

Serum Copper and Zinc Status in Hypothyroidism: A Case–Control Study Evaluating Their Impact on Thyroid Function

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Abstract

Background: Hypothyroidism is a common endocrine disorder with significant metabolic consequences. Apart from iodine, trace elements such as zinc (Zn) and copper (Cu) play an essential role in thyroid hormone synthesis, metabolism, and action. Alterations in these micronutrients may contribute to the pathophysiology of hypothyroidism.

Aim: To evaluate serum zinc and copper levels in patients with hypothyroidism and compare them with euthyroid healthy controls, and to assess their association with thyroid hormone levels.

Materials and Methods: This hospital-based case–control study included 100 subjects aged 18–65 years. Fifty patients with biochemically confirmed hypothyroidism constituted the case group, while fifty age- and sex-matched euthyroid individuals served as controls. Serum T3, T4, and TSH were estimated by chemiluminescence immunoassay. Serum zinc and copper levels were measured using spectrophotometric methods. Statistical analysis was performed using Student's t-test and correlation analysis.

Results: Mean serum zinc levels were significantly lower in hypothyroid patients compared to controls (32.3 ± 19.1 vs 86.0 ± 17.9 $\mu\text{g/dL}$; $p < 0.001$). Serum copper levels showed no statistically significant difference between cases and controls ($p > 0.05$). Serum zinc demonstrated a significant negative correlation with TSH and a positive correlation with T3 and T4 levels.

Conclusion: Hypothyroidism is associated with significantly reduced serum zinc levels, while serum copper levels remain largely unchanged. Zinc deficiency may play an important contributory role in thyroid dysfunction and may warrant attention during clinical evaluation of hypothyroid patients.

Keywords: Hypothyroidism, Zinc, Copper, Trace elements, Thyroid hormones.

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Introduction

Hypothyroidism is a common endocrine disorder characterized by deficient production or reduced biological action of thyroid hormones, resulting in a generalized slowing of metabolic processes throughout the body. Thyroid hormones play a vital role in regulating basal metabolic rate, thermogenesis, lipid and carbohydrate metabolism, cardiovascular function, growth, and neurological development. Deficiency of these hormones therefore leads to multisystem involvement, affecting nearly every organ system. Hypothyroidism represents one of the most prevalent endocrine disorders worldwide and

constitutes a major public health problem, particularly in developing countries such as India, where nutritional deficiencies and limited healthcare access further compound disease burden [1,2]. Although iodine deficiency is the most well-established nutritional cause of thyroid dysfunction, particularly in endemic regions, it has become increasingly evident that optimal thyroid function depends on an adequate supply of several micronutrients and trace elements. These micronutrients act as cofactors for enzymes involved in thyroid hormone synthesis, activation, transport, and cellular action. Among these, zinc

and copper have attracted considerable attention due to their essential roles in enzymatic reactions, antioxidant defense mechanisms, and endocrine regulation [3]. Zinc is a vital trace element required for normal growth, immune function, and endocrine regulation. In thyroid physiology, zinc is involved at multiple levels of hormone metabolism. It is necessary for the synthesis of thyrotropin-releasing hormone (TRH) in the hypothalamus and contributes to the structural integrity of thyroid hormone receptors through zinc-finger motifs.

Furthermore, zinc acts as a cofactor for iodothyronine deiodinase enzymes, which catalyze the peripheral conversion of thyroxine (T4) into the biologically active triiodothyronine (T3). Zinc deficiency can therefore impair thyroid hormone synthesis, reduce peripheral hormone activation, and diminish hormone-receptor binding at the cellular level, ultimately leading to features of hypothyroidism even in the presence of adequate iodine intake [4,5].

Copper is another essential trace element involved in thyroid hormone metabolism, although its role is less clearly defined compared to zinc. Copper is required for the activity of several oxidoreductase enzymes and plays a role in tyrosine metabolism, a critical step in the synthesis of thyroid hormones. It also contributes to phospholipid synthesis and oxidative processes that influence thyroid hormone production, secretion, and transport. Additionally, copper is a component of antioxidant enzymes such as superoxide dismutase, which protect thyroid tissue from oxidative damage during hormone synthesis [6,7].

The relationship between thyroid hormones and trace elements is complex and bidirectional. Thyroid hormones influence the intestinal absorption, tissue uptake, plasma transport, and renal excretion of zinc and copper. Conversely, deficiencies or imbalances of these trace elements can alter thyroid hormone synthesis, metabolism, and action, potentially exacerbating thyroid dysfunction. This interdependence suggests that alterations in trace element status may both contribute to and result from hypothyroid states [8].

Several clinical studies have attempted to evaluate serum zinc and copper levels in patients with hypothyroidism; however, the findings have been inconsistent. While many studies have reported significantly reduced serum zinc levels in hypothyroid patients, others have observed normal or variable copper levels, reflecting differences in dietary intake, geographic factors, disease severity, and methodological approaches [9–11]. These inconsistencies highlight the need for further region-specific studies, particularly in populations where nutritional deficiencies are common. India bears a substantial burden of hypothyroidism, with

a significant proportion of the population at risk for micronutrient deficiencies due to dietary patterns, socioeconomic factors, and malabsorption states. Understanding the status of trace elements such as zinc and copper in hypothyroid patients may provide valuable insights into disease pathogenesis and help identify potentially correctable factors that could improve clinical outcomes.

In this context, the present study was undertaken to evaluate serum zinc and copper levels in patients with hypothyroidism and to assess their association with thyroid hormone parameters, with the aim of contributing to a better understanding of the role of trace elements in thyroid dysfunction.

Materials and Methods

Study Design and Setting: This was a hospital-based case-control study conducted at Nalanda Medical College and hospital, Patna. Written informed consent was obtained from all participants.

Study Population: A total of 100 subjects aged between 18 and 65 years were included.

- **Cases (n = 50):** Patients with newly diagnosed or untreated primary hypothyroidism.
- **Controls (n = 50):** Age- and sex-matched euthyroid healthy individuals.

Inclusion Criteria

- Biochemically confirmed hypothyroidism (elevated TSH with low T3 and/or T4)
- Age 18–65 years

Exclusion Criteria

- Chronic liver or kidney disease
- Malabsorption syndromes
- Pregnancy
- Diabetes mellitus or other endocrine disorders
- Intake of zinc or copper supplements
- Acute or chronic inflammatory conditions

Sample Collection and Analysis: After overnight fasting, 5 mL of venous blood was collected under aseptic conditions. Serum was separated and stored at -20°C until analysis.

- **Serum T3, T4, TSH:** Chemiluminescence immunoassay
- **Serum Zinc and Copper:** Spectrophotometric method

Statistical Analysis: All collected data were entered into Microsoft Excel spreadsheets for data organization and preliminary processing. Statistical analysis was subsequently performed using the Statistical Package for the Social Sciences (SPSS) software. Continuous variables were expressed as mean \pm standard deviation (SD), while categorical variables were presented as frequencies and

percentages. The normality of data distribution was assessed prior to inferential analysis.

Comparisons between hypothyroid patients and euthyroid controls were carried out using Student’s independent t-test. Pearson’s correlation coefficient was employed to assess the relationship between serum trace element levels (zinc and copper) and thyroid hormone parameters (T3, T4, and TSH). All statistical tests were two-tailed, and a p-value of less than 0.05 was considered statistically significant.

Results

The mean age of hypothyroid patients was comparable to that of controls ($p > 0.05$). As expected, serum T3 and T4 levels were significantly lower and TSH levels were significantly higher in hypothyroid patients ($p < 0.001$) (Table 1).

Serum zinc levels were markedly reduced in hypothyroid patients compared to euthyroid controls (32.3 ± 19.1 vs 86.0 ± 17.9 $\mu\text{g/dL}$; $p < 0.001$). In contrast, serum copper levels showed no statistically significant difference between the two groups ($p > 0.05$) (Table 1).

Table 1: Comparison of Biochemical Parameters between Hypothyroid Patients and Controls

Parameter	Hypothyroid (Mean \pm SD)	Control (Mean \pm SD)	p-value
Age (years)	42.5 \pm 13.5	37.7 \pm 14.2	>0.05
T3 (ng/mL)	0.52 \pm 0.14	1.21 \pm 0.35	<0.001
T4 ($\mu\text{g/dL}$)	4.08 \pm 0.68	9.54 \pm 2.44	<0.001
TSH (mIU/L)	9.91 \pm 3.27	2.54 \pm 1.23	<0.001
Zinc ($\mu\text{g/dL}$)	32.3 \pm 19.1	86.0 \pm 17.9	<0.001
Copper ($\mu\text{g/dL}$)	104.7 \pm 30.0	103.2 \pm 22.4	>0.05

Serum zinc showed a significant positive correlation with T3 and T4 levels and a significant negative correlation with TSH levels, indicating an association between zinc deficiency and severity of hypothyroidism. Serum copper did not demonstrate any significant correlation with thyroid hormone parameters (Table 2).

Table 2: Correlation of Serum Zinc and Copper with Thyroid Hormones

Trace Element	T3	T4	TSH
Zinc	Positive correlation	Positive correlation	Negative correlation
Copper	Not significant	Not significant	Not significant

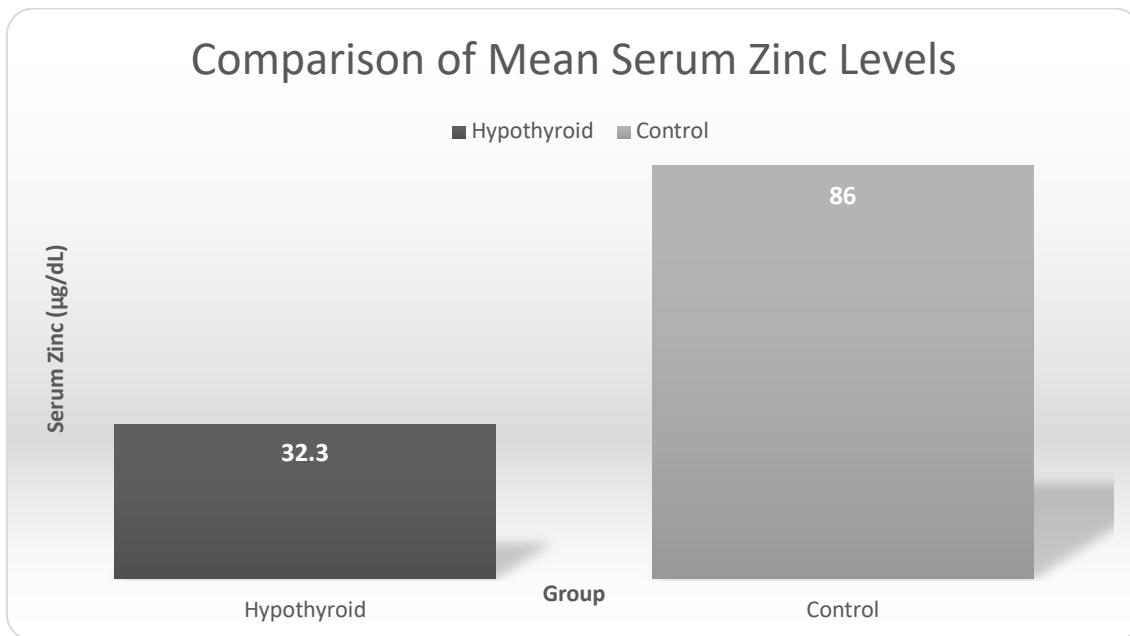


Figure 1: Comparison of Mean Serum Zinc Levels

Mean serum zinc levels were significantly reduced in hypothyroid patients compared to euthyroid controls ($p < 0.001$).

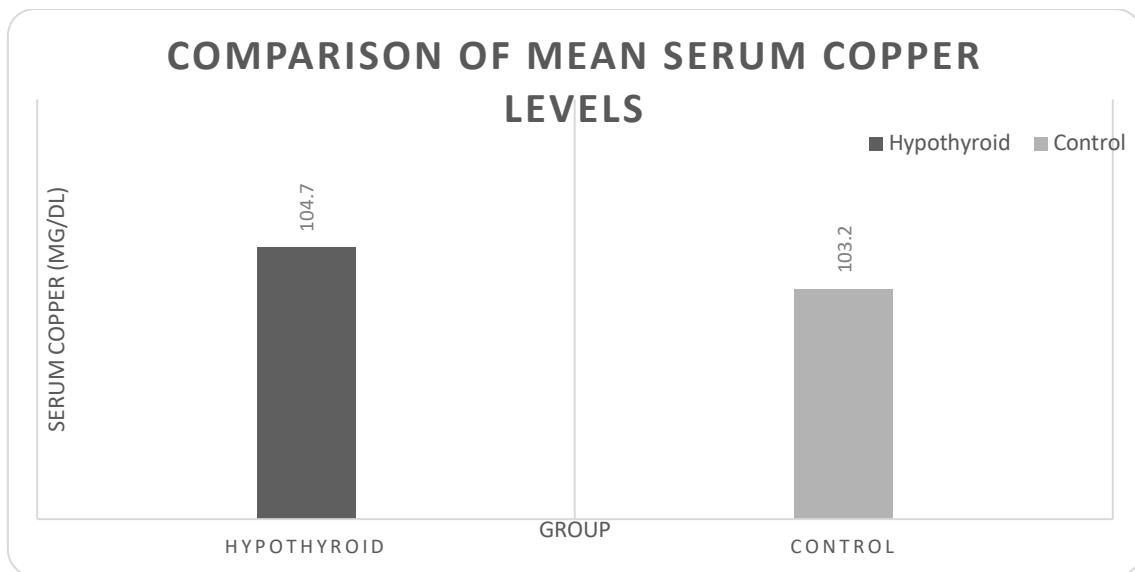


Figure 2: Comparison of Mean Serum Copper Levels

No statistically significant difference was observed in mean serum copper levels between hypothyroid patients and controls ($p > 0.05$).

Discussion

The present study demonstrates a significant reduction in serum zinc levels in patients with hypothyroidism when compared with euthyroid controls. This observation underscores the importance of zinc as a key micronutrient involved in thyroid hormone synthesis, metabolism, and action. The findings of this study support the growing body of evidence that micronutrient deficiencies, particularly zinc deficiency, may contribute to the pathophysiology and severity of hypothyroidism.

Several mechanisms may explain the reduced serum zinc levels observed in hypothyroid patients. Hypothyroidism is known to impair gastrointestinal motility and absorption, which may lead to decreased intestinal uptake of zinc. Additionally, thyroid hormones play an important role in regulating the transport and distribution of zinc across cell membranes and within tissues. Reduced thyroid hormone levels may therefore alter zinc homeostasis, resulting in decreased circulating zinc concentrations. Redistribution of zinc from plasma into tissues or increased urinary loss may further contribute to zinc depletion in hypothyroid states [12]. Zinc is essential for the activity of type-1 iodothyronine deiodinase, the enzyme responsible for peripheral conversion of thyroxine (T4) into the biologically active triiodothyronine (T3). Deficiency of zinc may thus impair this conversion, leading to reduced circulating T3 levels, as observed in the present study. Furthermore, zinc is a structural component of thyroid hormone receptors, which contain zinc-finger motifs that are critical for hormone-receptor binding and gene

transcription. Zinc deficiency may therefore reduce thyroid hormone action at the cellular level, even when hormone levels are marginally adequate [5].

The significant negative correlation observed between serum zinc and TSH levels in the present study suggests that increasing severity of thyroid dysfunction is associated with greater depletion of zinc stores. Elevated TSH reflects a compensatory response to declining thyroid hormone levels, and the inverse relationship with zinc further highlights the interdependence between zinc status and thyroid function. Similar associations have been reported in previous studies, which demonstrated reduced zinc levels in hypothyroid patients and improvement in thyroid hormone profiles following zinc supplementation [9,13].

In contrast to zinc, serum copper levels in the present study did not differ significantly between hypothyroid patients and euthyroid controls. This finding is consistent with several earlier studies reporting minimal or inconsistent alterations in copper levels in hypothyroidism [10,14]. Copper homeostasis is tightly regulated through intestinal absorption, hepatic storage, and biliary excretion, which may explain the relative stability of circulating copper levels despite thyroid dysfunction. Mild or moderate hypothyroidism may therefore be insufficient to produce measurable changes in serum copper concentrations.

Nevertheless, copper plays an important indirect role in thyroid hormone metabolism. Copper is required for the activity of enzymes involved in tyrosine metabolism, a key step in thyroid hormone synthesis. It also participates in antioxidant defense mechanisms that protect thyroid tissue from oxidative stress generated during hormone synthesis. Experimental studies have demonstrated that copper deficiency can exacerbate hypothyroid

states, suggesting that even subtle alterations in copper status may influence thyroid function under certain conditions [6]. The absence of significant copper alteration in the present study may be related to compensatory mechanisms, adequate dietary intake, or the relatively stable nature of serum copper levels.

The findings of the present study highlight the clinical relevance of assessing micronutrient status, particularly zinc, in patients with hypothyroidism. Zinc deficiency may not only contribute to the development and progression of hypothyroidism but may also impair the response to standard thyroid hormone replacement therapy. Identification and correction of zinc deficiency through dietary modification or supplementation could therefore represent a simple and cost-effective adjunct in the management of hypothyroid patients, especially in populations at risk for nutritional deficiencies.

In summary, the present study emphasizes the close association between zinc status and thyroid hormone metabolism and supports the role of zinc as an important modifiable factor in hypothyroidism.

Further large-scale and interventional studies are warranted to evaluate the therapeutic benefits of zinc supplementation and to clarify the complex interactions between trace elements and thyroid function.

Limitations

The present study has certain limitations that should be considered while interpreting the results. The sample size was relatively small, which may limit the generalizability of the findings to the wider population. Dietary intake of zinc and copper was not assessed; therefore, the influence of nutritional patterns on serum trace element levels could not be evaluated. Additionally, the study did not assess the long-term effects of zinc or copper supplementation on thyroid hormone levels or clinical outcomes, which restricts conclusions regarding potential therapeutic benefits.

Conclusion

Patients with hypothyroidism exhibit significantly reduced serum zinc levels, while serum copper levels remain largely unchanged. Zinc deficiency may contribute to impaired thyroid hormone metabolism and severity of hypothyroidism. Routine assessment of zinc status may be beneficial in the management of hypothyroid patients.

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