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CALCIUM AND MAGNESIUM LEVELS IN PATIENTS WITH PRIMARY HYPOTHYROIDISM

NIVOI KALCIJUMA I MAGNEZIJUMA KOD PACIJENATA SA PRIMARNIM HIPOTIREOIDIZMOM

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Summary

Introduction. The prevalence of Hashimoto's thyroiditis in the general population, along with the potential impact of altered calcium and magnesium concentrations, provided the impetus for this research. The objective of **o**ur study was to compare calcium and magnesium levels in newly diagnosed hypothyroid patients with those in patients undergoing thyrosubstitution therapy. **Material and Methods.** The study included three groups: patients newly diagnosed with hypothyroidism, patients with hypothyroidism on thyrosubstitution therapy, and a control group of euthyroid individuals matched for age and gender. We measured the concentrations of free triiodothyronine, free thyroxine, thyroid-stimulating hormone, thyroid peroxidase antibodies, thyroglobulin antibodies, total calcium, ionized calcium, magnesium, and phosphorus for all participants. **Results.** Newly diagnosed hypothyroid patients exhibited statistically significantly lower levels of free triiodothyronine, free thyroxine, calcium, and magnesium, and statistically significantly higher thyroid-stimulating hormone levels compared to both patients on thyrosubstitution therapy and euthyroid participants ($p<0.01$ for all comparisons). Additionally, total and ionized calcium, as well as magnesium levels, were found to be negatively correlated with thyroid-stimulating hormone levels ($p<0.05$ for all) and positively correlated with free triiodothyronine and free thyroxine levels ($p<0.05$ for all) in the newly diagnosed hypothyroid group. **Conclusion.** The observed associations between magnesium and calcium levels with thyroid function markers underscore the importance of evaluating the statuses of these elements in patients with primary hypothyroidism.

Key words: Hypothyroidism; Hashimoto Disease; Thyroiditis; Magnesium; Calcium; Blood; Thyroid Hormones

Sažetak

Uvod. Znanje o učestalosti Hašimotovog tireoiditisa u opštoj populaciji, kao i razumevanje potencijalnih posledica uzrokovanih promenama u koncentracijama kalcijuma i magnezijuma, inspirisalo je ideju za ovo istraživanje. Cilj našeg istraživanja bilo je upoređivanje nivoa kalcijuma i magnezijuma između pacijenata sa novodijagnostikovanim hipotireoidizmom i pacijenata na tireosupstitucionoj terapiji. **Materijal i metode.** Naše istraživanje obuhvatilo je tri grupe: pacijente sa novodijagnostikovanim hipotireoidizmom, pacijente sa hipotireoidizmom na tireosupstitucionoj terapiji i kontrolnu grupu eutireoidnih pacijenata, uparenih po uzrastu i polu. Merili smo koncentracije slobodnog trijodotironina, slobodnog tiroksina, tireostimulišućeg hormona, antitela na tireoidnu peroksidazu, antitela na tiroglobulin, ukupnog kalcijuma, jonizovanog kalcijuma, magnezijuma i fosfora kod svih učesnika. **Rezultati.** Ustanovili smo statistički značajno niže nivoe slobodnog trijodotironina, slobodnog tiroksina, kalcijuma i magnezijuma, kao i statistički značajno više nivoe tireostimulišućeg hormona kod pacijenata sa novodijagnostikovanim hipotireoidizmom u poređenju sa pacijentima na tireosupstitucionoj terapiji i eutireoidnim učesnicima ($p < 0,01$ za sva poređenja). Dodatno, nivoi ukupnog i jonskog kalcijuma, kao i nivo magnezijuma bili su u negativnoj korelaciji sa nivoima tireostimulišućeg hormona ($p < 0,05$ za sva merenja) i pozitivnoj korelaciji sa nivoima slobodnog trijodotironina i slobodnog tiroksina ($p < 0,05$ za sva merenja) u grupi pacijenata sa novodijagnostikovanim hipotireozomom. **Zaključak**. Povezanost nivoa magnezijuma i kalcijuma sa pokazateljima funkcije štitaste žlezde ističe važnost procene stanja ovih elemenata kod pacijenata sa primarnim hipotireoidizmom.

Ključne reči: hipotireoidizam; Hašimotova tireoiditis; tireoiditis; magnezijum; kalcijum; krv; tireoidni hormoni

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Introduction

Primary hypothyroidism is characterized by decreased levels of free thyroxine (fT4) and increased levels of thyroid-stimulating hormone (TSH) in the blood. Elevated TSH and reduced levels of thyroxine (T4) and triiodothyronine (T3) are crucial laboratory indicators of early thyroid gland dysfunction [1]. The clinical manifestations of thyroid function deficiency depend on the patient's age, comorbidities, and the rate

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Abbreviations

TSH – thyroid-stimulating hormone
T4 – thyroxine
T3 – triiodothyronine
TgAb – thyroglobulin antibodies
TPOAb – thyroid peroxidase antibodies
fT4 – free-thyroxine
fT3 – free-triiodothyronine

of hypothyroidism progression [2]. However, the absence of symptoms does not exclude hypothyroidism. Diagnosis is, therefore, established based on laboratory findings that indicate dysfunction of the hypothalamic-pituitary-thyroid axis [3].

Hashimoto's thyroiditis, or chronic lymphocytic thyroiditis, is the most common form of primary hypothyroidism. It is an autoimmune disorder marked by inflammation of the thyroid gland [4, 5]. In Hashimoto's thyroiditis, the presence of autoantibodies, such as thyroglobulin antibodies (TgAb) and thyroid peroxidase antibodies (TPOAb), signifies the destruction of thyrocytes and the initiation of an autoimmune process within the thyroid gland [4]. The autoimmune response against thyroid tissue in Hashimoto's thyroiditis is explained by two main pathophysiological mechanisms. The first involves antibody-mediated cell destruction and T-cell-stimulated cytotoxicity, while the second, more recently recognized mechanism involves cellular apoptosis [6]. In vitro studies have demonstrated high expression of pro-apoptotic molecules such as FasL, Fas, and Bax in thyrocytes [7]. Moreover, the stability of the redox system is crucial for protection against autoimmune triggers [8]. Imbalance in the redox system leads to increased production of reactive oxygen species (ROS), reactive nitrogen species (RNS), and reactive sulfides (RS) within cells [8, 9]. Accumulation of ROS results in oxidative stress, causing DNA damage and the accumulation of single-stranded DNA (ssDNA) and double-stranded DNA (dsDNA) [10, 11]. These forms of DNA can trigger autoimmune responses by inducing interferon genes and production of interferon gamma (IFN-γ), thereby initiating autoimmunity and inflammation [11]. Notably, the activity of the redox system is inversely correlated with the concentrations of anti-TPO antibodies and anti-TG antibodies, indicating that higher antioxidant capacity is associated with lower levels of autoantibodies [8].

Thyroid hormones have widespread effects on the metabolism of carbohydrates, fats, proteins, electrolytes, and minerals [12–15]. They also influence renal blood flow, glomerular filtration rate, tubular reabsorption, and mineral excretion, directly affecting the metabolism of calcium, magnesium, and phosphorus [16].

In hypothyroidism, there is a reduced mobilization of calcium from bone cells, leading to decreased total blood calcium levels [13]. This reduction prompts an increase in calcitonin, which enhances tubular reabsorption of phosphates, further lowering total blood calcium levels by increasing urinary excretion [17]. Hyperphosphatemia is also commonly observed in hypothyroidism, with several studies reporting low total calcium levels and elevated phosphate levels [18–20]. However, some studies suggest that both calcium and phosphate levels may remain within the normal reference range in hypothyroid patients [21].

Regarding magnesium levels in hypothyroidism, the evidence is inconsistent. Magnesium plays a key role in activating adenyl cyclase and cyclic 3',5'-nucleotide phosphodiesterase. Since thyroid hormones exert their effects via cAMP, magnesium ions may influence the thyroid gland response to stimulating hormones [22]. Magnesium is also an important protective cation, though the precise mechanism by which it influences the body's antioxidant capacity is not yet fully understood. Recent studies, however, suggest a beneficial role of magnesium in this context [23, 24]. Thyroid hormones play a crucial role in mitochondrial function, where magnesium is essential for oxidative phosphorylation as a component of complex V [24]. It also opposes atherosclerosis, reduces blood pressure, and promotes coronary vasodilation. Consequently, hypomagnesemia is linked to conditions such as arrhythmias, hypertension, and coronary vasospasm [25]. Some researchers have attributed hypomagnesemia in hypothyroidism to increased renal excretion of magnesium [26, 27]. Conversely, other studies have reported hypermagnesemia in hypothyroidism, potentially due to reduced urinary excretion of magnesium. Research by Jones et al. and McCaffrey and Quamme indicated that urinary magnesium excretion is decreased in hypothyroidism. They also suggested that magnesium elimination through feces is enhanced compared to euthyroid individuals, and the availability of magnesium for exchange between intracellular and extracellular spaces is reduced [28, 29].

Although changes in magnesium and calcium concentrations can be subtle, they may have significant long-term repercussion on cardiovascular function [30].

Given the prevalence of Hashimoto's thyroiditis in the general population, and the possible consequences of altered calcium and magnesium concentrations, we aimed to investigate the levels of calcium and magnesium and their relationship to thyroid function status indicators in affected patients.

The aim of this study was to assess the serum levels of calcium and magnesium in patients newly diagnosed with hypothyroidism and in those undergoing thyroid replacement therapy.

Material and Methods

The study was designed as a retrospective cross-sectional analysis and received approval by the Ethics Committee of the Clinical Center of Vojvodina. Data were sourced from the database of the Center for Laboratory Medicine at the Clinical Center of Vojvodina, covering patients referred to the Department from January 2020 to December 2020.

Based on the inclusion criteria, data were obtained from 72 patients of both genders diagnosed with primary autoimmune hypothyroidism, specifically Hashimoto's thyroiditis. These patients were divided into two groups of 36 individuals each. The first group included newly diagnosed hypothyroid patients who had

not yet initiated L-thyroxine therapy. The second group consisted of patients with hypothyroidism already undergoing L-thyroxine replacement therapy, with an average duration of 38 months. A control group of 30 clinically and biochemically healthy individuals was also included, matched for gender and age with the other two groups.

Exclusion criteria encompassed individuals younger than 18 years, pregnant women, patients with concurrent malignant diseases or other autoimmune disorders, those with liver insufficiency, terminal kidney failure, patients on thyroid suppressive therapy, and those taking supplements that could affect calcium, magnesium, or phosphorus levels.

For all enrolled patients, data on blood levels of free-triiodothyronine (fT3), free-thyroxine (fT4), TSH, TPOAb, TgAb, total and ionized calcium, magnesium, and phosphorus were extracted from their medical records for analysis.

Serum levels of fT3, fT4, TSH, TPOAb, and TgAb were determined using the chemiluminescence method on an automated Alinity analyzer (Abbott Diagnostics).

The concentrations of total calcium, magnesium, and phosphorus were measured using an automated Architect c8000 analyzer (Abbott Diagnostics), while ionized calcium levels were assessed using an AVL 910 analyzer (Roche Diagnostics).

Data were presented as absolute and relative numbers for descriptive variables, and as mean values with standard deviations for numeric variables with a normal distribution, as assessed by the Kolmogorov-Smirnov test.

Statistical comparisons of the analyzed variables were performed using the Student's t-test for continuous variables and the χ^2 test for categorical variables. Pearson correlation analysis was employed to evaluate the relationships between the studied parameters, with statistical significance set at a p-value <0.05. All statistical analyses were conducted using MedCalc software, version 9.2.0.1.

Results

The initial analysis focused on evaluating the gender distribution and age structure across the examined groups. As presented in **Table 1**, no statistically significant differences were observed.

As shown in **Table 2**, patients with newly diagnosed hypothyroidism had statistically significantly lower mean values of fT3, fT4, total calcium (Ca), and magnesium (Mg) compared to both patients on thyrosubstitution therapy and the control group ($p<0.01$ for all comparisons). Additionally, the mean TSH level was statistically significantly higher in newly diagnosed hypothyroid patients compared to both the treated group and the control group ($p < 0.01$ for all comparisons). Newly diagnosed hypothyroid patients also exhibited significantly lower levels of ionized calcium compared to the control group ($p=0.009$), with a borderline difference compared to the thyrosubstitution therapy group ($p=0.055$). Magnesium levels were significantly lower in newly diagnosed hypothyroid patients than in both the treated hypothyroid group and the control group ($p<0.01$ for both). In contrast, phosphorus levels were significantly higher in newly diagnosed hypothyroid patients compared to those undergoing thyroid replacement therapy ($p=0.009$). No statistically significant differences were observed between the group on thyroid replacement therapy and the control group in terms of thyroid hormones and electrolyte levels.

No statistically significant difference was found in the concentrations of TPOAb and TgAb between newly diagnosed hypothyroid patients and those on thyroid replacement therapy. However, both TPOAb and TgAb levels were significantly elevated in patients with hypothyroidism compared to the control group.

Table 3 presents the correlations between the concentrations of total Ca, Ca^{++}, Mg and P with TSH levels in patients newly diagnosed with hypothyroidism. Statistically significant negative correlation was observed between THS levels and the concentrations of total Ca, $Ca^{++}$and Mg levels in this patient. In contrast, no significant correlation was found between phosphorus levels and TSH.

Table 4 displays the correlations between the concentrations of total Ca, Ca^{++}, Mg, and P levels with the levels of fT3 in patients with newly diagnosed hypothyroidism. The data show a statistically significant positive correlation between fT3 levels and concentrations of both total and ionized Ca. Additionally, Mg levels also demonstrated a statistically significant correlation with fT3.

Table 1. Demographic data of the patients in relation to the examined groups
Tabela 1. *Demografski podaci pacijenata u odnosu na ispitivane*

Parameter *Parametar*	Group I Hypothyroidism *Grupa I Hipotireoidizam*	Group II Thyros. Therapy *Grupa II Tireosupst. terapija*	Control group *Kontrolna grupa*	p	p*	p**
Male/*Muško*	11 (31)	10 (28)	9 (30)	NS	NS	NS
Female/*Žensko*	25 (69)	26 (72)	21 (70)	NS	NS	NS
Age/*Godine*	54.58±11.38	54.86±9.60	50.93±11.06	NS	NS	NS

Legend: Data is shown as $\overline{X}$ ± SD or n (%); NS - not significant/*Legenda: Podaci su prikazani kao $\overline{X}$± SD ili n (%); NS – nije značajno*
p – Statistical significance between Group 1 (Newly diagnosed hypothyroidism) and Group II (thyrosubstitution therapy)/*Statistička značajnost između Grupe I (Novodijagnostikovani hipotireoidizam) i Grupe II (tireosupstituciona terapija)*
*p** – Statistical significance between Group I (newly diagnosed hypothyroidism) and control group (CG)/*Statistička značajnost između Grupe I (novodijagnostikovani hipotireoidizam) i kontrolne grupe (CG)*
*p*** – Statistical significance between group II (thyrosubstitution therapy) and the control group (CG)/*Statistička značajnost između Grupe II (tirosupstituciona terapija) i kontrolne grupe (CG)*

Table 2. Comparison of biochemical parameters between the examined groups and the control group
Tabela 2. *Komparacija biohemijskih parametara između ispitivanih grupa i kontrolne grupe*

Parameter *Parametar*	Group I Hypothyroidism *Grupa I Hipotireoidizam*	Group II Thyros. Therapy *Grupa II Tireosupst. terapija*	Control group *Kontrolna grupa*	p	p*	p**
fT_3 (pmo/l)	3.47±0.97	4.50±0.60	4.86±0.39	0.000	0.000	NS
fT_4 (pmo/l)	9.15±1.69	11.90±1.70	12.61±2.30	0.000	0.000	NS
TSH (mIU/l)	14.34±16.80	2.30±1.08	2.23±0.97	0.000	0.000	NS
TPO At (IU/l)	499.70±243.91	374.68±137.90	3.75±1.15	NS	0.000	0.000
Tg At (IU/l)	106.23±23.92	91.05±48.03	3.72±1.29	NS	0.000	0.000
Ca (mmol/l)	2.21±0.13	2.35±0.09	2.37±0.11	0.000	0.000	NS
Ca^{++}(mmol/l)	1.11±0.08	1.14±0.04	1.16±0.07	0.055	0.009	NS
Mg (mmol/l)	0.76±0.08	0.82±0.06	0.83±0.04	0.002	0.000	NS
P (mmol/l)	1.19±0.12	1.11±0.12	1.14±0.04	0.009	0.053	NS

Legend: Data is shown as X ± SD; fT_3 - free triiodothyronine; fT_4 - free thyroxine; TSH - thyroid-stimulating hormone; Ca - Calcium; Ca^{++} - ionized calcium; Mg - magnesium; P - phosphorus; NS - not significant
Legenda: Podaci su prikazani kao X ± SD; fT3 – slobodan trijodtironin; fT4 – slobodan tiroksin; TSH – tireostimulišući hormon; Ca – kalcijum; Ca^{++} – jonizovani kalcijum; Mg – magnezijum; P – fosfor; NS – nije značajno
p – Statistical significance between Group 1 (Newly diagnosed hypothyroidism) and Group II (thyrosubstitution therapy)/*Statistička značajnost između Grupe I (Novodijagnostikovani hipotireoidizam) i Grupe II (tireosupstituciona terapija)*
p* – Statistical significance between Group I (newly diagnosed hypothyroidism) and control group (CG)/*Statistička značajnost između Grupe I (novodijagnostikovani hipotireoidizam) i kontrolne grupe (CG)*
p** – Statistical significance between group II (thyrosubstitution therapy) and the control group (CG)/*Statistička značajnost između Grupe II (tirosupstituciona terapija) i kontrolne grupe (CG)*

Table 3. Correlations of examined parameters with TSH level in group of patients with newly diagnosed hypothyroidism
Tabela 3. *Korelacije ispitivanih parametara sa nivoom TSH u grupi pacijenta sa novootkrivenim hipotireoidizmom*

Parameter/*Parametar*	r/*r*	p/*p*
Ca (mmol/l)	-0.389	0.019
Ca^{++}(mmol/l)	-0.440	0.007
Mg (mmol/l)	-0.349	0.037
P (mmol/l)	-0.129	0.452

Legend: Ca – calcium; Ca^{++} – ionized calcium; Mg – magnesium; P – phosphorus
Legenda: Ca – kalcijum; Ca^{++} – jonizovani kalcijum; Mg – magnezijum; P – fosfor

Table 4. Correlations of the examined parameters with fT3 level in the newly diagnosed hypothyroid group
Tabela 4. *Korelacija ispitivanih parametara sa nivoom fT3 u grupi novodijagnostikovanog hipotireoidizma*

Parameter/*Parametar*	r/*r*	p/*p*
Ca (mmol/l)	0.422	0.010
Ca^{++}(mmol/l)	0.480	0.003
Mg (mmol/l)	0.413	0.012
P (mmol/l)	0.074	0.669

Legend: Ca – calcium; Ca^{++} – ionized calcium; Mg – magnesium; P – phosphorus
Legenda: Ca – kalcijum; Ca^{++} – jonizovani kalcijum; Mg – magnezijum; P – fosfor

Table 5. Correlations of the examined parameters with fT4 level in group of patients with newly diagnosed hypothyroidism
Tabela 5. *Korelacije ispitivanih parametara sa nivoom fT4 u grupi pacijenata sa novodijagnostikovanim hipotireoidizmom*

Parameter/*Parametar*	r/*r*	p/*p*
Ca (mmol/l)	0.355	0.034
Ca^{++}(mmol/l)	0.420	0.011
Mg (mmol/l)	0.473	0.004
P (mmol/l)	0.099	0.566

Legend: Ca – calcium; Ca^{++} – ionized calcium; Mg – magnesium; P – phosphorus
Legenda: Ca – kalcijum; Ca^{++} – jonizovani kalcijum; Mg – magnezijum; P – fosfor

Table 5 outlines the correlations between the concentrations of total Ca, Ca^{++}, Mg, and P with fT4 levels in the group of patients with newly diagnosed hypothyroidism. The results indicate a statistically significant positive correlation between fT4 levels and the concentrations of total Ca, Ca^{++}, and Mg. However, no significant correlation was observed between phosphorus levels and fT4 in this patient group.

Discussion

The values of the hypothalamic-pituitary-thyroid axis hormones in our study revealed statistically significant differences across the examined groups. Patients with newly diagnosed hypothyroidism had statistically lower levels of fT3, fT4 and TSH (fT_3: 3.47±0.97, fT_4: 9.15±1.69, TSH: 14.34±16.80) compared to those on thyroid substitution therapy (fT_3: 4.50±0.60, fT_4: 11.90±1.70, TSH: 2.30±1.08) and the control group (fT_3: 4.86±0.39, fT_4: 12.61±2.30, TSH: 2.23±0.97) ($p<0.01$ for all). These findings are consistent with the results of Kevitha et al. [31] and Shivakumar et al. [32]. High TSH levels in patients with newly diagnosed hypothyroidism, compared to euthyroid states, represent a compensatory response to insufficient secretion of thyroid hormones, which, as expected, are significantly lower.

The literature shows conflicting results regarding the concentrations of calcium ions, magnesium, and phosphorus in patients diagnosed with hypothyroidism. Furthermore, the underlying metabolic mechanisms causing these changes are not completely understood. Similar uncertainties persist regarding the electrolyte concentrations in this patient population.

Our study found that patients with newly diagnosed hypothyroidism had significantly lower concentrations of total calcium (2.21±0.13 vs. 2.35±0.09, p=0.000) and magnesium (0.76±0.08 vs. 0.82±0.06, p=0.002) compared to those on thyrosubstitution therapy and the control group (calcium: 2.21±0.13 vs. 2.37±0.11, p=0.000; magnesium: 0.76±0.08 vs. 0.83±0.04, p=0.000). Ionized calcium levels were also significantly lower in newly diagnosed hypothyroid patients compared to the control group (p=0.009). Phosphorus levels were significantly higher in newly diagnosed hypothyroid patients compared to those on thyrosubstitution therapy (1.19±0.12 vs. 1.11±0.12, p=0.009).

Our findings align with those of Saxena et al. [33], who reported significantly lower total calcium and higher phosphorus concentrations in hypothyroid patients. Similar results on total calcium and magnesium concentrations were observed in studies by Kaur et al. [34], Murgod and Soans [13], and other authors [20, 32, 35]. However, Shivakumar et al. [32] found lower phosphorus levels and higher calcium and magnesium levels, differing from our results and those of other studies.

Hypocalcemia in hypothyroidism may result from reduced thyroid hormone action on the mobilization of intracellular calcium and potassium from bone tissue [13]. This leads to increased calcitonin levels, promoting tubular phosphate reabsorption and enhancing calcium excretion through urine [24]. Hyperphosphatemia exacerbates the risk of hypocalcemia by maintaining the constant product of phosphorus and calcium concentrations, whereby elevated phosphorus levels lead to decreased total calcium levels to uphold this balance. Jones et al. [28] found that hypothyroidism is associated with increased urinary and fecal excretion of calcium, contributing to lower serum calcium levels. Studying laboratory rats, McCaffrey and Quamme [36], found that, despite hypocalcemia, there was elevated urinary excretion of calcium that was not responsive to blood calcium concentrations, suggesting dysregulation in renal calcium handling. Almost equal values of total and ionized calcium (2.35±0.09 vs. 2.37±0.11; 1.14±0.04 vs. 1.16±0.07), and phosphorus (1.11±0.12 vs. 1.14±0.04) in the group of patients undergoing thyroid replacement therapy and the euthyroid patients point out to the effect of thyroid hormones on metabolism of the above minerals.

Our study found significantly lower magnesium levels in newly diagnosed hypothyroid patients compared to those on thyroid replacement therapy (0.76±0.08 vs. 0.82±0.06, $p<0.002$) and controls (0.76±0.08 vs. 0.83±0.04, p=0.000). Mean serum magnesium levels across all groups (0.75-0.85 mmol/l) fall within a range that poses a high risk of magnesium deficiency, a condition affecting 20% of the Vojvodina population [37]. Magnesium levels in newly diagnosed hypothyroid patients are at the lower end of this range, suggesting a higher prevalence of deficiency in this subgroup.

Several studies have reported higher magnesium levels in hypothyroid patients [13, 32, 34], contrary to our findings. A comprehensive meta-analysis [38] concluded that magnesium concentrations do not statistically significantly differ between hypothyroid patients and the general healthy population. It highlighted considerable heterogeneity in the type, duration, and treatment of hypothyroidism across studies.

Some researchers link hypomagnesemia in hypothyroidism to increased renal magnesium excretion [26, 27], while others associate hypermagnesemia with urinary magnesium retention [28, 29]. It is suggested that hypothyroidism may elevate fecal magnesium excretion, which could explain the lower magnesium levels in newly diagnosed patients [28]. However, our study's limitation in measuring magnesium excretion fractions in urine and feces precludes definitive determination of this mechanism.

Our study also demonstrated significant negative correlations between total calcium, ionized calcium, and magnesium levels with TSH and positive correlations with fT3 and fT4 levels in newly diagnosed hypothyroid patients. Phosphorus did not show statistically significant correlations with any hormone in our study. Similar correlations between electrolyte levels and TSH have been reported by other studies [13, 20, 31, 32].

Stridevi et al. [35] found a significant negative correlation between TSH and total calcium but no significant correlation between TSH and magnesium or

phosphorus, unlike our study which found a correlation between magnesium and TSH. Un Nisa et al. [39] also reported significant negative correlations between magnesium and TSH, and significant positive correlations between magnesium and fT3 and fT4.

According to Wang et al. [40], lower serum magnesium levels (≤0.55 mmol/l) are linked with significantly higher rates of TPOAb positivity, TgAb prevalence, Hashimoto's thyroiditis, and clinically evident hypothyroidism, suggesting that low magnesium significantly increases the risk of thyroid hypofunction. Low serum magnesium levels may reduce immune tolerance and activate immune cells abnormally. Additionally, magnesium serves as a coenzyme in antioxidant pathways, including glutathione synthesis, which may diminish cellular antioxidant responses and promote accumulation of free radicals, leading to oxidative stress and tissue damage. Epidemiological studies have linked inadequate magnesium intake with several chronic inflammatory conditions and elevated serum C-reactive protein levels [39].

Considering our findings and those of other studies, it is important to monitor magnesium status in patients with Hashimoto's hypothyroidism, as low magnesium levels may exacerbate chronic inflammation in the thyroid. Furthermore, magnesium deficiency is linked to increased cardiovascular and metabolic risks. Hypothyroid patients often experience impaired quality of life, particularly in physical, vitality, and mental health domains [41–44]. Magnesium supplementation in deficient patients with primary autoimmune hypothyroidism may potentially support thyroid function and reduce cardiovascular and metabolic risks associated with the condition.

Conclusion

Our research demonstrates that total and ionized calcium, as well as magnesium levels, are significantly lower in patients with newly diagnosed hypothyroidism compared to those on thyroid replacement therapy and euthyroid controls. Conversely, phosphorus levels are significantly higher in newly diagnosed hypothyroid patients compared to those receiving thyroid replacement therapy. Additionally, we found that serum calcium and magnesium levels show significant negative correlations with thyroid-stimulating hormone (THS) levels and positive correlations with free-triiodothyronine (fT3) and free-thyroxine (fT4) levels in newly diagnosed hypothyroid patients. These findings highlight the critical association between magnesium and calcium levels and thyroid gland function, emphasizing the importance of assessing these elements in patients with primary autoimmune hypothyroidism. Regular monitoring and management of calcium and magnesium levels are crucial in hypothyroid patients, as dysregulation of these electrolytes may lead to suboptimal control of the underlying disease and negatively impact the quality of life. Correcting any deficiencies in these electrolytes could be essential for improving patient outcomes and overall health.

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