Journal of Babol University of Medical Sciences
JBUMS
e-ISSN: 2251-7170 p-ISSN: 1561-4107

Comparison of Serum Selenium Levels in Children with and without Subclinical Hypothyroidism

H. Ghaffari Hamedani (MD)[1], H. Parsian (PhD)[2], H. Shirafkan (PhD)[3], M. Pournasrollah (MD)[4], A. Mousapour (PhD)[5], Z. Panahivand (BSc)[6], M. Alijanpour (MD)[*6]

1.Student Research Committee, Babol University of Medical Sciences, Babol, I.R.Iran.
2.Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.
3.Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Science, Babol, I.R.Iran.
4.The Clinical Research Development Unit of Amirkola Children's Hospital, Babol University of Medical Sciences, Babol, I.R.Iran.
5.Department of Clinical Biochemistry, School of Medicine, Babol University of Medical Sciences, Babol, I.R.Iran.
6.Non-Communicable Pediatric Diseases Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.

***Corresponding Author: M. Alijanpour (MD)**
Address: Non-Communicable Pediatric Diseases Research Center, Amirkola Children's Hospital, Babol, I.R.Iran.
Tel: +98 (11) 32346963. **E-mail:** m.alijanpour@yahoo.com

Article Type
Research Paper

ABSTRACT

Background and Objective: Subclinical hypothyroidism is a condition without obvious symptoms, with a risk of developing into overt hypothyroidism of 2-5% per year. Given that the relationship between serum selenium concentration and thyroid function is unclear, the present study was conducted to compare serum selenium levels in children with and without subclinical hypothyroidism.

Methods: This case-control study was conducted on 103 children aged 3 to 18 years who referred to Amirkola Children's Hospital, Babol, in 2022-2023. The case group consisted of 53 children with normal T4 levels for age and TSH above the normal range of 5.5 MlU/L, and the control group consisted of 50 children with normal growth and thyroid tests and physical examination. T4 and TSH levels were measured by ELISA and selenium level was measured by atomic absorption spectrometry, and the two groups were compared.

Findings: Demographic data of the two groups including age, gender, body mass index, age group, maternal education, paternal education and place of residence did not show a significant difference. 103 children (53 and 50 children with and without subclinical hypothyroidism, respectively) were included in the study. The mean serum selenium was 74.9±26.54 µg/L (76.48 µg/L in the case group and 73.27 µg/L in the control group) and no significant difference was found between the two groups (p=0.883, CI: 0.34-3.48, MD=3.21). Selenium level of children with TSH less than 5.5 was 4.33 units higher than those with TSH greater than 5.5. However, this difference was not significant (p=0.982, CI: 0.43-2.34, OR=1.01).

Conclusion: The results of the study showed that there was no significant difference in serum selenium concentration in children with and without subclinical hypothyroidism.

Keywords: *Hypothyroidism, Selenium, Children.*

Received: Jun 11st 2024
Revised: Sep 17th 2024
Accepted: Oct 12nd 2024

Cite this article: Ghaffari Hamedani H, Parsian H, Shirafkan H, Pournasrollah M, Mousapour A, Panahivand Z, et al. Comparison of Serum Selenium Levels in Children with and without Subclinical Hypothyroidism. *Journal of Babol University of Medical Sciences*. 2025; 27: e29.

[DOI: 10.22088/jbums.27.1.29]

Introduction

Subclinical hypothyroidism is a condition in which the serum TSH level is reported to be higher than normal (greater than 5.5 mIU/L in children aged 5 months to 20 years) but the serum T4 level is within the normal range. This condition is a laboratory diagnosis, and the term subclinical refers to the presence of the disease without obvious symptoms (1). Therefore, its treatment is a matter of debate (2). The prevalence of subclinical hypothyroidism in children is 1.7%, which is lower than in adults (3).

The risk of progression of subclinical hypothyroidism to overt hypothyroidism is 2-5% per year, with this risk increasing with age, female gender, and higher TSH levels at diagnosis (4, 5). Although the disease is a completely asymptomatic biochemical diagnosis, several clinical manifestations, such as fatigue, weight gain, excessive sleeping, and weakness in physical activity, have been reported in affected children (6, 7). Selenium ion is a nutrient required for proper thyroid function and hormone synthesis in the thyroid gland (8, 9). Selenium is a micronutrient with antioxidant effects on cells. The thyroid gland contains high levels of selenium, which it uses to synthesize selenoproteins (10). In addition to protecting thyroid cells from free radicals, selenoproteins also help in the metabolism of thyroid hormones. However, the relationship between selenium deficiency and its effect on thyroid function and protection is unknown (11). A study by Parshukova et al. showed that low selenium levels were associated with lower thyroid hormone levels (12). In a study by Wu et al., high serum selenium levels were associated with a lower prevalence of subclinical hypothyroidism (13). However, the study by Federige et al. in this area did not confirm this and provided contradictory results (14).

Given the very small number of studies in this field and the existence of contradictory results, as well as the involvement of selenium ions in thyroid gland function and the effects of subclinical hypothyroidism on children's health, the present study was conducted to investigate the relationship between subclinical hypothyroidism and serum selenium levels in children aged 3-18 years referred to Amirkola Children's Hospital, Babol.

Methods

After approval by the Ethics Committee of Babol University of Medical Sciences with the code IR.MUBABOL.HRI.REC.1401.129, this case-control study was conducted on 103 children aged 3 to 18 years who referred to Amirkola Children's Hospital during the years 2022-2023. The inclusion criteria included children aged 3-18 years who referred to the hospital's Endocrinology Clinic for growth monitoring. All children underwent growth tests, including thyroid. If their T4 hormone levels were normal for their age but their TSH hormone was higher than 5.5 MIU/L, they were included in the case group, and if their growth and thyroid tests and physical examination were normal, they were included in the control group. Children with a body mass index below the 5th percentile, who are considered underweight or malnourished, those who took anticonvulsants, corticosteroids, or any type of supplement (tablets, syrups, pearls, etc.), and those with underlying heart, lung, kidney, liver, or malabsorption diseases were excluded from the study.

Convenience sampling was adopted according to the inclusion criteria. The sample size was calculated according to ($\mu 1=1.11$, SD1=0.37 and $\mu 2=0.87$, SD2=0.29), considering the difference in mean selenium levels in individuals with and without subclinical hypothyroidism in the study by Rostami et al. (15). The ratio of the two groups was considered to be 1 (R=1). Assuming an error level of 0.05 and a power of 80%, the minimum number of samples required in each group was 41. To examine the effect of the study's confounding variables, the final sample size was estimated to be 54 children in each group.

[DOI: 10.22088/jbums.27.1.29]

First, a detailed history about the characteristics of the children and parents was collected. The children in the study were first examined by a pediatric endocrinologist. For anthropometric measurements, weight (kg) was measured with a calibrated digital scale (made in Iran), and height was measured using a height meter by a medical student. Then, body mass index (BMI) was calculated using the formula weight (kg) divided by Square of height (m2). The obtained number was plotted on the standard BMI curve for girls and boys aged 2 to 20 years (based on CDC criteria). According to this criterion, children whose BMI percentile is below the 5th percentile are considered underweight, those between the 5th and 85th percentiles are considered normal weight, those between the 85th and 95th percentiles are considered overweight, and children whose BMI percentile is above the 95th percentile are considered obese (16).

Meanwhile, children with BMI below the 5th percentile, who were in the thin or malnourished range, and because selenium deficiency may be part of the laboratory symptoms of these patients and can distort the results of this study, were excluded from the study. In addition to BMI, demographic information including age, gender, age group, maternal and paternal education, and place of residence were examined, and the groups were matched in terms of age and gender. 4-5 ml blood samples were taken from the children. TSH and T4 levels were measured by laboratory method (ELISA) using a PISHTAZ kit (made in Iran) in the laboratory of the Children's Hospital. For selenium measurement, serum was separated from whole blood and then stored at -80 °C until the number of samples reached the required number. They were analyzed using the Atomic Absorption Spectrophotometry technique with a spectrophotometer (made by Hanon Company, China) (17) and with the relevant hollow cathode. Serum selenium level was measured in the atomic absorption laboratory of the Biochemistry Department of Babol University of Medical Sciences. The normal serum selenium level for this age group was considered to be 11±84.3 μg/L (18).

Data were statistically analyzed using SPSS version 23 software. Descriptive analysis was performed using mean and standard deviation (for quantitative data), frequency, and percentage (for qualitative data). T-test and Chi-square tests were used to examine the parameters between the two groups. Linear and logistic regressions were used to examine the effect of subclinical hypothyroidism on selenium level by controlling for possible confounding factors and $p<0.05$ was considered significant.

Results

Demographic information included age, gender, body mass index, age group, maternal and paternal education, and place of residence. Out of 108 children, five children (one case and four controls) were excluded from the study because blood selenium levels were not measured. 103 children (53 children with subclinical hypothyroidism and 50 controls) were included in the study. The mean age of the children in the study was 8.20±4.01 years (case group 8.15±4.01 and control group 8.26±4.05) and the body mass index was 18.99±4.85 kg/m2 (case group 18.74±4.56 and control group 19.30±5.22), and no statistically significant differences were found in terms of age and body mass index in the case and control groups (Table 1).

In addition, the mean TSH and T4 in all subjects was 8.08±2.45 mg/L and 8.91±1.70 μg/dL, respectively. The mean TSH in the case and control groups was 7.24±1.08 mg/L and 2.78±0.92 mg/L, respectively, and there was a statistically significant difference between the two groups ($p<0.001$). Furthermore, the mean T4 in the case and control groups was 8.67±1.89 μg/dL and 9.17±1.46 μg/dL, respectively, but no statistically significant difference was found between the two groups.

[DOI: 10.22088/jbums.27.1.29]

The mean difference in selenium levels between the case and control groups in the study children was 3.21, which decreased to 0.72 and 5.12 in girls and boys, respectively. However, these differences were not statistically significant. When comparing selenium levels by age group of children aged 2-10 years and 11-18 years with hypothyroidism, the differences were not statistically significant (Table 2).

Table 1. Demographic characteristics of children by group

Variable	Total Number(%)	Case group Number(%)	Control group Number(%)	p-value
Gender				
Girl	45(43.68)	23(51.1)	22(48.9)	0.951
Boy	58(62.32)	30(51.7)	28(48.3)	
Age group				
2-10	79(79.70)	41(51.9)	38(48.1)	0.872
11-18	24(23.33)	12(50)	12(50)	
Maternal education				
High school diploma	41(39.80)	21(51.2)	20(48.8)	0.994
Academic education	62(60.20)	32(51.6)	30(48.4)	
Paternal education				
High school diploma	48(46.60)	25(52.08)	23(47.91)	0.341
Academic education	55(53.4)	28(50.9)	27(49.1)	
Residence				
City	80(77.63)	40(50)	40(50)	0.583
Village	23(22.57)	13(56.5)	10(43.5)	

Table 2. Difference in mean selenium levels in the two groups by gender and age

Selenium	Raw mean difference	95% CI	p-value T-test
Total children	3.21	-7.20 – 13.62	0.541
Gender			
Girl	0.72	-13.86 – 15.31	0.921
Boy	5.12	-9.98 – 20.22	0.503
Age			
2-10 years	5.69	-6.75 – 18.14	0.363
11-18 years	-4.98	-24.53 – 14.57	0.602

Selenium level in children with TSH<5.5 was 4.33 units higher than in children with TSH>5.5. However, this difference was not statistically significant (p=0.98, CI: 0.43-2.34, OR=1.01). Rural children also had a mean selenium level of 1.31 units lower than urban children, which was not statistically significant (p=0.881, CI: 0.34-3.48, OR=1.09). In addition, a one-unit increase in BMI increased mean selenium by 0.47 units, but this difference was also not statistically significant (p=0.332, CI: 0.87-1.04, OR=0.95) (Table 3).

[DOI: 10.22088/jbums.27.1.29]

Table 3. Fitting of logistic regression model to investigate the association between subclinical hypothyroidism and selenium deficiency in children

Variables	Regression coefficient (B)	SE (B)	OR	95% CI	p-value
TSH (below 5.5, above 5.5)	0.01	0.43	1.01	0.43 – 2.34	0.982
Place of residence (urban/rural)	0.08	0.59	1.09	0.34 – 3.48	0.881
BMI	-0.04	0.04	0.95	0.87 – 1.04	0.332

Discussion

The results of the present study showed that there was no significant difference in serum selenium concentration between the two groups. This result was inconsistent with a study by Wu et al. and a study by Dabbaghmanesh et al. (13, 19). Wu et al. conducted a study to evaluate the difference between the prevalence of thyroid diseases in two regions with different selenium concentrations in China, comparing 3038 people from the Zhejiang region with 3114 people from the Ningshan region. According to the results of this study, the prevalence of thyroid diseases, including subclinical hypothyroidism, was significantly lower in the region with sufficient selenium concentration compared to the region with low selenium concentration. The region with high selenium was associated with a lower chance of subclinical hypothyroidism (13).

In a study by Dabbaghmanesh et al., the relationship between thyroid hormone status, goiter prevalence, and serum selenium concentration was investigated in 1188 Iranian children aged 8 to 13 years and showed that serum selenium concentration was significantly lower in children with goiter than in children without goiter. There was also a significant difference in serum selenium concentration between girls and boys, with boys having significantly lower concentrations than girls (19). It is possible that in the presence of selenium deficiency in the body, the function of iodothyronine deiodinases is reduced; as a result, the production of the active form of T3 from T4 is reduced. This mechanism potentially leads to increased production of TSH by stimulating the hypothalamic-pituitary axis (20). The thyroid gland contains high amounts of selenium in the form of selenoproteins. This organ has the highest selenium content per gram of tissue (21). However, the fact that selenium ions play an effective role in regulating the function of thyroid hormones has not yet been fully proven (11). The difference between our results and the reported results is probably due to the differences in the populations studied, including age, geographical location, and the nature of thyroid disorders. It can also be said that the normal cut-off point for selenium ions in the population and soil of each region needs to be determined. Because the normal level of serum selenium levels may vary in different regions.

However, the results of the present study were consistent with those of Wang et al. (22) and Moravej et al. (23). In a case-control study by Moravej et al. in 120 Iranian children, no significant association was found between selenium deficiency and hypothyroidism (23). In a 6-year cohort study by Wang et al., 549 people living in areas with normal selenium levels and 641 people living in areas with inadequate selenium concentrations were studied. The rate of improvement in thyroid function in patients with subclinical hypothyroidism in areas with selenium deficiency was higher than in those living in areas with normal selenium levels (0.46% vs. 6.30%, p=0.008) (22). Moreover, in a systematic review and meta-analysis by Winther et al., which was conducted to evaluate the therapeutic role of selenium supplements in the treatment of autoimmune thyroiditis, according to the results of the meta-analysis that measured the

[DOI: 10.22088/jbums.27.1.29]

therapeutic effects of these supplements over a period of 3, 6, and 12 months, no significant relationship was found between changes in serum TSH levels and selenium supplementation at any of the treatment time periods (24). Regarding the limitations of the study, it was conducted as a case-control study with a limited sample size. A noteworthy strength of the study was its focus on the pediatric population.

In the present study, no significant difference was found between the two groups of case and control in terms of serum selenium concentration. It is suggested that a study be conducted in a larger population and using various study designs with follow-up of TSH levels to explain the complex mechanism of thyroid function status in children.

Conflict of interest: The authors declare that there is no conflict of interest in the present study.

Acknowledgment

We would like to thank the Vice Chancellor for Research and Technology of Babol University of Medical Sciences for supporting the research, as well as the Student Research Committee and the Clinical Research Development Unit of Amirkola Children's Hospital.

[DOI: 10.22088/jbums.27.1.29]

References

1.Kliegman R, St Geme JW. Nelson textbook of pediatrics, 21st ed. Philadelphia: Elsevier; 2019. p.2920.

2.Metwalley KA, Farghaly HS. Subclinical hypothyroidism in children: updates for pediatricians. Ann Pediatr Endocrinol Metab. 2021;26(2):80-5.

3.Melmed S, Polonsky KS, Larsen PR, Kronenberg HM. Williams Textbook of Endocrinology, 13rd ed. Elsevier; 2015. p.1888.

4.Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA. 2004;291(2):228-38.

5.Peeters RP. Subclinical Hypothyroidism. N Engl J Med. 2017;376(26):2556-65.

6.Bona G, Prodam F, Monzani A. Subclinical hypothyroidism in children: natural history and when to treat. J Clin Res Pediatr Endocrinol. 2013;5(Suppl 1):23-8.

7.van der Gaag E, van der Palen J, Schaap P, van Voorthuizen M, Hummel T. A Lifestyle (Dietary) Intervention Reduces Tiredness in Children with Subclinical Hypothyroidism, a Randomized Controlled Trial. Int J Environ Res Public Health. 2020;17(10):3689.

8.Schomburg L. Selenium, selenoproteins and the thyroid gland: interactions in health and disease. Nat Rev Endocrinol. 2011;8(3):160-71.

9.Gorini F, Sabatino L, Pingitore A, Vassalle C. Selenium: An Element of Life Essential for Thyroid Function. Molecules. 2021;26(23):7084.

10.Avery JC, Hoffmann PR. Selenium, Selenoproteins, and Immunity. Nutrients. 2018;10(9):1203.

11.Andrade GRG, Gorgulho B, Lotufo PA, Bensenor IM, Marchioni DM. Dietary Selenium Intake and Subclinical Hypothyroidism: A Cross-Sectional Analysis of the ELSA-Brasil Study. Nutrients. 2018;10(6):693.

12.Parshukova O, Potolitsyna N, Shadrina V, Chernykh A, Bojko E. Features of selenium metabolism in humans living under the conditions of North European Russia. Int Arch Occup Environ Health. 2014;87(6):607-14.

13.Wu Q, Rayman MP, Lv H, Schomburg L, Cui B, Gao C, et al. Low Population Selenium Status Is Associated With Increased Prevalence of Thyroid Disease. J Clin Endocrinol Metab. 2015;100(11):4037-47.

14.Federige MAF, Romaldini JH, Miklos ABPP, Koike MK, Takei K, Portes ES. Serum selenium and selenoprotein-P levels in autoimmune thyroid diseases patients in a select center: a transversal study. Arch Endocrinol Metab. 2017;61(6):600-7.

15.Rostami R, Nourooz-Zadeh S, Mohammadi A, Khalkhali HR, Ferns G, Nourooz-Zadeh J. Serum Selenium Status and Its Interrelationship with Serum Biomarkers of Thyroid Function and Antioxidant Defense in Hashimoto's Thyroiditis. Antioxidants (Basel). 2020;9(11):1070.

16.Centers for Disease Control and Prevention. BMI Frequently Asked Questions. 2024. Available from: https://www.cdc.gov/bmi/child-teen-calculator/bmi-categories.html

17.Horncastle DCJ. Atomic absorption spectrophotometry. Med Sci Law. 1973;13(1):3-22.

18.Safaralizadeh R, Kardar GA, Pourpak Z, Moin M, Zare A, Teimourian S. Serum concentration of selenium in healthy individuals living in Tehran. Nutr J. 2005;4:32.

19.Dabbaghmanesh MH, Sadegholvaad A, Ejtehadi F, Omrani G. Low serum selenium concentration as a possible factor for persistent goiter in Iranian school children. Biofactors. 2007;29(2-3):77-82.

20.Ventura M, Melo M, Carrilho F. Selenium and Thyroid Disease: From Pathophysiology to Treatment. Int J Endocrinol. 2017;2017:1297658.

21.Duntas LH, Benvenga S. Selenium: an element for life. Endocrine. 2015;48(3):756-75.

22.Wang S, Chen P, He Y, Wei J, Tian L, Wu Y, et al. A follow-up study on factors affecting the recovery of patients with hypothyroidism in different selenium environments. BMC Endocr Disord. 2024;24(1):14.
23.Moravej H, Rakhshandehroo S, Ilkhanipoor H, Amirhakimi A, Rostami K, Yazdani N, et al. Role of Selenium Deficiency in Pediatrics with Acquired Hypothyroidism. Int J Prev Med. 2021;12:83.
24.Winther KH, Wichman JE, Bonnema SJ, Hegedüs L. Insufficient documentation for clinical efficacy of selenium supplementation in chronic autoimmune thyroiditis, based on a systematic review and meta-analysis. Endocrine. 2017;55(2):376-85.

[DOI: 10.22088/jbums.27.1.29]