk factors that predispose to autism among preschool and school children living in Al-Madinah Al-Manawarah.

Study design: Case-control.

The study was conducted at Al-Amal psychiatric hospital, Al-Madinah Al-Monawarah.

The study included 30 children diagnosed with autism or ASD, attending the pediatric psychiatry outpatient clinic and autism day care center at Al-Amal psychiatric hospital, during the period from February to April 2014.

The diagnosis of autism or autism spectrum disorders was done by the pediatric psychiatry consultant based on the diagnostic criteria of DMS V. DC (2013)

All attending children during the working day who fit the inclusion criteria were enrolled in the study until the study sample was completed.

Inclusion criteria:

1 - Parents consenting the research.

2- Males and females of age range 2-10 years.

3- Diagnosis of Autism or ASD

Exclusion criteria:

1. Autism associated with genetic syndromes.

2. Patients following special diet as gluten & casein free diet.

3. Known food allergy leading to avoidance of certain food.

4. Mother or primary care taker not available to give detailed diet history.

Thirty six age, sex, and socioeconomic matching children served as the control group, were enrolled from the University and Nabaa AL-Maref Nursery for the young age group (2 -6 years old).

There was difficulty to access male primary schools for the older age group, (7 -10 years old), so all control of that age was selected from family members of the researchers.

Mean age of autism group was 58.66 ±19.87 months (29-108). Mean age of the control group was 59.38±20.11 months (24-108). There was no significant difference between both groups (P=.884)

Methods:

Mothers were interviewed regarding some relevant information as detailed history of early feeding practices, sun exposure and exposure to some environmental toxins.

Dietary study:

Before taking diet history, all mothers of autistic children were asked about food habits and dietary intake in the period before diagnosis of autism. All mothers reported that children followed the same food pattern before the onset of the disease. Eleven mother (36.6%), reported trying to shift to more healthy food after diagnosis but all children resisted any changes in diet habits so these results represent typical pattern of food intake.

Dietary history using 24 hour recall:

In this method the mothers were asked to recall the exact foods and beverages intake during the 24 hour period. As the autism is associated with behaviors that can impacts food intake. Mothers were asked in details about the usual dietary intake of the family with special focus on the child eating pattern before the onset of the disease as well as his/her current diet.

Quantities of foods and beverages consumed were estimated in household measures. The conversion of household measures to grams were done manually. Food analysis was done using the software Arab Food Analysis Programme (Version 1, Arab nutrition center).

Food frequency questionnaire:

The target food proposed to be associated with reduction or increase risk of autism was grouped into categories and the frequency of intake of those food items were assessed in details.

Anthropometry:

Weight, standing height: were taken from each subject using the standard techniques.

Statistical analysis:

Descriptive analysis (mean, standard deviation and Student's t test) were done using (SPSS17). The comparative outcomes of anthropometry, clinical, & dietary data were analyzed by using the Chi-square test for categorizing data. The minimal level of significance will set at $P < 0.05$.

Ethical issues:

The research was explained to parents in simple language and all data were taken from mothers. All data were kept confidential.

Results and Discussion :

Sun **exposure**:

Table (1) demonstrate that there was significant difference in sun exposure between both groups.

Table 1: Sun exposure among children of both group

	Subjects	**Frequency of sun exposure**				**P value**
		Daily	Weekly	Monthly	Never	
Mothers	Autism	5 (16.7%)	0 (0.0%)	21(70%)	4(13.3%)	.3
	Control	8(22.2%)	3(8.3)	20(55.6%)	5(13.9%)	
First 2 years	Autism	11(36.7%)	4(13.3%)	3(10%)	12(40%)	.03*
	Control	7(19.4%)	16(44.4%)	5(13.9%)	8(22.2%)	
Current exposure	Autism	8(26.7%)	5(16.7%)	1(3.3%)	16(53.3%)	.02*
	Control	15(41.7%)	9(25%)	5(13.9%)	7(19.4%)	

* Significant difference

BMI:

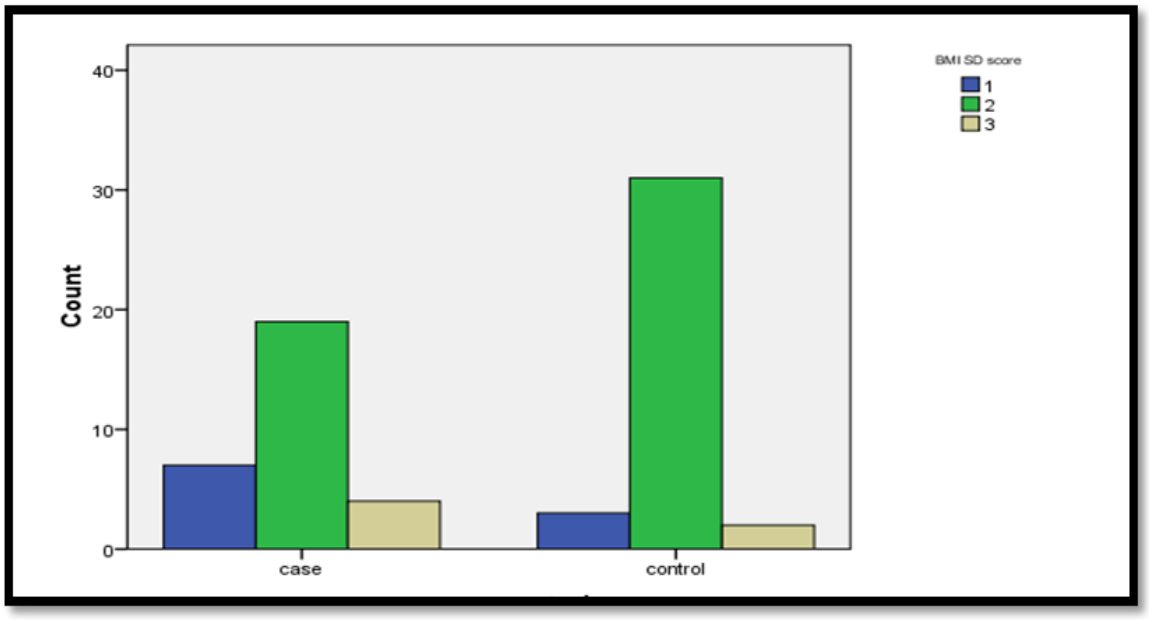

Fig. (1): Distribution of BMI categories between both groups

1= Thinness, 2= Normal, 3= Obesity

Chi-Square =4.64 P=.098

Assessment of dietary intake using 24 hour recall:

There was no significant difference in mean energy, carbohydrates, protein and total fat consumption between both groups. The autism group had significantly lower omega-3 intake than the control group (mean level 0.029±0.003 & 0.268±0.049 g/day respectively, P=.01).

Minerals:

There was highly significant difference in iron consumption between both groups (6.66±0.400&10.23±0.601 mg/day respectively). While there was no significant difference in calcium consumption between both groups with both groups had consumption much below the recommended levels.

Dietary intake of vitamins:

There was no significantly difference in mean consumption of both water soluble and fat soluble vitamins between both groups. As regards vitamin D consumption, there was a huge problem in dietary intake with almost all children from both groups had diet containing less than 50% of the recommended amounts.

Table (2): Mean daily dietary intake among normal children & children with autism

	Autism (n=30)	Control (n=36)	P
Energy (Kcal/d)	1330±54.10	1576±46.30	.051*
Protein (g/d)	38±2.00	48±2.50	.091
Omega-3(g/d)	0.029±0.003	0.268±0.049	.011*
Total Fat (g/d)	46±2.40	54±2.10	.159
Carbohydrates (g/d)	199±8.70	234±6.70	.076
Iron mg/day	6.66±0.400	10.23±0.601	.007*
Calcium mg/day	332±5.38	331±5.60	.797
Folic acid (µg/d)	173±1.28	203±9.79	.440
vitamin B12 (µg/d)	0.45±2.27%	0.55±1.9%	.365
vitamin D(mcg)	1.31±0.019	1.60±0.060	.515

* Significant difference

Food frequency:

Dairy products & eggs:

Milk and dairy products are consumed daily by significantly larger proportion of control children compared to autistic children. One third and 20% of autistic children reported no milk or dairy product consumption respectively, in comparison to 5.6% and 11.1% of the control group.

One third autistic children reported no egg consumption respectively, in comparison to 0.0% of the control group. Table (3) clarifies results of food frequency questionnaire.

Vegetables and fruits:

There was no significant difference in consumption of fruits (dried or fresh) and vegetables (fresh and cooked) between both groups. Less than half of all the studied children consume fresh fruits on daily bases.

Consumption of fresh and cooked vegetables followed this low pattern, in which only four children among both groups consumed cooked vegetables on daily bases.

Table (3): Statistical comparison between the autistic and the control group regarding the frequency of food item consumption .

Food items	Subjects	Frequency of intake				P value
		Daily	Weekly	Monthly	Never	
Milk	Autism	17 (56.7%)	3 (10.0%)	0(0%)	10 (33.3%)	.011*
	Control	22(61.1%)	11(30.6%)	1(2.8%)	2(5.6%)	
Dairy products	Autism	15 (50.0%)	9 (30.0%)	0(0%)	6 (20%)	.269
	Control	25(69.4%)	7(19.4%)	0(0)%	4(11.1%)	
Eggs	Autism	7(23.3%)	11(36.7%)	2(6.7%)	10(33.3%)	.001*
	Control	7(19.4%)	28(77.8%)	1(2.8%)	0(0%)	
Fresh fruits	Autism	13(43.3%)	13(43.3%)	1 (3.3%)	3 (10.0%)	.542
	Control	17(47.2%)	15(41.7%)	3(8.3%)	1 (2.8%)	
Cooked vegetables	Autism	4(13.3%)	9(30%)	3(10%)	14(46.7%)	.506
	Control	4(11.1%)	15(41.7%)	6(16.7%)	11(30.6%)	
Fresh vegetables	Autism	6(20%)	11(36.7%)	3(10%)	10(33.3%)	.082
	Control	12(33.3%)	17(47.2%)	4(11.1%)	3(8.3%)	
Tuna	Autism	0 (0%)	7(23.33%)	5(16.7%)	18(60%)	.059*
	Control	2(5.56%)	17(47.2%)	6(16.7)	11(30.6%)	
other fish types	Autism	0(0%)	5(16.7%)	9(30%)	16(53.3%)	.016*
	Control	0(0%)	11(30.6%)	18(50%)	7(19.4%)	
Liver	Autism	0(0%)	1(3.3%)	5(16.7)	24(80%)	.027*
	Control	0(0%)	2(5.6%)	18(50%)	16(44.4%)	
Meat Include (chicken)	Autism	10(33.3%)	11(36.7%)	0(0%)	9(30%)	.017*
	Control	18(50%)	16(44.4%)	1(2.8%)	1(2.8%)	
Butter	Autism	4(13.3%)	4(13.3%)	3(10%)	19(63.3%)	.003*
	Control	4(11.1%)	10(27.7%)	14(38.8%)	8(22.2%)	
Olive oil	Autism	5(16.6%)	4(13.3%)	3(10%)	18(60%)	.020*
	Control	8(22.2%)	11(30.5%)	9(25%)	8(22.2%)	
sweetly Juice	Autism	21 (70.0%)	5 (16.7%)	1 (3.3%)	3 (10.0%)	.164
	Control	29(80.5%)	7(19.4%)	0(0.0%)	0(0.0%)	
soft drink	Autism	16 (53.3%)	2(6.7%)	10 (33.3%)	2(6.7%)	.140
	Control	3(8.3%)	13(36.1%)	9(25%)	11(30.5%)	
fast-food	Autism	1(3.3%)	9(30.0%)	6(20.0%)	14(46.6%)	.010*
	Control	3(8.3%)	13(36.1%)	16(44.4%)	4(11.1%)	
Sweets	Autism	13(43.3%)	9(30.0%)	2(6.7%)	6(20.0%)	.094
	Control	23(63.8%)	11(30.5%)	1(2.7%)	1(2.7%)	
Processed meat	Autism	0(0.0%)	1(3.3%)	1(3.3%)	28(93.3%)	.082
	Control	0(0.0%)	2(5.5%)	2(5.5%)	32(88.8%)	

* Significant difference

Food choices among autistic patients:

Table (4) summarizes the number of children refusing certain food items from both groups. As shown in the table higher numbers of autistic children exclude many food items from their diet.

Table (4): Proportion of children excluding food items from their diet

	Autism	Control
Milk	10 (33.3%)	2(5.6%)
Other dairy products	6 (20%)	4(11.1%)
Eggs	10(33.3%)	0(0%)
Fresh fruit	3 (10.0%)	1 (2.8%)
Dried fruit	21(70%)	25(69.4%)
Cooked vegetables	14(46.7%)	11(30.6%)
Fresh vegetables	10 (33.3%)	3(8.3%)
Tuna	18 (60%)	11(30.6%)
Salmon	27 (90%)	28(77.8%)
other fish types	16(53.3%)	7(19.4%)
Ghee	21(70%)	15(41.6%)
Butter	19(63.3%)	8(22.2%)
olive oil	18(60%)	8(22.2%)
Sweetly Juice	3 (10.0%)	0(0.0%)
Soft drink	2(6.7%)	11(30.5%)
French-fries	3(10.0%)	2(5.5%)
Fast-food	14(46.6%)	4(11.1%)
Sweets	6 (20.0%)	1(2.7%)
Processed meat	28 (93.3%)	32(88.8%)

Parents of children with ASDs often report that their children are highly selective eaters, with very restricted repertoires of food acceptance that may be limited to as few as five foods. Picky eating, also referred to as food selectivity, is a significant problem because it may be associated with inadequate nutrition as a result of the restricted diet **(Dovey *et al.*, 2008).**

We found that among the studied autistic children, his diet behavior started long before diagnosis. Food selectivity was shown by the high prevalence of 'never food' among children with autism compared to the control. This reflects refusal of large varieties of food groups exposing those children to poor nutrition. Although we found no significant difference in BMI between groups, overweight and thinness has higher

prevalence among the autistic children compared to the control. Obesity and overweight were reported among autistic children in other studies **(Bicer and Alsaffar, 2013).**

Food selectivity refers to picky eating, frequent food refusals, limited repertoires of foods, but also includes excessive intake of a few foods, and selective intake of certain food categories such as carbohydrates (**Cermak *et al.*, 2010**).The presence of obesity cannot exclude nutritional deficiencies affecting mainly the micronutrients. Interestingly, vitamin and mineral deficiency may occur in both under nutrition and over nutrition. For example, the globalized high-energy and low-nutrient density Western dietary patterns and trends, typified by snacking, breakfast skipping, fast foods, soft drinks and convenience foods, are nutritionally unbalanced, and intake of micronutrients in fails to meet recommended daily allowance values **(Cetin *et al.*, 2010).**

Although only minority of the studied children were underweight, yet we found that the intake of many micronutrients in both groups is below the international recommendations for healthy life and especially for healthy brain and bones

A recent study indicates that the dietary intake of selected nutrients by an apparently healthy Saudi population is imbalanced **(Al-Daghri, 2012).**

Consistent with previous findings on food selectivity in children with AU/ASD, we found that they consumed more servings of sweetened non-dairy beverages and soft drinks and significantly fewer servings of milk, eggs, tuna, fish, meat, and liver than did the control children **(Hertz-Picciotto *et al.*, 2010 and El-Ansary *et al.*, 2011)**.

The majority of the previous food is loaded with nutrients. Omega-3 polyunsaturated fatty acids (PUFAs) have been found to be a basic component of normal neural development and maintenance of neural health **(Wainwright, 2002).** We found significant lower omega3 consumption (almost 10 times less) among the autistic children compared to the control. Omega- 3 can be found in fish and our results indicate that autistic children had significantly low fish consumption compared to control children.

The autistic children in this study consumed milk and eggs in significantly lower levels than the control group. The apparent increase in the prevalence of autism over the last 20 years corresponds with increasing medical advice to avoid the sun, advice that has probably lowered vitamin D levels and would theoretically greatly lower activated vitamin D (Calcitriol) levels in developing brains **(Cannell, 2008).**

In our study we demonstrated very low dietary vitamin D consumption among all the studied children from both groups. The situation of vitamin D in autistic children may be more compromised by the significantly lower sun exposure when compared to the control group.

The autistic children had significantly lower iron consumption. This may be related to significantly lower animal meat and liver compared to control children. Evidence suggests that brain iron deficiency at any time in life may disrupt metabolic processes and subsequently change cognitive and behavioral functioning. Nonhematologic manifestations of iron deficiency include decreased cognitive performance, and behavioral disturbances **(Beard and Connor 2008).**

There is strong evidence that iron deficiency anemia is associated with poorer performance on developmental ratings in infants and with lower scores on cognitive function tests and educational achievement tests in children **(Grantham-McGregor S, Ani 2001 and Bruner *et al.*, 1996).**

Conclusions:

This study revealed that children with autism suffer from many nutrient deficiencies, some of which may be a risk factor in genetically susceptible children. Supplementation may be the key to improving brain impairment in those children.

The pandemic of vitamin D deficiency affects Saudi children and needs careful diagnosis and management in order to lessen the impact of this vitamin deficiency on the health of those children. Other nutrients deficiencies like folic acid, vitamin B12 and calcium are affected also

Recommendations:

Professional dietetic consultation should be included in the health team who manage children with autism. Mothers of autistic children

should be educated about the importance of proper nutrition and nutrients needed for behavior and brain functions.

- Nutrition education and counseling regarding child nutrition should be established, it is much better to be included in an already going successful programs like the compulsory program of premarital examination, prenatal visits and vaccination.
- Vitamin D campaign and social marketing of its impact in prevention of many diseases which are common in KSA.

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تقييم العوامل الغذائية المساهمة في ظهور التوحد بين الأطفال السعوديين في المدينة المنورة

التوحد هو حالة من التطور العصبي ناتجة عن مسببات غير معروفة والتي عادة ما يتم تشخيصها في السنوات الثلاث الأولى من العمر. وقد ربطت عدة دراسات سابقه بين انخفاض تناول بعض العناصر الغذائية والتوحد وأمراض واضرابات التوحد.

الاهداف:

التعرف على عوامل الخطوره الغذائيه والتي يمكن ان تساهم في ظهور التوحد بين أطفال عمر ما قبل المدرسة وعمر المدرسة الذين يعيشون في المدينة المنورة.

طريقة العمل:

تمت مقارنة ثلاثة وثلاثين طفلا يعانون من اضطرابات امراض التوحد / او المصابين بالتوحد، في عمر ٢-١٢ سنة. و ستة وثلاثين من الأطفال الاصحاء في نفس العمر كمجموعه ضابطه من حيث مؤشر كتلة الجسم وتناول الطعام، وذلك باستخدام استبيان استرجاع المتناول خلال ٢٤ ساعه السابقه والاستبيان الخاص بالتاريخ الغذائي للطفل.

النتائج المتحصل عليها:

اظهرت الدراسة ان الأطفال الذين يعانون من التوحد او اضرابات مرض التوحد قد استهلكوا كمية مماثلة من الطاقة والبروتين والعديد من العناصر الغذائية الأخرى. وكثير منها أقل من التوصيات الدولية للأطفال في تلك الفئة العمرية، وكلاهما استهلكوا كميات أقل بكثير في عنصري الأوميغا- ٣ والحديد من المجموعة الضابطة.

الخلاصه:

الأطفال الذين يعانون من اضرابات مرض التوحد في المملكة العربية السعودية تستهلك أقل من الكمية الموصى بها من بعض العناصر الغذائية.

كما انهم يعانون أكثر من انخفاض تناول أوميغ- ٣ والحديد، جنبا إلى جنب مع انخفاض المتناول من العديد من المواد الغذائية الاخرى مما يعرضهم اكثر لظهور التوحد.