

# Assessment of Serum Calcium and Phosphorus in Patients with Hypothyroidism: A Hospital-Based Cross-Sectional Study

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## ABSTRACT

**Introduction:** Hypothyroidism is a clinical status resulting from a deficiency of thyroid hormones or, more rarely, from their impaired activity at the tissue level. Divalent ions, such as calcium and phosphorus are required as cofactors for many enzymes in various metabolic pathways that are directly or indirectly regulated by thyroid hormones. So, a decrease in thyroid hormone can result in mineral disturbances, which lead to an increased incidence of osteoporosis, metabolic syndrome, and cardiovascular diseases. **Aims:** To assess the alteration of serum calcium and phosphorus in patients with hypothyroidism. **Methods:** A Hospital-based comparative cross-sectional study was conducted at Nepalgunj Medical College Teaching Hospital, Kohalpur, Nepal. A total of 130 participants, aged 18–60 years, were selected for the study. Out of these, 65 participants diagnosed with hypothyroidism were recruited into the hypothyroid group, and 65 euthyroid, healthy individuals visiting the hospital for routine check-ups were recruited into the euthyroid group. Blood samples were collected over a six-months period, starting from September 27, 2024, and analyzed for free triiodothyronine, free thyroxine, thyroid-stimulating hormone, calcium, and phosphorus to assess the alterations in calcium and phosphorus levels in hypothyroidism. **Results:** Our study showed that serum calcium levels were significantly decreased, while serum phosphorus levels were significantly increased, in both subclinical hypothyroidism and overt hypothyroidism ( $p < 0.05$ ) compared to euthyroid individuals. Among the hypothyroid group, serum thyroid-stimulating hormone manifested a significant negative correlation with calcium ( $r = -0.275$ ,  $p = 0.02$ ) and a positive correlation with phosphorus ( $r = 0.166$ ,  $p = 0.186$ ). **Conclusion:** The present study concludes that hypothyroid participants exhibited serum electrolyte disturbances, such as decreased calcium and increased phosphorus in comparison to euthyroid participants.

**Keywords:** Hypothyroidism, Serum Calcium, Phosphorus, Thyroid hormones

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## INTRODUCTION

Approximately 300 million people worldwide suffer from thyroid dysfunction.<sup>1</sup> In Nepal prevalence of thyroid dysfunction varies between 22.42% to 29.0%<sup>2-4</sup> whereas prevalence of hypothyroidism ranges between 12.41% to 25%.<sup>2-4</sup> Hypothyroidism is a medical condition characterized by increased thyroid stimulating hormone (TSH) with normal or decreased thyroid hormones.<sup>5</sup> The divalent ions like calcium and phos-

phate are required for many enzymes as a cofactor in various metabolic pathways, which are directly or indirectly regulated by thyroid hormones.<sup>6</sup> Hypocalcemia and hyperphosphatemia are common mineral disturbances in hypothyroidism.<sup>7,8</sup> According to some literature, hypothyroidism causes a drop in serum calcium and phosphorus<sup>6,9</sup> however other studies reported an increase in serum phosphorus and a decrease in serum calcium.<sup>10</sup> Even in another study, normal levels of serum calcium and phosphorus were observed.<sup>11</sup> Metabolism of cal-

cium and phosphorus are often altered in thyroid disorders<sup>12</sup> and some studies indicates that abnormalities in the metabolism of these divalent cations are linked to metabolic disorders, hypertension, and cardiovascular diseases.<sup>13,14</sup> Since the impact of thyroid hormones on serum calcium and phosphorus is yet unclear and there is a paucity of data about the impact of thyroid hormones on serum calcium and phosphorus from western region of Nepal. So, the current study was undertaken with an aim to assess serum calcium and phosphorus levels in patients with hypothyroidism and compare them with euthyroids in a tertiary care hospital at Kohalpur and the data generated through the present study will help to formulate standard treatment guidelines for better patient care as needed.

## METHODS

A hospital-based comparative cross-sectional study was conducted at the Department of Biochemistry of Nepalgunj Medical College Teaching Hospital (NGMCTH), Kohalpur, from September 2024 to March 2025. Ethical clearance for the study was obtained from the Institutional Review Committee of NGMCTH (Ref: 19/081-082 dated September 27, 2024), and oral and written consents were obtained from all participants before enrollment in the study. The participants were of both sexes, with an age range between 18 and 60 years. On the basis of participants self-reporting as well as on the basis of recent clinical and laboratory examination, participants having hepatic disorders, diabetes mellitus, cardiovascular disorders, pregnant women, bone diseases and taking mineral supplements were excluded from the study. Using the following formula, a convenient sampling technique was employed to determine the sample size.<sup>2</sup>

Prevalence of hypothyroidism (P): 12.41%<sup>2</sup>

Error (d)= 8 %

Z= 1.96

q =1-p = 0.875

Sample size (n) =  $Z^2pq/d^2$

$$= (1.96)^2(0.1241)(0.875)/(0.08)^2$$

$$=65$$

A total of 130 participants were enrolled in the study. Out of which 65 participants attending the medicine outpatient department of NGMCTH diagnosed with hypothyroidism were enrolled in the hypothyroid group which were further stratified into subclinical hypothyroidism (SCH) and overt hypothyroidism (OHY) and an equal number of age and sex matched healthy individual having normal thyroid function test who attended the hospital for routine health checkup were enrolled in the euthyroid group. Three milliliters of fasting venous blood were collected in a gel tube under aseptic conditions. They were subjected to centrifugation for 5 minutes at 3500 revolutions per minute (RPM) to separate serum for biochemical analysis. Serum thyroid-stimulating hormone (TSH) was estimated by sandwich immunoluminometric assay, while serum free triiodothyronine (FT3) and free thyroxine (FT4) were assessed by competitive immunoluminometric assay using Maglumi 800. Serum calcium and phosphorus was estimated by

Arsenazo III and phosphomolybdate method respectively using Mindray BS 430 wet chemistry analyzer. Thyroid function test, included FT3, FT4 and TSH. Data was entered in a Microsoft Excel spreadsheet and analyzed using Statistical Package for the Social Sciences (SPSS) version 25. The data was not normally distributed so all the biochemical parameters were expressed as median with inter quartile range (IQR). The Mann-Whitney test was applied to compare the biochemical parameters of hypothyroid and euthyroid group. Spearman's correlation was employed to see the correlation of TSH with calcium and phosphorus among the hypothyroid group. A p-value <0.05 was considered statistically significant.

## RESULTS

Out of 130 participants in the current study, the majority of participants were female in both the hypothyroid group (43) and the euthyroid group (45) and the majority of participants belonged to the age group 51 – 60 years in both the hypothyroid and euthyroid group.

Parameters	Median (Interquartile range)		
	Total participants	Hypothyroid group	Euthyroid group
Age (years)	44.91 ± 10.36 (23 – 60)	45.92 ± 10.43 (23 – 60)	43.89 ± 10.26 (25 – 59)
Age group (years)	≤ 30	17 (13.0%)	8 (12.3%)
	31 - 40	37 (28.4%)	20 (30.8%)
	41 - 50	21 (16.1%)	10 (15.4%)
	>50	55 (42.3%)	27 (41.5%)
Sex	Male	42 (32.3)	20 (30.8%)
	Female	88 (67.7)	45 (69.2%)
TSH (μIU/ml)	4.21 (2.57 – 12.1)	12.1 (8.3 – 24.5)	2.57 (1.73 – 3.11)
FT4 (ng/dl)	1.23 (1.1 – 1.43)	1.15 (0.74 – 1.34)	1.3 (1.2 – 1.49)
FT3 (pg/ml)	2.89 (2.13 – 3.21)	2.49 (1.23 – 2.90)	3.1 (2.56 – 3.35)
Calcium (mg/dl)	9.14 (2.57 – 12.1)	8.6 (7.91 – 9.41)	9.7 (9.01 – 10.12)
Phosphorus (mg/dl)	3.25 (2.93 – 3.75)	3.66 (2.93 – 3.92)	3.12 (2.91 – 3.37)

TSH: Thyroid stimulating hormone, FT4: Thyroxine, FT3: Free triiodothyronine

**Table I: Baseline characteristics of the hypothyroid group and euthyroid group**

Table I shows that the majority of the participants in both the hypothyroid group and the euthyroid group belonged to the age group ≥50 years, which was about 43.0% and 41.5%, respectively. Serum TSH and phosphorus levels increased, while serum FT3, FT4 and Calcium Levels decreased in the hypothyroid group compared to the euthyroid group. Age was expressed in mean ± SD (minimum - maximum age).

Parameters	Median (Interquartile range)			p value a vs c	p value b vs c
	SCH <sup>a</sup> (n = 33)	OHY <sup>b</sup> (n = 32)	Euthyroid group <sup>c</sup>		
Age (years)	44 (34 – 56)	47 (31 – 55)	45 (35 – 54)	0.719	0.957
TSH ( $\mu$ U/ml)	9.76 (6.40 – 16.6)	22.5 (11.5 – 49.4)	2.57 (1.73 – 3.11)	0.001	0.001
FT4 (ng/dl)	1.23 (1.14 – 1.39)	0.59 (0.18 – 0.71)	1.3 (1.2 – 1.49)	0.034	0.001
FT3 (pg/ml)	2.65 (2.21 – 3.12)	1.16 (1.05 – 1.69)	3.1 (2.56 – 3.35)	0.023	0.001
Calcium (mg/dl)	8.7 (8.17 – 9.66)	8.51 (7.91 – 9.17)	9.7 (9.01 – 10.12)	0.001	0.001
Phosphorus (mg/dl)	3.50 (3.05 – 3.89)	3.73 (2.91 – 3.98)	3.12 (2.91 – 3.37)	0.02	0.003

TSH: Thyroid stimulating hormone, FT4: Thyroxine, FT3: Free triiodothyronine, SCH: Subclinical hypothyroidism, OHY: Overt hypothyroidism, n: Number of participants, a vs cMann-Whitney U test between SCH and euthyroid group, b vs c Mann-Whitney U test, between OHY and euthyroid group. P < 0.05 was considered statistically significant and was indicated in bold type.

**Table II: Comparison of biochemical profile of participants between the hypothyroid group and the euthyroid group**

Table II represents that serum calcium, FT3 and FT4 were significantly decreased in the SCH and OHY compared to euthyroid group while serum TSH and phosphorus were significantly increased in the SCH and OHY compared to euthyroid group. Mann-Whitney U test was used to generate p value.

Group	Parameter	Calcium	Phosphorus
Hypothyroid group	TSH	r: -0.275* p value: 0.027	r: 0.166 p value: 0.186

r denotes Spearman's correlation coefficient; a p-value < 0.05 was considered statistically significant and was indicated in bold type

**Table III: Spearman's correlation of TSH with calcium and phosphorus in the hypothyroid group**

Table III shows that serum calcium was negatively correlated with TSH, and this correlation was statistically significant (r = -0.275, p = 0.02). In contrast, there was no correlation between serum phosphorus and TSH.

## DISCUSSION

The current study enrolled 65 participants diagnosed with hypothyroidism into the hypothyroid group and an equal number of euthyroid healthy participants into the euthyroid group to assess the alteration of serum calcium and phosphorus in hypothyroidism. Our study manifested female predominance with majority and minority of the participants belonged to the age group >50 years and  $\leq$ 30 years respectively as well as the median age of the participants in SCH, OHY and euthyroid was 44 years, 47 years and 45 years respectively, which shows that

the age differences between the comparison group were not statistically significant. However, serum calcium was significantly decreased while serum phosphorus was significantly increased in both SCH and OHY compared to the euthyroid group, respectively.

In the current study, approximately 66.2% of the participants in the hypothyroid group were female, suggesting that hypothyroidism was more prevalent in women than in men, which is consistent with the findings of the Regmi et al study (2010).<sup>15</sup> The higher incidence of hypothyroidism in females may be caused by estrogen, which is thought to be an antagonist of FT3 and FT4 since it competes with them for receptor protein binding sites.<sup>16</sup> The present study reveals that serum calcium was significantly decreased (p<0.001) in both the SCH [8.7 (8.17 – 9.66)] and OHY [8.51 (7.91 – 9.17)] compared to the euthyroid group [9.7 (9.01 – 10.12)], as well as in hypothyroid participants' serum calcium, was negatively correlated with serum TSH (r: -0.275, p = 0.02) and was statistically significant. The findings of our study was in consistent with the similar studies done by Dhungana A et al<sup>16</sup> and Saxena S et al.<sup>10</sup> The possible explanation of hypocalcemia in hypothyroidism is due to decreased outflow of calcium from the cells and due to increased production of calcitonin in hypothyroidism, which promotes increased tubular excretion of calcium<sup>17</sup> as well as due to depressed bone turnover due to decreased thyroid hormone since thyroid hormones acts on osteoblast to stimulate osteoclastic bone resorption via nuclear receptors.<sup>8,9</sup>

In the current study, serum phosphorus was increased in both the SCH [3.50 (3.05 – 3.89)] and OHY [3.73 (2.91 – 3.98)] compared to the euthyroid group [3.12 (2.91 – 3.37)] and was statistically significant. This finding was in agreement with the study conducted by Saxena S. et al<sup>10</sup> and Dhungana A et al.<sup>6</sup> However, In contrast to our study Modi A et al<sup>9</sup> reported a significant decrease in serum phosphorus in hypothyroidism, and possibly this could be due to decreased bone turnover because in hypothyroidism the effect of thyroid hormone on osteoblast diminishes resulting in decreased osteoclastic bone resorption.<sup>9</sup> In our study, in hypothyroid participants, serum phosphorus was positively correlated with serum TSH, but was not statistically significant (r value = 0.166, p = 0.186), which is similar to the study done by Bharti A et al<sup>18</sup> where they also reported a positive correlation of serum phosphorus with serum TSH. In contrast to our study, Modi et al<sup>9</sup> reported a significant negative correlation of serum phosphorus with serum TSH (r value = -0.69, p value < 0.05). In our study serum phosphorus was increased and the possible reason behind this is due to increased calcitonin in hypothyroidism which is responsible for increased tubular reabsorption of phosphorus.<sup>17</sup> The small sample size of our hospital-based study is a limitation. Clarifying the relationship between calcium, phosphorus, and TSH can be made easier with a larger sample size and a general population investigation. Additionally, further examination of confounding variables, such as vitamin D, parathyroid hormone, and calcitonin, would have been beneficial for a better understanding of mineral metabolism and balance.

## CONCLUSION

Our study concludes that serum calcium levels were significantly decreased while serum phosphorus levels were significantly increased in hypothyroid individuals compared to euthyroid healthy participants. Serum calcium and serum TSH showed a strong negative association in hypothyroidism, whereas serum phosphorus and serum TSH showed a positive correlation in hypothyroidism. So, our study recommends that hypothyroid individuals should have their serum calcium and phosphorus levels routinely checked to detect and treat the disease resulting from the malfunction in mineral metabolism and prevent the additional consequences associated with it.

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