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Research Article

# Study of Macro- and Microelement Status in Patients with Nodular Goiter Residing in Kyiv Region

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**Abstract**

Sixty-one residents of Kiev region (16 individuals with nodular goiter and 45 individuals without thyroid pathology - the control group) were examined. When studying urinary iodine excretion, median urinary iodine concentration in the control group was 65.0 $\mu$g/l, while in patients with nodular goiter, it was 72.15 $\mu$g/l indicating mild iodine deficiency. In patients with nodular goiter, there were observed decreased serum levels of calcium - 74.17 mg/l ($p<0.05$), magnesium - 17.67 mg/l, zinc - 0.73 mg/l ($p<0.05$) and selenium - 0.03 mg/l ($p<0.05$) as compared to those in the control group. The relative risk of developing nodular goiter in decreased serum calcium concentration was 1.66 (95% confidence interval 1.07-2.09), ($p<0.05$); in decreased serum concentration of both calcium and selenium, it was 2.30 (95% confidence interval 1.147-4.085), ($p<0.05$); in low serum magnesium concentration, the relative risk was 2.6 (95% confidence interval 1.11-6.09) ($p<0.05$).

**Keywords**

iodine deficiency; thyroid gland; nodular goiter; urinary iodine excretion; macro- and microelements; relative risk of developing diseases

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## Problem statement and analysis of the recent research

Nodular goiter (NG) is considered a multifactorial disease [1, 2]. This disorder occurs due to complex interaction of exogenous and numerous endogenous factors. In case of thyroid disfunction caused by various factors (iodine deficiency, inadequate iodine metabolism, inherited defects, etc.) hypophysis can stimulate the thyroid gland leading to increased thyroid stimulating hormone (TSH) production which results in the formation of proliferative and hyperplastic nodules [3].

A number of authors believe that autocrine growth factors such as insulin-like growth factor, epidermal growth factor, fibroblast growth factor play a significant role in the stimulation of thyrocyte proliferation. These biological components are physiological modulators of both thyrocyte proliferation and apoptosis [4, 5]. According to its mechanism of action, iodine bounds to tyrosyl residues of thyroglobulin (Tg), as well as to lipids forming iodinated lactones and aldehydes. The latter are considered as physiological inhibitors of autocrine growth factors and their decreased concentration in thyroid glands results in thyrocyte growth stimulation.

ND occurs not only due to iodine deficiency; other trace element deficiency is associated with its development as well. Trace elements (iron (I), calcium (Ca), selenium (Se), etc.) deficiency increases the risk of ND development [6-9]. Se and zinc (Zn) are proven to play a significant role in iodine metabolism and their inadequate intake has a negative impact on the thyroid gland. The effect of copper (Cu), manganese and bromine on goiter pathogenesis is still studying [10, 11].

We have earlier reported the presence of iodine deficiency almost throughout the whole territory of Ukraine and a constant lack of iodine in the diet of people living in northern regions of Ukraine [12-15]. We consider that the correlation between the imbalance of macro- and trace elements in humans and NG prevalence play a significant role in ND occurrence, whereas their mechanisms of action are remaining unclear.

The objective of the research was to determine the features of macro- and microelement provision of the population of Kyiv region and their role in the ND development.

## 1. Materials and methods

The study included 61 adult volunteers at the age of 29-46 years residing in Kyiv region. All the participants were divided into two groups: the control group comprised 45 (21 males and 24 females) volunteers at the age of (39.48±0.66) years; the study group included 16 (10 females and 6 males) volunteers with ND at the age of (39.0±1.26) years.

Urinary iodine concentrations (UIC) were measured using the Sandell-Kolthoff reaction method modified by Dunn et al. [16]. The results of the study were interpreted according to the WHO recommendations [17]. The study of UIC undergoes constant external quality control in the Center for Disease

Control and Prevention (Atlanta, USA).

Thyroid ultrasound measurements were performed using ultrasonographic scanner Terason 2000 with linear sensor and a frequency of 10 MHz. The thyroid size was determined according to the recommendations of Brunn J et al. [18]. ND was defined when thyroid volume exceeded 15 cm3 for males and 13 cm3 for females [19].

Serum macro- and microelements concentrations were studied using inductively coupled plasma-atomic emission spectroscopy (ICP-AES) according to the standard procedure in the laboratory of analytical chemistry and toxicological compound monitoring of Institute of Occupational Health of the NAMS of Ukraine. The ICP-AES system consisted of spectrophotometer Optima 2100 DV (Perkin Elmer, USA). Blood samples of subjects were preliminary subjected to microwave treatment. The upper and lower limits of element concentration in the blood samples were within the following ranges: 17-28 mg/l for magnesium (Mg), 90-112 mg/l for Ca, 0.6-1.2 mg/l for Zn, 0.6-1.68 mg/l for I, 0.7-1.55 mg/l for Cu and 0.046- 0.14 mg/l for Se [20].

Thyroid function was examined by the level of TST, free thyroxine (FT4), Tg. The levels of total FT4 and TSH were measured by radioimmunoassay analysis using reagent pack (Amersham, UK). To study the levels of antibodies to Tg and thyroxine peroxidase in the serum, an enzyme immunoassay method was used using standard kits (Medizin, Germany).

Statistical processing of data was carried out in accordance with the requirements of evidence-based medicine and biostatistics, applying the approaches of modern non-infectious epidemiology [21, 22]. During the statistical analysis, the software package SPSS 11.0 and MedStat were used. [23].

## 2. Results and discussion

When studying urinary iodine excretion, median UIC in the control group was 65.0 [40.75-109.45] $\mu$g/l; in patients with nodular goiter, it indicated mild iodine deficiency as well (Table 1). In the control group, 28.8 % of individuals had normal median urinary iodine levels (>100 $\mu$g/l), while 6.7 % of volunteers had severe iodine deficiency (<20 $\mu$g/l). Among patients with NG, 31.2 % individuals had normal median urinary iodine levels (>100 $\mu$g/l), and 6.2 % of volunteers had severe iodine deficiency (<20 $\mu$g/l).

Tg value is considered a criterion of more stable iodine deficiency. In the control group, Tg level (9.3 [5.2-18.55] $\mu$g/l) was similar to that in the study group, i.e., there was observed no significant difference between both groups. TSH level greater than 4 mIU/l was observed in 6.3% of participants in the study group and 2.2% of participants in the control group. Ultrasound examination revealed that the median of thyroid volume was 10.75 [9.08-12.625] $cm^3$, whereas in the control group, this parameter was 11.05 $cm^3$ [9.6-12.85]. The activation of immune processes in the thyroid gland was observed in people with NG. Elevated level of thyroid peroxidase antibody (TPOAb) titers of (24.4 [17.75-29.9] IU/ml) was observed in the study group (p<0.05 as compared to the control group).

The experimental data of macro- and microelement distribution in the blood serum were summarized and analyzed. Abnormal distribution of the sample results was detected; therefore, the values of the median and quartile intervals of the series are given.

In the control group, the median serum Ca level was 90.13 [72.34-103.94] mg/l, whereas in the study group, it was lower (74.17 [52.36-88.91] mg/l, p<0.05, according to the Mann-Whitney U-test) (Fig. 1).

In the control group, the median serum Mg level was found to be 21.65 [19.41-26.67] mg/l and in the study group, it was 17.66 [14.73-22.72] mg/l (p<0.05, according to the Mann-Whitney U-test).

In the control group, the median serum Zn level was 0.88 [0.77-1.15] mg/l being higher the median serum Zn level in the study group - 0.72 [0.51-0.84] mg/l (p<0.05, according to the Mann-Whitney U-test).

In the control group, the median serum Fe level was 0.84 [0.67-1.12] mg/l. Fe level less than 0.6 mg/l was observed in 22.5 % of the participants, while in 2.5 % of individuals, the level of Fe exceeded normal values. In the study group, the median serum Fe level was 0.96 mg/l [0.47-1.41]. In 31.25% of cases, Fe levels were less than optimal iron levels.

In the control group, the median serum Cu level was 0.91 [0.81-1.26] mg/l. In the study group, it was 0.92 [0.79-1.08] mg/l. Cu deficiency was detected in 12.5 % patients with NG.

In the control group, the median serum Se level was 0.039 [0.03-0.11] mg/l. Se deficiency was detected in 67.5% of volunteers. In the study group, serum Se level was 0.029 [0.024-0.047] mg/l (p<0.05, according to the Mann-Whitney U-test) which being significantly lower than that in the control group (Fig. 1).

The correlation between different element concentration in the control group and the study group was investigated (Table 2). In the study, a significant (p<0.05) correlation between Ca and Mg content was found (correlation coefficient (r) was 0.526). In the control group, a significant (p<0.01) correlation was found between Ca and Cu content (r = 0.429).

In the control group, Fe level correlated with TPOAb level, r = 0.332 (p<0.05). In the study group, there was correlation (r = 0.511, p<0.05) between Fe level and thyroid gland volume, Cu level and Tg concentration (r = 0.595, p<0.05), Mg level and Tg level (r = 0.599, p<0.05).

The relative risk (RR) of NG development was estimated in accordance with essential element level in the blood serum on the basis $\chi 2$ for a 4-fold conjunction table with Fisher's correction.

In case of low Mg level, RR = 2.6 (95% CI 1.11-6.09), (p<0.05), whereas in low serum Ca content, RR = 1.66 (95 % CI 1.07-2.09). In simultaneous Ca and Se deficiency, RR = 2.30 (95 % CI 1.147-4.085), (p<0.05).

## 3. Conclusions

1. Mild iodine deficiency was observed in volunteers of both the control group (72.1 $\mu$g/l) and the study group

**Table 1.** Median UIC and thyroid status studied volunteers residing in Kyiv region

| Parameters | Control group Median [Q1 – Q3] | Study group Median [Q1 – Q3] |
|---|---|---|
| (n) | 45 | 16 |
| UIC, $\mu$g/l | 65.0 [40.75-109.45] | 72.15 [47.45-111.45] |
| Tg, $\mu$g/l | 9.3 [5.2-18.55] | 8.65 [4.45-15.875] |
| Thyroid volume, $cm^3$ | 11.05 [9.6-12.85] | 10.75 [9.08-12.625] |
| TSH, mIU/l | 1.2 [0.8-1.95] | 1.7 [1.0-2.1] |
| FT4, pmol/l | 16.3 [12.8-19.8] | 14.95 [13.4-16.5] |
| TPOAb, IU/ml | 19 [5.0-26.55] | 24.4 [17.75-29.9]* |
| TgAbs, IU/ml | 18 [7.0-23.5] | 13.25 [8.425-24.55] |

*Notes:*
**Q1 – Q3** – 1-3 quartiles;
* $p<0.05$ as compared to the control group according to the Mann-Whitney U-test.

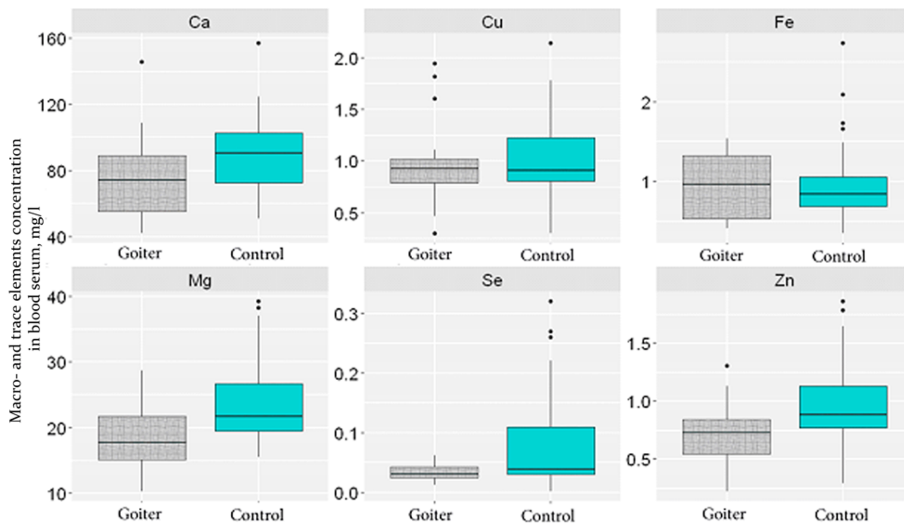


**Figure 1.** Analysis of serum macro- and trace element concentration in individuals with NG and the control group.
*Note:*
* $p<0.05$ – as compared to the control group.

**Table 2.** Correlation between macro- and microelements and thyroid status parameters in both groups

| Correlation links between parameters | Control group (n=45) | | Study group (n=16) | |
|---|---|---|---|---|
| | rspearman | p | rspearman | p |
| Ca/Mg | 0.286 | 0.063 | 0.526 | 0.036 |
| Ca/Cu | 0.429 | 0.004 | 0.107 | 0.692 |
| Fe/ TPOAb | 0.332 | 0.03 | -0.192 | 0.477 |
| Fe/ Thyroid volume | -0.005 | 0.947 | 0.511 | 0.043 |
| Mg/TgAbs | -0.034 | 0.827 | 0.599 | 0.014 |
| Cu/Tg | -0.041 | 0.794 | 0.595 | 0.015 |

(65.0 $\mu$g/l) residing in Kyiv region.

2. Volunteers of the study group were found to have lower serum Ca and Mg levels as compared to the control group.

3. Patients with NG had lower serum Se concentration as compared to the control group.

4. Patients with NG had lower serum Zn concentration as compared to the control group.

5. There was a significant correlation between Ca and Mg concentration in patients with NG.

6. In case of low Mg level, RR = 2.6 (95% CI 1.11-6.09), ($p<0.05$), whereas in low serum Ca content, RR = 1.66 (95 % CI 1.07-2.09). In simultaneous Ca and Se deficiency, RR = 2.30 (95 % CI 1.147-4.085), ($p<0.05$).

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