

Comparison of dietary macro and micronutrient intake with physical activity levels among children with and without autism: a case-control study

Jalal Moludi^{1,2}, Behzad Ebrahimi³, Vahid Maleki², Somaiyeh Saiedi², Arash Tandoroost², Hamed Jafari-Vayghyan⁴, Shahab Alizadeh⁵, Kurosh Djafarian⁵

¹Nutrition Research Center, faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran. ²Student Research Committee, Faculty of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran; ³Department of Food Science and Technology, Maragheh University of Medical Science, Maragheh, Iran; ⁴School of Health, Arak University of Medical Sciences, Arak, Iran; ⁵Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics, Tehran University of Medical Sciences, Tehran, Iran - E-mail: kdjafarrin@yahoo.com

Summary. *Background:* Physical activity is an important part of healthy lifestyle especially for autistic children. A few studies have previously compared the differences of diet intake and physical activity patterns in autistic and healthy children. This study was aimed to compare the macro- and micronutrient intake and physical activity patterns between children with and without autism. *Materials and Methods:* The present case-control study was conducted on 59 boys aged 6 to 13 years with autism and healthy children. Dietary intake of subjects was measured by Food Frequency Questionnaire (FFQ). The physical activity level was recorded for seven days using an ActiGraph accelerometer which categorized by the time of each participant spent, in sedentary, moderate and vigorous activity. *Results:* The findings revealed that there were significant differences in intake of many dietary factors including energy ($p < 0.05$), carbohydrate ($p < 0.05$), sugar ($p < 0.05$), fructose ($p < 0.01$), vitamin D ($p < 0.05$), Vitamin C ($p < 0.01$), Calcium ($p < 0.01$), Iron ($p < 0.05$), Magnesium ($p < 0.05$) and Manganese ($p < 0.05$) between autistic and healthy children. Furthermore, sedentary and moderate activity levels were significantly higher in children with autism compared with healthy children ($p < 0.05$). Percent calories from fat was positively associated with heavy physical activity ($r = 0.258$, $p < 0.05$). multivariate linear regression analysis showed that after control for change in BMI and dietary energy intake the calorie from fat, vitamin C and caffeine were negatively associated with physical activity level ($r = -0.571$, $p < 0.05$ Vs. $r = -0.573$, $p < 0.05$ Vs. $r = -0.371$, $p < 0.01$, respectively). *Conclusion:* It is concluded that there is a significant difference in food intake and physical activity levels in children with autism compared with healthy children. The potential role of diet especially calorie from fat, vitamin C, and caffeine should be considered to have applicable physical activity recommendations for children with ASD.

Key words: actigraph, autism, children, dietary intakes, micronutrient, physical activity

Abbreviations

ASD: Autism spectrum disorders
FFQ: Food frequency questionnaire
BMI: Body mass index
CPM: Count per minute

Introduction

Autism spectrum disorders (ASD) is a group of heterogeneous neurodevelopmental disabilities characterized by impaired emotional functioning, social and behavioral interaction that manifest during child-

hood (1, 2). Worldwide, the prevalence of this disability increasing annually which has become a relatively common neurodevelopmental disorder (3). Increased risk of being overweight/obese is one of the problems affecting the children with ASD (4, 5). It is well established that the type of diet, physical inactivity and side effects of antipsychotic medications that these children used may contribute to more body weight gain than healthy children (6, 7).

In addition to obesity, recent studies have shown that some of the associated behaviors and symptoms of ASD are related to dietary intake (8, 9). In children with ASD limited diets due to the food selectivity, dietary habits, chewing problems, family food choices, aberrant eating, gastrointestinal symptoms and mealtime behavior may affect dietary intake (10, 11). Therefore, we accomplished that in comparison to healthy children, nutritional status of children with ASD may be endangered due to the insufficient intake of vitamins and minerals. However, unlike the studies investigating the dietary intake of children with ASD, there are limited numbers of studies have compared them to age-matched healthy children (12-14).

The social and behavioral impairments experienced by these children appear to make participation in physical activity more difficult (15). There are still some methodological problems among studies measuring physical activity levels. Children with ASD have difficulties in completing self-report questionnaires and completing them by parents is not an accurate procedure. In addition, these questionnaires cannot use to monitor physical activity behavior (16). The lack of an appropriate method to record exercise activity in individuals with ASD causes impossibility to compare them with healthy children in accurate way (17). Nevertheless, ActiGraph activity monitor which can collect data such as body movements over extended periods of time may be a useful and more user-friendly method versus other methods to record exercise activity especially for children with autism (18).

There are relatively rare studies regarding physical activity and dietary intake in children with ASD. Therefore, this case- control study firstly aimed to investigate macro- and micronutrients intake and physical activity levels among children with and without ASD, Secondly, to determine the impact of macro- and micronutrients

intake on the physical activity levels of these subjects. The interaction of dietary intake and physical activity levels on body mass index was also assessed.

Materials and methods

Participants

A group of 59 boys (aged 6 to 13 years), including 30 autistic subjects and 29 healthy ones were selected by the cluster sampling method from two autistic schools, and four healthy children's schools located in Tehran, Iran from December to March 2014. Subject with autism who participated in the study diagnosed according to the diagnostic and statistical Manual of Mental Disorders (19). Children who have mental retardation and severe behavior problems were excluded. The study was ethically approved by the ethics committee of Tehran University of Medical Sciences, Tehran, Iran (Reference no.: tums 91022717958).

Anthropometric measurements

All participants (n=59) were weighed and measured in light clothing without shoes using a digital scale (Seca Hamburg, Germany) with accuracy nearest to 0.05 kg, and by Seca stadiometer, with accuracy about 0.1 cm. The body mass index (BMI) was calculated as the weight (kg) divided by the square of the height (m).

Physical activity determination

Physical activity was assessed using an accelerometer (ActiGraph, GTX3, USA). This 25-gram device was closed around the wrist of subjects, and information on physical activity levels was recorded. Validity and reliability of this method was determined by previous studies (15). Physical activity was measured by ActiGraph accelerometers during walking hours for 7 consecutive days. At the end of this time the physical activity levels summarized as sedentary (counts/min 25-250), moderate (counts/min 250-499), and heavy (counts/min \geq 500) (20).

Dietary assessment

The food frequency questionnaire (FFQ), validated for children with autism was used (21), in order to evaluate the pattern of food intake and also energy

intake in children. The parents of study participants reported their children mean frequency of consumption of each food item in a day, week, month, or year and the portion size during the past year. Then mean weekly consumption of food items was calculated. The data were analyzed by Nutritionist IV software.

Statistical analysis

For data analysis, descriptive statistics (mean, standard deviation), as well as inferential statistics (independent t-test, Kolmogorov-Smirnov, Pearson correlation coefficient), were applied using SPSS 19 software (SPSS Inc. IL, Chicago, USA). The normal distribution of the samples was determined by the Kolmogorov-Simonov test. Independent student t-test was used to compare case and control groups. Bivariate Pearson correlations were assessed between physical activity levels and dietary variables. Multivariate linear regression analysis was used to assess significant correlation among the physical activity and dietary factors. In this study a *P* value of less than 0.05 was considered significant.

Results

One of the 30 subjects participated in the control group of current study was excluded because of lack of cooperation, and ultimately 59 subjects were included in the study. Independent t-test results showed that there were no significant differences in mean age, BMI, height, and weight between two study groups ($p > 0.05$). In line with the study purposes, the average intake of macro- and micronutrients in children with autism and healthy children was evaluated. There were significant differences in energy ($p < 0.05$), carbohydrate ($p < 0.05$), sugar ($p < 0.05$), fructose ($p < 0.01$), vitamin D ($p < 0.05$), Vitamin C ($p < 0.01$), Calcium ($p < 0.01$), Iron ($p < 0.05$), Magnesium ($p < 0.05$) and Manganese ($p < 0.05$) intake between autistic and healthy children. The intakes of the presented nutrients were higher in healthy children (Table 1). We also evaluated the average level of physical activity in children with autism and healthy children. According to the table 2, moderate activity level was significantly lower in children with autism versus healthy children ($p = 0.035$), while sedentary physi-

Table 1. Demographic and micronutrients and macronutrients intake in case and control groups

Variables	Cases (n = 30) (Mean \pm SD)	Controls (n = 29) (Mean \pm SD)	P-value
Age (year)	10.3 \pm 2.37	9.83 \pm 1.97	0.410
Height (cm)	140.16 \pm 16	138.2 \pm 11.12	0.582
Weight (kg)	36.12 \pm 14.63	37.94 \pm 10.18	0.550
BMI (kg/m ²)	18.85 \pm 4.03	19.49 \pm 3.12	0.500
Energy (kcal)	2148.21 \pm 668.61	1806.54 \pm 555.25	0.045
Carbohydrate (16)	279.01 \pm 80.31	242.26 \pm 56.71	0.032
Protein(16)	68.78	57.03	0.063
Fat(16)	86.10	71.02	0.139
Sugar (16)	70.16 \pm 37.08	52.82 \pm 24.54	0.010
Fructose (16)	11.63 \pm 9.78	5.85 \pm 4.13	0.008
Linolenic acid (16)	0.40 \pm 0.72	0.31 \pm 0.28	0.054
Vitamin D (μ g)	1.39 \pm 1.28	0.95 \pm 1.47	0.025
Vitamin C (mg)	91.34 \pm 68.08	60.80 \pm 37.03	0.005
Calcium (mg)	688.86 \pm 286.40	547.53 \pm 286.04	0.006
Iron (mg)	13.56 \pm 4.67	11.75 \pm 3.96	0.013
Magnesium (mg)	228.12 \pm 81.22	182.63 \pm 54.13	0.021
Zinc (mg)	8.32 \pm 3.92	7.04 \pm 2.89	0.180
Manganese (mg)	2.30 \pm 1.68	1.73 \pm 0.70	0.021

BMI, body mass index; data are presented as mean \pm SD; $p < 0.05$ is significant

Table 2. The comparison of physical activity levels* in case and control groups.

Activity level	Cases (n = 30) (mean \pm SD)	Controls (n = 29) (mean \pm SD)	p-value
Sedentary (7th day)	331.84 \pm 117.37	286.61 \pm 104.43	0.124
Sedentary (5th day)	341.98 \pm 119.99	309.58 \pm 117.03	0.280
Sedentary (2th day)	313.06 \pm 122.47	254.75 \pm 100.36	0.047
Moderate (7th day)	180.67 \pm 105.46	217.98 \pm 111.78	0.190
Moderate (5th day)	181.51 \pm 121.606	203.06 \pm 114.35	0.058
Moderate (2th day)	178.73 \pm 109.815	243.51 \pm 120.26	0.035
Heavy (7th day)	20.06 \pm 27.113	17.94 \pm 21.01	0.073
Heavy (5th day)	21.40 \pm 31.133	16.13 \pm 18.25	0.413
Heavy (2th day)	18.61 \pm 26.521	20.96 \pm 26.50	0.073

Data are presented as mean \pm SD and $p < 0.05$ is significant. Physical activity was measured by ActiGraph accelerometers worn during 7 consecutive days: 7th day (Activity recorded in seven days), 5th day (Activity recorded in five days), and 2nd day (Activity recorded in two days)

Table 3. Pearson correlation coefficients between physical activity with demographic characteristics, dietary intakes, and BMI

Variables		BMI	Kilocalories	Carbohydrate*	Protein*	Fat*	Iron	Zinc	Manganese
PA 2day	r	-0.20	.094	-0.135	-0.173	0.233	0.033	.157	-0.080
	P	0.167	0.508	0.339	0.220	0.096	0.817	0.265	0.573
PA 5day	r	-0.186	0.061	-0.121	-0.175	.209	-0.25	.125	0.014
	P	0.188	0.667	0.395	0.216	0.137	0.860	0.378	0.920
PA 7day	r	-0.190	0.079	-0.159	-0.191	.258	-0.12	0.138	-0.030
	P	0.178	0.577	0.261	0.175	0.045	0.935	0.329	0.830

PA: physical activity, r: Pearson correlation coefficients, p: p value; p < 0.05 is significant. * Percent calories from fat, Carbohydrates, Protein

cal activity was higher in autistic children ($p = 0.047$). About heavy physical activity, there was no any significant difference between groups ($P > 0.05$).

Bivariate Pearson correlation coefficients between physical activity, which measured by mean daily CPM (counts per minute), and demographic characteristics, dietary factors, and BMI were shown in Table 3. In all subject, there was a significantly positive correlation between heavy physical activity level and dietary fat intake ($r = 0.258$, $p = 0.045$). Other dietary factors were not correlated with physical activity levels ($P > 0.05$).

Multivariate linear regression was used to assess the correlation of five factors (caffeine intake, vitamin C, percent calorie from fat, protein and carbohydrates) with physical activity (total sum of physical activity), after controlling for the influence of total energy intake and BMI in all boys. It was shown that the calorie from fat, vitamin C and caffeine were negatively associated with physical activity level ($r = -0.571$, $p < 0.05$ vs. $r = -0.573$, $p < 0.05$ vs. $r = -0.371$, $p < 0.01$, respectively) (Table 4).

Table 4. Multivariate linear regression analysis for relationship between physical activity and some dietary intakes

Variable	Coefficient	95% C.I		P value
		Lower	Upper	
percent calorie from fat	-0.571	0.93	7.83	0.040
percent calorie from carbohydrate	-0.169	-2.81	1.53	0.550
percent calorie from protein	0.208	-1.624	6.37	0.237
vitamin C	-0.573	-4.039	-1.46	0.001
Caffeine	-0.371	-1.96	-0.37	0.008

p < 0.05 is significant. Values were adjusted for energy intake and BMI

Discussion

This study was aimed to compare the dietary intake and physical activity levels between children with autism and healthy children. In addition, we assessed the association of dietary intake with physical activity levels in these two groups. This study revealed that the level of moderate physical activity is lower in autistic children than in healthy children, while sedentary physical activity was higher in autistic children. From the perspective of the authors, this finding could explain the differences in physical activity levels between autistic and healthy children.

By reviewing previous studies in the literature, it can be found that the activity level of children with autism might have some differences with the healthy children. In line with the present study, Pan et al (22) and Ghaheri et al (23) indicated that activity levels in children with autism is lower than healthy children. Nevertheless, Sandt et al (24) reported that there is no significant difference in physical activity between autistic and normal children. Bandini et al (15) reported that the moderate and severe activity in children with autism is equal to other children. However, this finding was different from the perspective of children's parents, which they reported their autistic children have a low level of physical activity.

Interestingly there was no correlation between physical activity levels and BMI of subjects. In contrast, Must et al described that autistic children tend to engage in lower level of physical activity during the weekend, which may be related to a subsequent increase of their BMI (25).

We also found that there is a significant clinical deficiency in nutrients intake of children with autism. There are several studies have examined the micronutrients intake of autistic patients. In agreement with our study, they have reported that the intake of micronutrients in these patients is lower than normal controls (26, 27). However, some other studies have reported that there are not any differences in nutrients intake between normal and autistic children (28). Micronutrients are essential components in the production of neurotransmitters, and people who suffered from mental illnesses need more micronutrients, therefore, it is suggested that higher intake of nutrients may improve mental performance in these patients (29). Recent studies have proposed that adenosine triphosphate level (ATP) in patients with mental disorders is influenced by the proportion of micronutrients they consume (29). Therefore, regardless of the subclinical insufficiency, adequate intake of micronutrients is associated with better mental performance.

The comparison of micronutrients intake in autistic children with dietary recommended intake (DRI) has revealed that intakes of calcium, magnesium, vitamin C, and vitamin D are lower than the required amounts. Blaurock-Busch et al (30) demonstrated that in children with autism, the intake of arsenic, cadmium, barium, lead, cerium, magnesium, and zinc is lower than DRI (30, 31). Furthermore, in a study that was conducted by Elder and colleagues, it has been shown that autistic children have a low intake of zinc, selenium, vitamin D and omega-3 fatty acids(11). Micronutrients intake may have a positive impact on the level of physical activity. The results of Rucklidge's study (32) showed that higher intake of micronutrients in adults with autism is associated with a reduction in tension and stress caused by the tremor. In our study, healthy children who had a better status in term of micronutrients intake had a higher physical activity level.

Intake of toxic metals such as mercury and arsenic might effect on the pathogenesis of autism and physical activity level in children with this disorder. Since children have higher absorption levels, they are more susceptible to the risk of toxic metals associated autism; meanwhile, nutrients deficiencies such as iron, zinc, and copper could exacerbate this state (33-35).

Yasuda et al (36) in a study emphasized on the positive role of these micronutrients in the ASD. In agreement with their study, in the present study, intake of the essential trace element 'copper' was significantly different in autistic and healthy children, which might contribute to the observed differences in physical activity level between these two groups.

In some studies, consumption of a high-fructose diet has been reported to be in association with occurrence of the negative symptoms of autism (11, 37, 38, 39). In this study, there was a significant difference in fructose consumption between the two groups, which could be considered as one of the involving factors in activity level differences between children with and without autism. However, some studies have not found any relationship between dietary fructose limitation and reduction in negative symptoms of autism (40).

The study limitations

A number of caveats need to be considered in the interpretation of the present findings. Briefly, the relatively small sample size might limit the power to detect very moderate associations and also limit the generalizability of the results. In addition, the study subjects were limited to male students, and thus replication of our results using larger samples in both genders is necessary. Finally, the case-control design of our study, in which we could not determine the causality or mechanism of the relationship between macro-and micronutrients intake and autism could be considered as study's limitations.

Conclusion

This study revealed inadequate intake of several important nutrients in autistic children compared with healthy ones. Moreover, our findings showed that there was a significant positive correlation between calorie from fat intake and heavy physical activity level in children. It could be recommended that in order to increase the level of physical activity in children with autism, the potential role of diet especially calorie from fat, vitamin C, and caffeine should be considered.

Acknowledgments

The authors thank the Tehran University of Medical Sciences directors for allowing us to conduct this comparative case-control study to compare the macro- and micronutrient intake and physical activity patterns between children with and without autism. This study was supported by grants from the Tehran University of Medical Sciences (TUMS), Tehran, Iran.

References

- Brown TA, Barlow DH. Dimensional versus categorical classification of mental disorders in the fifth edition of the Diagnostic and statistical manual of mental disorders and beyond: Comment on the special section. *Journal of abnormal psychology*. 2005;114(4):551.
- Mazefsky CA, Herrington J, Siegel M, Scarpa A, Maddox BB, Scahill L, et al. The role of emotion regulation in autism spectrum disorder. *Journal of the American Academy of Child & Adolescent Psychiatry*. 2013;52(7):679-88.
- Baio J. Prevalence of Autism Spectrum Disorders: Autism and Developmental Disabilities Monitoring Network, 14 Sites, United States, 2008. *Morbidity and Mortality Weekly Report. Surveillance Summaries*. Volume 61, Number 3. Centers for Disease Control and Prevention. 2012.
- Curtin C, Anderson SE, Must A, Bandini L. The prevalence of obesity in children with autism: a secondary data analysis using nationally representative data from the National Survey of Children's Health. *BMC pediatrics*. 2010;10(1):11.
- Zimmer MH, Hart LC, Manning-Courtney P, Murray DS, Bing NM, Summer S. Food variety as a predictor of nutritional status among children with autism. *Journal of autism and developmental disorders*. 2012;42(4):549-56.
- Rimmer JH, Rowland JL, Yamaki K. Obesity and secondary conditions in adolescents with disabilities: addressing the needs of an underserved population. *Journal of Adolescent Health*. 2007;41(3):224-9.
- Stigler KA, Potenza MN, Posey DJ, McDougle CJ. Weight gain associated with atypical antipsychotic use in children and adolescents. *Pediatric Drugs*. 2004;6(1):33-44.
- Emond A, Emmett P, Steer C, Golding J. Feeding symptoms, dietary patterns, and growth in young children with autism spectrum disorders. *Pediatrics*. 2010;126(2):e337-e42.
- Shearer T, Larson K, Neuschwander J, Gedney B. Minerals in the hair and nutrient intake of autistic children. *Journal of Autism and Developmental Disorders*. 1982;12(1):25-34.
- Curtin C, Hubbard K, Anderson SE, Mick E, Must A, Bandini LG. Food selectivity, mealtime behavior problems, spousal stress, and family food choices in children with and without autism spectrum disorder. *Journal of autism and developmental disorders*. 2015;45(10):3308-15.
- Elder JH. The gluten-free, casein-free diet in autism: an overview with clinical implications. *Nutrition in Clinical Practice*. 2008;23(6):583-8.
- Alkazemi D, Rahman A, AlSaad S, Kubow S. Parental perceptions and concerns of weight status in children with autism spectrum disorders in Kuwait. *Research in Autism Spectrum Disorders*. 2016;22:1-9.
- Bicer AH, Alsaffar AA. Body mass index, dietary intake and feeding problems of Turkish children with autism spectrum disorder (ASD). *Research in developmental disabilities*. 2013;34(11):3978-87.
- Bicer AH, Alsaffar AA. Dietary intake and physical activity levels of male adolescents with autism spectrum disorder (ASD) and normal to high body mass index (BMI)—A case series study. *Research in Autism Spectrum Disorders*. 2016;31:1-10.
- Bandini LG, Gleason J, Curtin C, Lividini K, Anderson SE, Cermak SA, et al. Comparison of physical activity between children with autism spectrum disorders and typically developing children. *Autism*. 2013;17(1):44-54.
- Dale D, Welk GJ, Matthews CE. Methods for assessing physical activity and challenges for research. *Physical activity assessments for health-related research*. 2002:19-34.
- Draheim CC. Cardiovascular disease prevalence and risk factors of persons with mental retardation. *Mental retardation and developmental disabilities research reviews*. 2006;12(1):3-12.
- Puyau MR, Adolph AL, Vohra FA, Butte NF. Validation and calibration of physical activity monitors in children. *Obesity*. 2002;10(3):150-7.
- Diagnostic A. *statistical manual of mental disorders*. American Psychiatric Association. Washington, DC. 1994:886.
- Freedson PS, Melanson E, Sirard J. Calibration of the Computer Science and Applications, Inc. accelerometer. *Medicine and science in sports and exercise*. 1998;30(5):777-81.
- Aghaeinejad M, Djafarian K, Mahmoudi M, Maskooni M. Comparison of energy and macronutrients intake between children with autism and healthy children. *International Research Journal of Applied and Basic Sciences*. 2013;5(6):667-70.
- Pan C-Y, Tsai C-L, Chu C-H, Hsieh K-W. Physical activity and self-determined motivation of adolescents with and without autism spectrum disorders in inclusive physical education. *Research in Autism Spectrum Disorders*. 2011;5(2):733-41.
- Ghaheri B, Sheikh M, Memari A, Hemayattalab R. Investigating Level of Daily Physical Activity in Children with High Functioning Autism and its Relation with Age and Autism Severity. *Arak Medical University Journal*. 2013;16(8):0-.
- Sandt DR, Frey GC. Comparison of physical activity levels between children with and without autistic spectrum disorders. *Adapted Physical Activity Quarterly*. 2005;22(2):146-59.
- Must A, Phillips SM, Curtin C, Anderson SE, Maslin M, Lividini K, et al. Comparison of sedentary behaviors between children with autism spectrum disorders and typically developing children. *Autism*. 2013;1362361313479039.
- Hyman SL, Stewart PA, Schmidt B, Lemcke N, Foley JT, Peck R, et al. Nutrient intake from food in children with autism. *Pediatrics*. 2012;130(Supplement 2):S145-S53.

27. Sharp WG, Berry RC, McCracken C, Nuhu NN, Marvel E, Saulnier CA, et al. Feeding problems and nutrient intake in children with autism spectrum disorders: a meta-analysis and comprehensive review of the literature. *Journal of autism and developmental disorders*. 2013;43(9):2159-73.
28. Lockner DW, Crowe TK, Skipper BJ. Dietary intake and parents' perception of mealtime behaviors in preschool-age children with autism spectrum disorder and in typically developing children. *Journal of the American Dietetic Association*. 2008;108(8):1360-3.
29. Gately D, Kaplan BJ. Database analysis of adults with bipolar disorder consuming a micronutrient formula. *Clinical Medicine Insights Psychiatry*. 2009;2:3.
30. Blaurock-Busch E, Amin OR, Rabah T. Heavy metals and trace elements in hair and urine of a sample of arab children with autistic spectrum disorder. *Maedica (Buchar)*. 2011;6.
31. Blaurock-Busch E, Amin OR, Dessoki HH, Rabah T. Toxic metals and essential elements in hair and severity of symptoms among children with autism. *Maedica: A Journal of Clinical Medicine*. 2012;7:38-48.
32. Rucklidge J, Johnstone J, Harrison R, Boggis A. Micronutrients reduce stress and anxiety in adults with Attention-Deficit/Hyperactivity Disorder following a 7.1 earthquake. *Psychiatry Research*. 2011;189(2):281-7.
33. Geier DA, Kern JK, Geier MR. A prospective study of pre-natal mercury exposure from maternal dental amalgams and autism severity. *Acta Neurobiol Exp*. 2009;69(2):189-97.
34. Adams JB, Audhya T, McDonough-Means S, Rubin RA, Quig D, Geis E, et al. Toxicological status of children with autism vs. neurotypical children and the association with autism severity. *Biological trace element research*. 2013;151(2):171-80.
35. Elsheshtawy E, Tobar S, Sherra K, Atallah S, Elkasaby R. Study of some biomarkers in hair of children with autism. *Middle East Current Psychiatry*. 2011;18(1):6-10.
36. Yasuda H, Yoshida K, Yasuda Y, Tsutsui T. Infantile zinc deficiency: association with autism spectrum disorders. *Scientific reports*. 2011;1.
37. El Seedy GM, El Daly RS, el hafiz Emara EA. The Effectiveness of Using Glutine and Casine Free Meals Provided With Some Sources from Omega 3 and Magnesium in Decreasing the Symptoms of Autistic Children. *Journal of American Science*. 2013;8:9.
38. Elder JH, Shankar M, Shuster J, Theriaque D, Burns S, Sherrill L. The gluten-free, casein-free diet in autism: results of a preliminary double blind clinical trial. *Journal of autism and developmental disorders*. 2006;36(3):413-20.
39. Gholizadeh F, Moludi J, Yagin NL, Alizadeh M, Nachvak SM, Abdollahzad H, Mirzaei K, Mostafazadeh M. The relation of Dietary diversity score and food insecurity to metabolic syndrome features and glucose level among pre-diabetes subjects. *Primary care diabetes*. 2018 Aug 1;12(4):338-44.
40. Whiteley P, Haracopos D, Knivsberg A-M, Reichelt KL, Parlar S, Jacobsen J, et al. The ScanBrit randomised, controlled, single-blind study of a gluten-and casein-free dietary intervention for children with autism spectrum disorders. *Nutritional neuroscience*. 2010;13(2):87-100.

Correspondence:

Kurosh Djafarian

Department of Clinical Nutrition, School of Nutritional Sciences and Dietetics

Tehran University of Medical Sciences, Tehran, Iran.

E-mail: kdjafarrin@yahoo.com