SERUM MAGNESIUM LEVELS IN HYPOTHYROID AND EUTHYROID PATIENTS AT A TERTIARY CARE CENTER: A COMPARATIVE CROSS-SECTIONAL STUDY

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ABSTRACT

INTRODUCTION

Magnesium (Mg) plays a role in thyroid hormone metabolism, immune regulation, and oxidative stress control. However, studies comparing Mg levels in hypothyroid and euthyroid individuals have yielded inconsistent results. Region-specific data from Western Nepal are limited.

MATERIAL AND METHODS

This cross-sectional analytical study included 150 primary hypothyroid and 150 euthyroid adults attending a tertiary care center in Southwestern Nepal between May 2023 and April 2024. Thyroid status was assessed using serum TSH, free T4 (fT4), and free T3 (fT3). Serum Mg levels were measured. Group comparisons and correlations were analyzed using non-parametric tests, with $p < 0.05$ considered statistically significant.

RESULTS

Mg levels were significantly higher in hypothyroid individuals compared to euthyroid controls ($p = 0.001$), with the difference significant only in the 21–40 year age group ($p = 0.008$). Median Mg levels in both groups were within the reference range. When classified into euthyroid, subclinical, and overt hypothyroid categories, both hypothyroid groups showed higher Mg levels than the euthyroid group. Mg exhibited weak but significant positive correlations with TSH, age, and BMI.

CONCLUSION

Hypothyroid individuals exhibited higher serum Mg levels than euthyroid controls, predominantly in the 21 – 40 year age group. Well-designed clinical trials are warranted to evaluate the therapeutic potential and clinical relevance of Mg in thyroid dysfunction.

KEYWORDS

Hypothyroidism, Magnesium, Thyroid hormones

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INTRODUCTION

Hypothyroid disorders are a global health concern and are highly prevalent in Nepal. Primary hypothyroid disorders are the most common type, with Hashimoto's thyroiditis (HT) and iodine deficiency as the leading causes.[1-3]

Magnesium (Mg), the fourth most abundant cation, is implicated in several aspects of energy metabolism as well as thyroid function. It is essential for Adenosine Triphosphate (ATP) activation and serves as a co-factor for many enzymes. It is involved in thyroid hormone metabolism, modulates thyroid hormone receptor sensitivity, and influences the bioavailability of selenium, which is required for deiodination of thyroxine (T4) to the more active triiodothyronine (T3). Mg also has immunomodulatory effects including T cell activation, reduction of proinflammatory cytokines, and oxidative stress mitigation. Additionally, Mg regulates vitamin D function, which affects calcium homeostasis, influencing several aspects of hormone release and immune function. These effects may contribute to the development of autoimmune thyroid disorders (AITDs), especially HT. Thyroid hormones, in turn, influence Mg absorption and regulation.[4-6]

Despite the known physiological interplay between Mg and thyroid function, studies comparing Mg levels in hypothyroid and euthyroid individuals have produced inconsistent results.[7-9] Such variability may arise from differences in population characteristics, including dietary intake or iodine sufficiency across regions. However, region-specific data from Nepal are limited, particularly from Western Nepal, where unique dietary habits and nutritional status may influence both thyroid function and Mg levels. This study aimed to compare serum Mg concentrations between primary hypothyroid and euthyroid individuals attending a tertiary care center in Southwestern Nepal.

MATERIAL AND METHODS

This hospital-based cross-sectional study was conducted from May 2023 to April 2024 at the Department of Biochemistry in collaboration with the Internal Medicine Department of Universal College of Medical Sciences (UCMS), Bhairahawa, Lumbini province, Nepal. Ethical approval for the study was taken from the Institutional Review Committee of UCMS (UCMS/IRC/020/23). The study population included patients recommended for the thyroid function test (TFT) from the Internal Medicine OPD of UCMS by physicians. Patients were considered hypothyroid if they had a clinical diagnosis of primary hypothyroidism or elevated TSH levels at the time of the study. Euthyroid controls were patients referred for TFT with normal TSH and fT4 levels and no history of thyroid dysfunction or thyroid medication use. Patients with secondary hypothyroidism, malignancy, multiple endocrine disorders, liver diseases, CKD, OP poisoning and patients supplemented with minerals were excluded. A total of 300 participants were selected using purposive sampling, comprising 150 primary hypothyroid patients and 150 euthyroid controls. The sample size was calculated using $n = 2 (Z_\alpha + Z_\beta)^2/d^2$ to detect a small-to-moderate effect (Cohen's $d = 0.4$) for comparison of two means, with a two-tailed $\alpha = 0.05$ ($Z_{\alpha/2} = 1.96$) and 90% power ($Z_\beta = 1.28$). This yielded a minimum of 131.22 participants per group. After accounting for a 10% non-response rate, the sample was adjusted to 144.34 and rounded to 150 per group.

Both verbal and written consent was obtained from the participants. Each participant was required to fill out a proforma that included their socio-demographic status. Anthropometric data (height and weight) were taken using standard measuring scales.

Serum thyroid hormones were analyzed via chemiluminescence assay (MAGLUMI 2000) and Mg by Xylidyl Blue-End Point (Selectra PROs). The same serum sample collected for TFT was used for magnesium analysis. Samples were analyzed immediately when possible; if delayed, they were stored at 2–8°C and analyzed within 48 hours. The following reference ranges were used for TFT parameters as per manufacturer's instructions viz a viz free triiodothyronine (fT_3): 2.0-4.2 pg/ml, thyroxine (fT_4): 0.89-1.72 ng/dl, and thyroid stimulating hormone (TSH): 0.3-4.5 µIU/ml. The participants were categorized as euthyroid (normal fT_4, and TSH), subclinical hypothyroid (elevated TSH, normal fT_4), and overt hypothyroid (elevated TSH, decreased fT_4).[10,11] The reference range for Mg was 1.5 - 2.6 mg/dl.

The data were entered in Microssoft excel and exported to the statistical package for social sciences (SPSS) version 20 for analysis. Shapiro-Wilk test was done to assess the normality of the numerical data (fT_3; fT_4; TSH; Mg, age, and BMI). Since all the values deviated significantly from normality, they were expressed in their median values along with the interquartile ranges (IQR). Mann-Whitney U test, Kruskal-Wallis test, Chi-squared test, and Spearman's correlation were performed for analysis. A p-value of <0.05 was considered statistically significant.

RESULTS

Out of the total 300 participants, the majority were female (n = 238; 79.3%). Among the females, six were pregnant, of whom four belonged to the euthyroid group. The median age and BMI of the participants were 40 years (IQR: 30.2–53) and 23.5 kg/m² (IQR: 20.3–27.1), respectively. The median serum Mg level was 2.2 mg/dL (IQR: 1.9–2.4).

Table 1 presents the association of socio-demographic characteristics and dietary habits with thyroid status. No statistically significant differences were observed between the study groups in terms of sex, religion, smoking status, alcohol consumption, or intake of Mg-rich foods. However, age group was significantly associated with thyroid status ($p = 0.005$).

Table 2 shows the comparison of numerical parameters between the hypothyroid and euthyroid groups. Age ($p = 0.001$), serum Mg ($p = 0.001$), and TSH levels ($p < 0.001$) were significantly higher in the hypothyroid group compared to the euthyroid group. Conversely, median fT3 and fT4 levels were significantly lower in the hypothyroid group (both $p < 0.001$). Given the significant age difference between study groups, serum Mg levels were further analyzed across different age groups **(table 3)**. Among participants aged 21–40 years, serum Mg levels were significantly higher in the hypothyroid group compared to

the euthyroid group ($p = 0.005$). No significant differences in Mg levels were found across the remaining age groups.

Further categorization of thyroid status into euthyroid, subclinical hypothyroid, and overt hypothyroid groups revealed a significant difference in serum Mg levels among the groups (Figure 1). Mg levels were significantly lower in the euthyroid group compared to both the subclinical ($p = 0.004$) and overt hypothyroid groups ($p = 0.007$). However, no significant difference was observed between subclinical and overt hypothyroid groups ($p = 0.414$). Serum Mg levels showed a statistically significant but weak positive correlation with age, BMI, and TSH levels (Table 4).

Table 1. Comparison of categorical variables between the study groups

		Hypothyroid n (%)	Euthyroid n (%)	*p*-value n (%)
Sex	Female	123 (82)	115 (76.7)	0.254
	Male	27 (18)	35 (23.3)	
Age group (years)	≤20 years	4 (2.7)	11 (7.3)	0.005
	21-40	58 (38.7)	80 (53.3)	
	41-60	67 (44.6)	43 (28.7)	
	>60	21 (14)	16 (10.7)	
Religion	Hindu	137 (91.3)	141 (94)	0.376
	Non-Hindu	13 (8.7)	9 (6)	
	No	142 (94.7)	146 (97.3)	
Smoking	Past	5 (3.3)	0 (0)	0.074
	Yes	3 (2)	4 (2.7)	
Alcohol	No	138 (92)	134 (89.3)	0.126
	Past	4 (2.7)	1 (0.7)	
	Yes	8 (5.3)	15 (10)	
Mg rich diet	Occasional	26 (17.3)	30 (20)	0.553
	Regular	124 (82.7)	120 (80)	

p-values obtained from chi-square analysis. $p < 0.05$ considered statistically significant.

Table 2. Comparison of numerical parameters between the study groups

	Hypothyroid (n = 150)	Euthyroid (n = 150)	*p*-value
Age (years)	46 (33.7 - 55)	37 (17 - 50)	0.001
BMI (Kg/m2)	23.7 (20.7 - 26.9)	22.8 (19.7 -27.8)	0.489
TSH (µIU/ml)	7.1(5.8 -11.8)	2.7 (1.7 - 3.4)	<0.001
fT3 (pg/ml)	2.5 (2.2 - 3.1)	3.1 (2.8 - 3.3)	<0.001
fT4 (pg/ml)	1 (0.9 -1.2)	1.2 (1 - 1.4)	<0.001
Mg (mg/dl)	2.3 (1.9 - 2.5)	2.1 (1.9 - 2.3)	0.001

Values presented as median (IQR). *p*- values from Mann-Whitney U test.
$p < 0.05$ considered statistically significant.

Table 3. Serum Mg levels between hypothyroid and euthyroid across different age groups

Variables		Thyroid		*p*-value
		Hypothyroid	Euthyroid	
Mg Levels across different age groups	≤ 20 years (n = 15)	1.98 (1.83 – 2.46)	1.98 (1.88 – 2.29)	0.896
	21 – 40 years (n = 138)	2.30 (1.96 – 2.50)	2.02 (1.84 – 2.31)	0.008
	41- 60 years (n = 110)	2.23 (1.97 – 2.41)	2.13 (1.95 – 2.42)	0.530
	> 60 years (n = 37)	2.31 (2.29 – 2.87)	2.23 (2.06 – 2.41)	0.089

Values presented as median (IQR). *p*-values from Mann-Whitney U test.
$p < 0.05$ considered statistically significant.

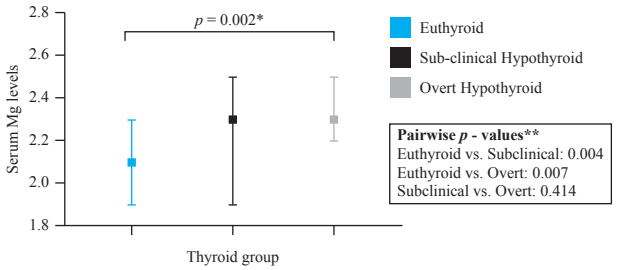

Figure 1. Median Mg levels among the study groups
[*p value from Kruskal-Wallis-H test. **p values from Mann-Whitney U test]

Table 4. Correlation of Mg levels with age, BMI and TFT parameters.

	Correlation coefficient (ρ)	*p* - value
Age	0.152	**0.009**
BMI	0.181	**0.043**
TSH	0.210	**<0.001**
fT_3	-0.090	0.120
fT_4	0.055	0.342

p-values from Spearman correlation analysis
$p < 0.05$ considered statistically significant

DISCUSSION

Mg plays essential roles in cellular regulation and has been implicated in maintaining normal thyroid function. Mg deficiency appears to enhance innate immunity, impair adaptive immunity, and increase oxidative stress. These mechanisms seem to play an important role in the pathogenesis of Hashimoto's thyroiditis (HT). Studies have shown increased Tg-Ab levels and HT prevalence in patients with Mg deficiency.[6, 12, 13]

This cross-sectional study, involving 150 primary hypothyroid and 150 euthyroid patients, aimed to compare Mg levels between the two groups. We found that serum Mg levels were significantly higher in the hypothyroid group compared to euthyroid patients, both within reference ranges. However, this association was confounded by significantly higher age among hypothyroid patients. Although multiple linear regression could not be performed due to unmet assumptions, subgroup analysis by age revealed that the higher Mg levels in hypothyroid patients were significant only in the 21 - 40 year age group. When thyroid status was further categorized into euthyroid, subclinical hypothyroid and overt hypothyroid groups, we found that serum Mg levels were significantly higher in both hypothyroid groups compared to the euthyroid group. Additionally, Mg levels showed a weak but significant positive correlation with TSH, age, and BMI.

The existing literature shows conflicting findings. A previous study from Nepal also reported increased serum Mg levels in hypothyroid patients, consistent with our results.[8] Other studies by Shivkumar et al,[14] Hiremath K et al,[15] and Chowdhry et al[16] also reported similar findings. The probable reason for increased serum Mg levels is thought to be reduced renal clearance in hypothyroid patients.[17] In contrast, other studies have reported reduced serum Mg levels in hypothyroid patients compared to their euthyroid counterparts.[18, 19] A systematic review and meta-analysis of 14 observational studies found no significant difference in

serum Mg levels between hypothyroid and euthyroid individuals, although the included studies were highly heterogeneous.[9]

These discrepancies highlight key considerations. Although Mg has diverse physiological roles supported by experimental evidence, this doesn't guarantee clinical relevance. Observational studies, including ours, can generate hypotheses but have limitations and often overemphasize biological plausibility. They cannot confirm whether Mg deficiency significantly contributes to thyroid disorders or whether supplementation is truly beneficial in hypothyroid treatment. A randomized trial by Rabbani et al found that Mg Oxide, combined with Zinc and Vitamin A, improved fT_4 levels and reduced inflammation in hypothyroid patients.[4] However, the short follow-up, use of multiple supplements, and absence of patient-important outcomes limit its conclusions. Well-designed RCTs with longer follow-up and clinically meaningful endpoints are needed to determine Mg's therapeutic role. Until then, recommendations should not rely solely on observational data or mechanistic rationale.

This study had several limitations. As a hospital-based study, the findings may not be generalizable to the broader community. The cross-sectional design limits causal inference and is prone to both known and unknown confounders. The use of purposive sampling may introduce selection bias. Additionally, six of the female participants were pregnant. As different TSH cut-off values apply in pregnancy, this may have introduced minor variation in thyroid classification.

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CONFLICT OF INTEREST

None

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