Original Article

# Role of Selenium Deficiency in Pediatrics with Acquired Hypothyroidism

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## Abstract

**Background:** Although selenium is one of the nutrients that has an important role in the metabolism of thyroid hormones, it has been investigated in rare studies. This study aimed to evaluate role of selenium deficiency in children and adolescents with acquired hypothyroidism. **Methods:** This case and control study was conducted on 60 acquired hypothyroidism and 60 healthy children who had been referred to the pediatrics endocrine clinic in *Shiraz*, *Iran*, from November 2018 to April 2019. Some information such as age, gender, weight, height, duration of disease, and level of plasma selenium were recorded. Plasma selenium level was measured by atomic absorption spectrophotometer. Data were analyzed using SPSS software 21.0. **Results:** The mean of selenium level in the case and control groups were 93.77 ± 24.90 μg/dl and 85.96 ± 25.20 μg/dl, respectively. There was no significant difference between the two groups in the mean levels of selenium. Independent t-test showed no significant difference in the mean levels of selenium in male and female samples in the case group, but this difference was significant in the control group. **Conclusion:** Selenium deficiency may not have significant role as a cause of acquired hypothyroidism in pediatric and adolescent age group, in south of *Iran*. Thus, it does not seem necessary to routinely check the level of selenium for patients with thyroid dysfunction.

**Keywords:** *Deficiency, hashimoto disease, hypothyroidism, selenium, selenoproteins*

## Introduction

Since acute or chronic exposure to heavy metals can have effects on people's health, their monitoring in the human body fluids, such as blood serum, is considered as an indicator.[1]

These days, thyroid disorders such as hypothyroidism are very common. There are two types of hypothyroidism in infants and children that presents at birth (congenital) and develops after birth, usually during late childhood > three years old (YO) or adolescence (acquired). The most common cause of acquired hypothyroidism in children and adolescents is autoimmune hypothyroidism (Hashimoto thyroiditis).[2]

A study showed that thyroid gland needs the different nutrients to synthesize its hormones.[3] In this regards, selenium is one of an important factors to metabolize thyroid hormones.[4]

Thyroid gland includes high levels of selenium that attach to many selenoproteins and protect the gland from an excess of hydrogen peroxide generated to product the thyroid hormones.[5-7]

In this regards, Parshukova *et al*.[8] confirmed that low serum selenium levels have an effect on the thyroid hormone levels in North European Russia. Also, another study in China showed that higher plasma selenium was related to lower chance to be affected by hypothyroidism.[9]

Since selenium is not produced in the human body and low access to the selenium may cause abnormalities of thyroid metabolism disorders.[7] It is needed for proper functioning of the immune system and is an important factor in the metabolism of thyroid hormones.[4]

Despite the expected relationship between selenium and thyroid function, few studies have revealed the positive influence of selenium supplementation on thyroid hormone levels.[10] Moreover, rare studies in *Iran* have investigated effects of selenium deficiency in thyroid disorders including pediatrics with acquired hypothyroidism. Therefore, this study aimed to evaluate role of selenium deficiency in children and adolescents with acquired hypothyroidism in southern *Iran*.



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## Materials and Methods

### Study design

This case-control study was performed from November 2018 to April 2019.

### Selection and description of participants

The study population included children who referred to the pediatric endocrine clinic and health care centers in *Shiraz*, *Iran*. The case group were selected from children with hypothyroidism who were referred to the pediatric endocrine clinic of Imam Reza and control group were selected from healthy children who were referred to health care center in Imam Reza by convenience sampling method. As Imam Reza clinic is a referral center, children in case and control groups were from both urban and rural areas in Fars province. The sample size was estimated based on the sampling formula, $\alpha = 0.05$, and $\beta = 0.20$, about 120 (60 for each group) while considering 20% attrition:

$$N = \frac{Z1-\propto/2^2 - P(1-P)}{d^2}$$

Figure 1 shows the participation flow chart. In the case group, children aged 4 to 18 Y/O with acquired hypothyroidism were enrolled in the study. Case groups were treated with levothyroxine at a dose of 2-5 μg/kg/day (As needed according to the results of the blood test). Healthy children aged 4 to 18 Y/O who did not take medication and had normal physical exam (thyroid gland palpitation), normal laboratory test (T4 (thyroxine) and thyroid stimulating hormone (TSH)), and normal weight and height (between 25 to 75 percentiles) were included in the control group. Weight was measured by Balas device with accuracy of 50 grams. Height was also measured by Balas device with accuracy of 0.1 cm (Manufactory country: Iran). Children who had other associated disorders and did *not* agree to *participate* in the *study* were excluded from the study.

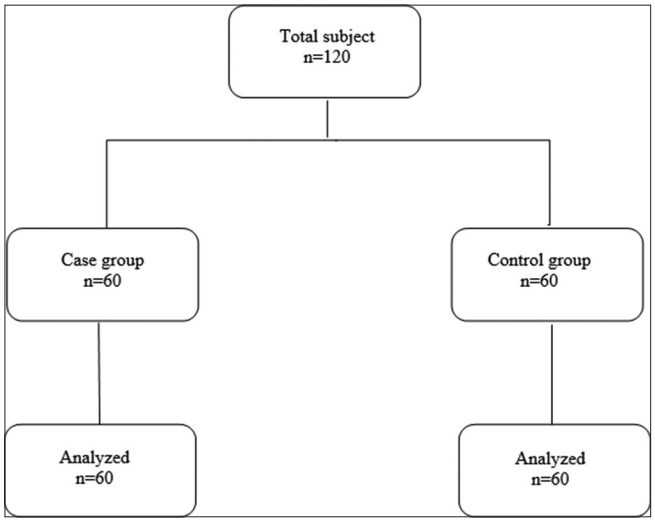


**Figure 1: Flow diagram of participants in the study**

### Technical information

Acquired hypothyroidism was diagnosed by a pediatric endocrinologist based on clinical assessment and laboratory tests (T4 and TSH). The clinical assessment included weight and height measurement, check the size of the thyroid gland, presence of goiter, and other clinical symptoms of hypothyroidism such as cold intolerance, skin dryness, etc., But the definitive diagnosis of hypothyroidism was based on a blood sample test. To measure T4 and TSH, the clotty blood sample (2cc) was taken using Electro Chemiluminescence Immunity method on Roche cobas e411 analyzer. The patients who had T4 less than normal (4.6–12 μg/dl) and TSH more than normal (0.5–6 μU/ml) in two consecutive blood tests were included in the study as hypothyroidism cases.

Then, demographic information including age, gender, weight, height, and duration of disease (in the case group) were recorded. After that, to measure selenium level, the clotty blood sample (2cc) was taken from case and control group. All the samples both from the healthy children and the children with acquired hypothyroidism were taken in the morning before breakfast. Centrifugation at the rate of 10000 rpm for 10 min separated off the serum. The plasma was kept at temperature -70°C. To measure plasma selenium levels, samples were diluted with Nickel Nitrate and Nitric Acid as in the simple Campillo method.[11]

Plasma selenium levels of all participants in the case and control groups were measured by atomic absorption spectrophotometer (Autonomic absorption, Varian 500 FS, English). The selenium measurement was performed by the furnace of the atomic absorption device with a width of 1 nm and a wavelength of 156 nm. Finally, the means of plasma selenium level of the two groups were compared.

Goiter that is defined as an enlarged thyroid, is a typical but nonspecific finding of acquired thyroid disease. In this study an expert endocrinologist done visual inspection including three positions, and palpated thyroid gland from either side of the patient. World Health Organization has classified goiter into three grade (grade 0: No visible or palpable goiter, grade 1: Goiter is palpable but not visible in chin-neutral position, and grade 2: Goiter is visible and palpable in chin-neutral position).[12]

The research was reviewed and approved by an Institutional Review Board (Ethics approval number: IR.SUMS.REC.1396.15426). Informed consent was taken from the parents of the children in both case and control group.

The Statistical Package for the Social Sciences software (SPSS: An IBM Company, version 21.0, IBM Corporation, Armonk, NY, USA) was used for data analysis. Demographic data were summarized using descriptive statistics (Mean and Standard Deviation, and frequency). Moreover, analytic data were analyzed by

Independent T-test and Chi-square test. *P* value < 0.05 was considered to be statistically significant.

## Results

A total of 60 healthy children and 60 children with acquired hypothyroidism aged 4-18 Y/O were enrolled in the study. Based on our results, 58.34% of the participants were girls and 41.66% were boys. The mean age of children in the case and control groups were 10.76 ± 3.9 and 11.91 ± 4.51 Y/O, respectively. As shown in the Table 1, statistical tests revealed no significant differences between two groups based on demographic features such as age, weight, and height (*P* > 0.05). Amongst patients of the case group, 55.9% of the parents were relative (first or second cousins).

Duration of thyroid disease in the case group was as below: 18 patients (30%) less than 3 Y/O, 21 patients (35%) between 3 and 6 Y/O, and 21 patients (35%) more than 6 Y/O.

Amongst patients in the case group, 23 patients (38.3%) had goiter. Only 34.5% of patients in the case group had positive family history of hypothyroidism.

As depicted in Table 1, there was no significant difference in the mean of plasma selenium levels between the case (93.70 ± 24.90 μg/dl) and control groups (85.96 ± 25.20 μg/dl) (*P* = 0.09).

In addition, selenium deficiency was not reported in any of participants based on the cut-off point (*P* = 0.09).

As shown in Table 2, Independent t-test showed that there was no significant difference in the mean plasma levels of selenium between male and female cases in the case group (*P* = 0.51), but this difference was significant in the control group (*P* = 0.03).

**Table 1: Comparison of demographic data and Selenium level between case and control groups (*n*=120)**

| Variable | Mean±SD | | *P* |
|---|---|---|---|
| | Case | Control | |
| Age (Y/O) | 10.76±3.96 | 11.91±4.51 | >0.05* |
| Weight (kg) | 36.07±16.55 | 39.43±16.19 | |
| Height (cm) | 133.55±39.91 | 143.27±22.30 | |
| Plasma Selenium Level (μg/dl) | 93.70±24.90 | 85.96±25.20 | 0.09* |

Y/O=Years Old; SD=Standard Deviation. *Significant at 0.05 type one error

**Table 2: Mean of Selenium level according to gender in case and control groups (*n*=120)**

| Variable | Group | Mean±SD | | *P* |
|---|---|---|---|---|
| | | Female | Male | |
| Selenium | Case | 95.57±23.61 | 91.22±26.70 | 0.51* |
| | Control | 92.02±27.04 | 77.72±20.16 | 0.03* |

SD=Standard Deviation. *Significant at 0.05 type one error

## Discussion

This study was carried out to evaluate the role of selenium deficiency as a risk factor in children and adolescents with acquired hypothyroidism.

According to laboratory cut off points, there was no selenium deficiency in participants of this study. In addition, there was no difference between the mean of plasma selenium level amongst case and control groups. This result shows that selenium deficiency doesn't have a vital effect amongst children with acquired hypothyroidism in this geographic region. In this regard, different studies have shown different results. Two studies from Brazil have shown that selenium level in that region has influenced thyroid function.[10,13] Also, Kawai *et al*.[14] have explained the effect of selenium deficiency on thyroid function. Also, another study conducted in Iraq reported that the plasma selenium level in the hypothyroidism patients were significantly less than the healthy samples.[15] On the contrary, Jang *et al*.[16] who evaluated hypothyroidism patients in Korea, have found that selenium deficiency isn't a common result amongst these patients.

Some studies have also been conducted in *Iran*. Nazemi *et al*.[17] revealed that selenium level of water and soil was low in different regions of our country. Moreover, another study showed that administration of selenium to hypothyroidism women leads to thyroid function improvement.[18] But, study by Nourbakhsh *et al*.[19] revealed that there was no difference in selenium and selenoprotein levels among hypothyroidism and healthy children and adolescents. The diversity of geographical and environmental factors can be the reason why Iranian researchers have different findings regarding the role of selenium in thyroid disorders.

On the other hand, most of the studies related to selenium and thyroid disorders have been performed on adult populations, while our study's target population was children and adolescents. Therefore, age may be an important role in selenium deficiency.

Our study showed that in Fars, one of the main provinces of southern *Iran*, selenium deficiency cannot be considered as an important risk factor to cause acquired hypothyroidism.

There is only about 10–15 mg selenium in each person's body.[20] Researches have showed that the mean of plasma selenium level in Iranian healthy children aged 1–16 years is 84.2 ± 11.36 ng/dl.[21] Our results showed that this mean was 9 ng/dl more than mean of selenium level of Iranian healthy children in case and 1 ng/dl more than mean of selenium level of Iranian healthy children in control group. Therefore, it seems that there was suitable selenium in the diet of our study population (Shiraz) compared to Iranian children. The lowest serum selenium levels in healthy Iranian children have been reported in the study of Mahyar *et al*.[22] In Qazvin and the study of Amiri *et al*.[23]

and the highest serum selenium levels was in the study of Khoshdel *et al*.[24] from Shahrekord, *Iran*. Differences in studies can be related to differences in type of nutrition and geographical location, and possibly factors such as age, gender, diet, and the amount of selenium in different areas. Also, enzymatic changes, increased free radicals and ultimately neurological disorders are other factors that can have an effect on the selenium levels.[25,26] According to controversy the selenium level in different Iranian studies, it is recommended that selenium levels be assessed in the different age groups of children across the country as a national plan.

Our study had some limitations in the sample size and geographical area of study. Thus, further studies with larger sample size in the different geographic regions of *Iran* are recommended.

In spite of our limitation, the strength of this study was the age of the participants. So far, except for the present report, there are very limited data about selenium level in children with acquired hypothyroidism.

## Conclusion

Selenium deficiency cannot be considered as major risk factors to cause acquired hypothyroidism among children and adolescents in south of *Iran*. Thus, it does not seem necessary to routinely perform screening the level of selenium for patients with thyroid dysfunction. It is recommended that selenium levels in children with hypothyroidism be measured at the first diagnosis and compared with a healthy group in another study.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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