Determination of serum zinc and phosphorus levels in patients with hypothyroidism

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Abstract

Background

Various studies reported that serum zinc (Zn) and phosphorus (P) levels altered in patients with hypothyroidism and vice versa, but results were found inconsistent.

Aim

It was aimed to find the association between serum Zn and P in patients with hypothyroidism. **Material and**

Method

In this case-control study, a total of 100 subjects (50 newly diagnosed patients of hypothyroidism and 50 controls) were enrolled aged between 25 and 60 years. Biochemical parameters such as thyroid profile, serum Zn, and P were estimated in each subject. A $p < 0.05$ was considered statistically significant.

Result

The mean level of body mass index (BMI), thyroid-stimulating hormone (TSH), and serum P was found significantly elevated in cases compared to controls ($p < 0.001$). However, the mean level of triiodothyronine (T3), thyroxine (T4), and serum Zn was found significantly reduced in cases compared to controls ($p < 0.001$). The serum Zn has shown a significant negative correlation with T3 and BMI among cases ($r = -0.313$ $p < 0.05$, $r = -0.338$ $p < 0.05$, respectively). However, Serum P has shown a significant positive correlation with TSH and BMI among cases ($r = 0.310$ $p < 0.05$, $r = 0.449$ $p < 0.01$, respectively). Regression analysis indicated that serum Zn significantly predicted hypothyroidism ($p < 0.00$). Similarly, Serum P significantly predicted hypothyroidism ($p < 0.007$).

Conclusion

Results showed that serum Zn levels were significantly reduced and serum P levels were significantly elevated in cases compared to controls. The serum Zn and serum P both may act as predictors for hypothyroidism and its complications.

INTRODUCTION

Hypothyroidism is defined as serum thyroid-stimulating hormone (TSH) levels elevated and thyroxine (T4) levels reduced from the normal reference range [1, 2]. The reference range of TSH is mainly considered 0.4 – 4.0 mIU/L [3]. A study was conducted in eight major cities in India and reported a 10.95% overall prevalence of hypothyroidism [4]. Hypothyroidism affects overall body functions from metabolism to immunity to the nervous system [5]. Hypothyroidism affects the metabolism of essential trace elements such as zinc (Zn), copper (Cu), iron (Fe), manganese (Mn), and iodine (I) [6].

Zn is an essential element required for the proper functioning of the deiodinase enzyme and conversion of T4 into triiodothyronine (T3). Zn deficiency also inhibits the synthesis of Thyrotropin-releasing hormone (TRH). Moreover, Zn deficiency may cause hypothyroidism, and hypothyroidism may result in Zn deficiency [7]. Zn is also required to stimulate the gene expression of thyroglobulin and thyroperoxidase [8]. Absorption and excretion of Zn are affected by thyroid hormones [9].

Phosphorous (P) is a predominant intracellular anion present as phosphate. The normal plasma inorganic phosphate (Pi) concentration in an adult is 2.5 to 4.5 mg/dl. It is an essential component of the body that plays a vital role in the constituent of cell membrane structure, nucleic acids, cellular energy adenosine triphosphate (ATP) synthesis, and intracellular signaling proteins. It is required to maintain acid-base homeostasis through a phosphate buffer system [10].

The average daily consumption of phosphate for adults is about 1000 mg mainly absorbed through jejunum. Active absorption of phosphate occurs through sodium-dependent phosphate co-transporter type IIb (NPT2b) [11]. An experimental study illustrated that sodium-dependent phosphate co-transportation is mainly regulated by the T3 thyroid hormone [12].

In this context, it is important to find the association of serum Zn and P with thyroid hormone. The present study is aimed to find the association between serum Zn and P levels in patients with hypothyroidism.

MATERIALS & METHODS

Subject Selection

In this case-control study, a total of 100 subjects (50 newly diagnosed patients of hypothyroidism and 50 age and gender-matched healthy controls) were enrolled from the Out-Patient Department of Medicine, University Medical Hospital. Subjects aged between 25 and 60 years. A detailed demographic and medical history was taken from each subject. Written consent was taken from each subject.

Inclusion and exclusion criteria

Newly diagnosed patients of hypothyroidism were considered as cases (TSH ≥ 5.0μIU/mL) [13]. The subject who has a medical history of any chronic disease such as diabetes, cardiovascular disease, dyslipidemia, liver dysfunction, kidney dysfunction, typhoid, jaundice, or any infectious disease such as hepatitis, sexually transmitted disease, HIV, tuberculosis, or pregnant woman was also excluded from the study.

Laboratory Investigations

Sample collection

a total of 5ml venous blood was collected into a plain vial under aseptic conditions. For the separation of the serum sample centrifugation was done at 3000rpm for 5 minutes. Transferred the upper pale-yellow supernatant into a fresh micro-centrifuge tube and store it at -20 ^{0}C deep fridge till further laboratory investigation.

Thyroid Profile

TSH, T4, and T3 were analyzed by using a commercially available kit by Mini-Vidas Compact Automated Immunoanalyzer System based on the Enzyme-Linked Fluorescent Assay (ELFA) principles (BioMerieux S.A. France) [14].

Serum Zinc

Serum zinc was determined by the Nitro PAPS Colorimetric method [15].

Serum Phosphorus

Serum phosphorus was determined by phosphomolybdate *UV-VS* Spectrophotometric method [16].

Statistical Analysis

Statistical analysis was performed using SPSS 20.0 (IBM SPSS Statistics, US). Student unpaired t-test was used to compare the mean of variables between cases and controls. Data were represented as Mean ± SD. Pearson correlation analysis was done among cases. Regression analysis was also performed. A p-value of < 0.05 was considered statistically significant.

RESULT

The mean level of BMI, TSH, and serum P was found significantly elevated in cases compared to controls ($p = 0.004$, $p < 0.001$, and $p = 0.01$, respectively). However, the mean level of T3, T4, and serum Zn was found significantly reduced in cases compared to controls ($p < 0.001$, $p = 0.007$, and $p < 0.001$, respectively), illustrated in Table 1 **&** Fig. 1a & 1b.

Table 1
Characteristic of the case and controls

S. No.	Parameters	Control (N = 50)	Case (N = 50)	P. Value
1	Age (Year)	35.38 ± 6.79	36.68 ± 8.91	0.41
2	Gender(M\F)	25/25	25/25	1.00
3	BMI (kg/m^2)	24.11 ± 3.71	26.41 ± 2.47	0.004**
4	T3 (nmol/L)	1.91 ± 0.31	1.55 ± 0.37	< 0.001**
5	T4 (nmol/L)	110.38 ± 20.68	98.68 ± 21.80	0.007**
6	TSH (µIU/mL)	2.61 ± 0.98	10.07 ± 3.09	< 0.001**
7	Serum Zn (µg/dL)	90.45 ± 15.81	77.22 ± 14.50	< 0.001**
8	Serum P (µg/dL)	4.12 ± 0.81	4.57 ± 0.90	0.01*

***p < 0.01, considered statistically significant.*

**p < 0.05, considered statistically significant.*

BMI: Body mass index, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid-stimulating hormones, P: Phosphorus, Zn: Zinc

The serum Zn has shown a significant negative correlation with T3 and BMI among cases ($r= -0.313$ $p < 0.05$, $r= -0.338$ $p < 0.05$, respectively). However, Serum P has shown a significant positive correlation with TSH and BMI among cases ($r = 0.310$ $p < 0.05$, $r = 0.449$ $p < 0.01$, respectively), illustrated in Table 2 **&** Fig. 2.

Table 2
Correlation of Serum Zn and Serum P with parameters of hypothyroidism

S. No.	Parameters	Serum Zn (r)	Serum P (r)
1	Age (years)	-0.223	0.097
2	T3 (nmol/L)	**-0.313***	-0.029
3	T4 (nmol/L)	-0.129	0.062
4	TSH (µIU/mL)	0.060	**0.310***
5	Serum Zn (µg/dL)	1	-0.053
6	Serum P (µg/dL)	-0.053	1
7	BMI (kg/m^2)	**-0.338***	**0.449****

***Correlation is significant at the 0.01 level (2-tailed).*

**Correlation is significant at the 0.05 level (2-tailed).*

BMI: Body mass index, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone, P: Phosphorus, Zn: Zinc

Regression analysis indicated that serum Zn significantly predicted hypothyroidism (F (6, 43) = 8.026, p < 0.00). The R^2 = 0.528 depicts that model 1 explains 52.8% of variations in hypothyroidism due to serum Zn. Similarly, Serum P significantly predicted hypothyroidism (F (6, 43) = 3.475, p < 0.007). The R^2 = 0.327 depicts that model 2 explains 32.7% of variations in hypothyroidism due to serum P, illustrated in Table 3.

Table 3
Model Summary

Model	R	R Square	Adjusted R Square	Std. Error of the Estimate	Change Statistics				
					R Square Change	F Change	df1	df2	Sig. F Change
1	0.727[a]	0.528	0.462	10.63126	0.528	8.026	6	43	0.000*
2	0.571[b]	0.327	0.233	0.78932	0.327	3.475	6	43	0.007*

(Model 1): [a] Dependent Variable: Serum Zn

Predictors: (Constant), BMI, T3, T4, TSH, Age, Serum P

(Model 2): [b] Dependent Variable: Serum P

Predictors: (Constant), BMI, T3, T4, TSH, Age, Serum Zn

*$p < 0.05$ considered statistically significant

BMI: Body mass index, T3: Triiodothyronine, T4: Thyroxine, TSH: Thyroid stimulating hormone, P: Phosphorus, Zn: Zinc

DISCUSSION

Results showed that the mean level of BMI and serum P was found significantly elevated and serum Zn was reduced in cases compared to controls. In addition, the serum Zn has shown a significant negative correlation with T3 and BMI among cases. However, Serum P has shown a significant positive correlation with TSH and BMI among cases. Regression analysis indicated that serum Zn and P both may act as significant predictors for hypothyroidism and its complications.

It was reported that the morbid obesity category has shown a three-fold increment in the levels of TSH [17]. Another study reported that BMI has shown a significant association with hypothyroidism in young individuals [18]. Similarly, a positive association was found between BMI and serum TSH [19]. Another study reported that TSH levels increase with increases in BMI in females and T4 levels decrease with increases in BMI in males [20]. It was suggested that hypothyroidism influences normal metabolic activity and leads to excessive fat accumulation and body weight [21].

For the biosynthesis of thyrotropin-releasing hormone, the enzyme requires Zn as a cofactor. Zn deficiency affects the functions of the thyroid hormone. The study reported that serum Zn levels were found significantly low in patients with hypothyroidism [22, 23]. In addition, Khan et al reported that the serum Zn has shown a significant negative correlation with T4 [24]. Assessment of serum Zn levels is essential in patients with hypothyroidism because several studies reported that Zn deficiency may increase the disease complications and be associated with hypertension [25], type 2 diabetes mellitus [26], immune dysfunction [27], and liver cirrhosis [28]. A recent study reported that Zn supplementation may prevent the incidence of hypothyroidism [29]. Another study reviewed that Zn supplementation improves thyroid functions and increases the levels of T3 in overweight or obese individuals [30].

A study reported that levels of TSH and serum P were significantly elevated in cases compared to controls [31, 32]. Similarly, serum P was found significantly high in patients with hypothyroidism compared to controls [33]. However, Gammage et al reported that serum P levels were decreased in hypothyroidism patients [34]. Diana et al reported that serum P has a significant positive correlation with TSH and BMI [35]. However, Kotb et al suggested that serum P may act as a significant predictor of hypothyroidism complications such as uremic pruritis [36]. It was suggested that the management of serum P can play a significant role in weight loss in individuals and chronic diseases [11, 37]. Assessment of serum P levels is essential in patients with hypothyroidism, because elevated serum phosphorus levels may increase the disease complications and be associated with microvascular dysfunction [38], coronary artery calcification [39], chronic kidney disease [40], and cardiac arrest [41].

Limitations of the study

This study has been conducted with small sample size. This study is part of a post-graduate degree and has to complete in a time-restricted manner. Further study is required to confirm the current findings in a large sample size.

CONCLUSION

Results showed that serum Zn levels were significantly reduced and serum P levels were significantly elevated in cases compared to controls. In addition, the serum Zn has shown a significant negative correlation with T3 while serum P has shown a significant positive correlation with TSH among cases. The serum Zn and serum P both may act as predictors for hypothyroidism and its complications.

Declarations

FUNDING: This study was not funded by any funding agency or company.

ETHICAL APPROVAL: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee (IEC Approval No. IEC/IIMS&R/2022/15) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

INFORMED CONSENT: Written informed consent was obtained from all individual participants included in the study.

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CONFLICTS OF INTEREST: Authors declared that they have no conflict of interest.

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Figures

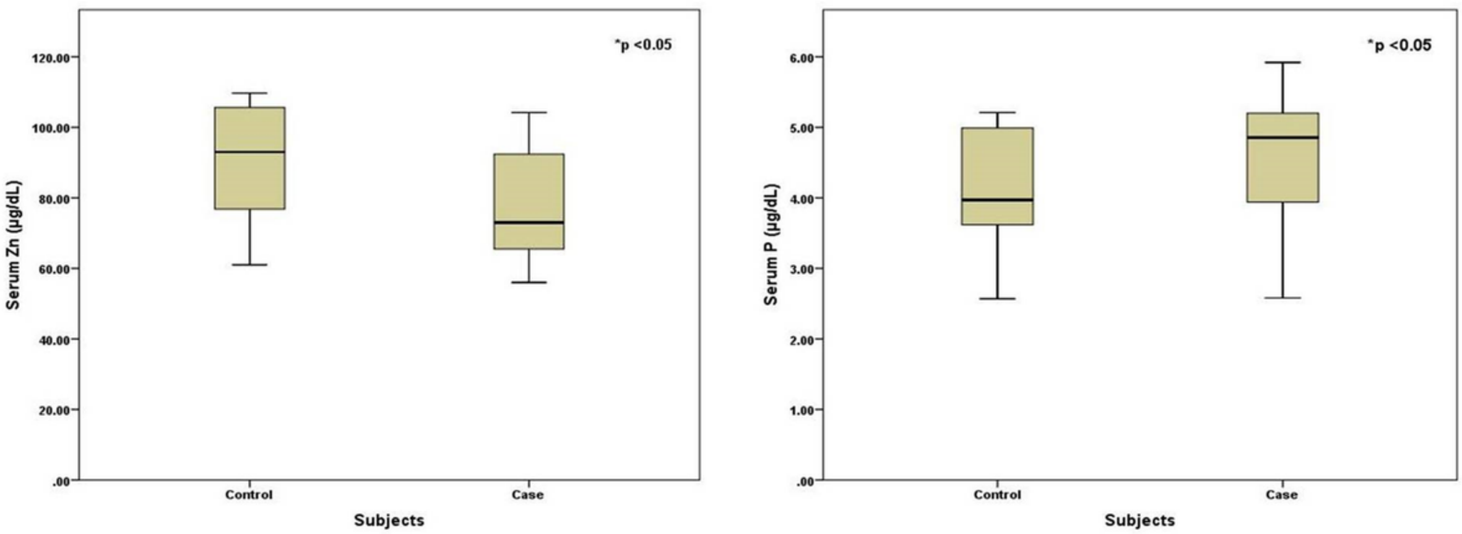

Figure 1

a:Serum Zn levels in cases and controls

b:Serum P levels in cases and controls

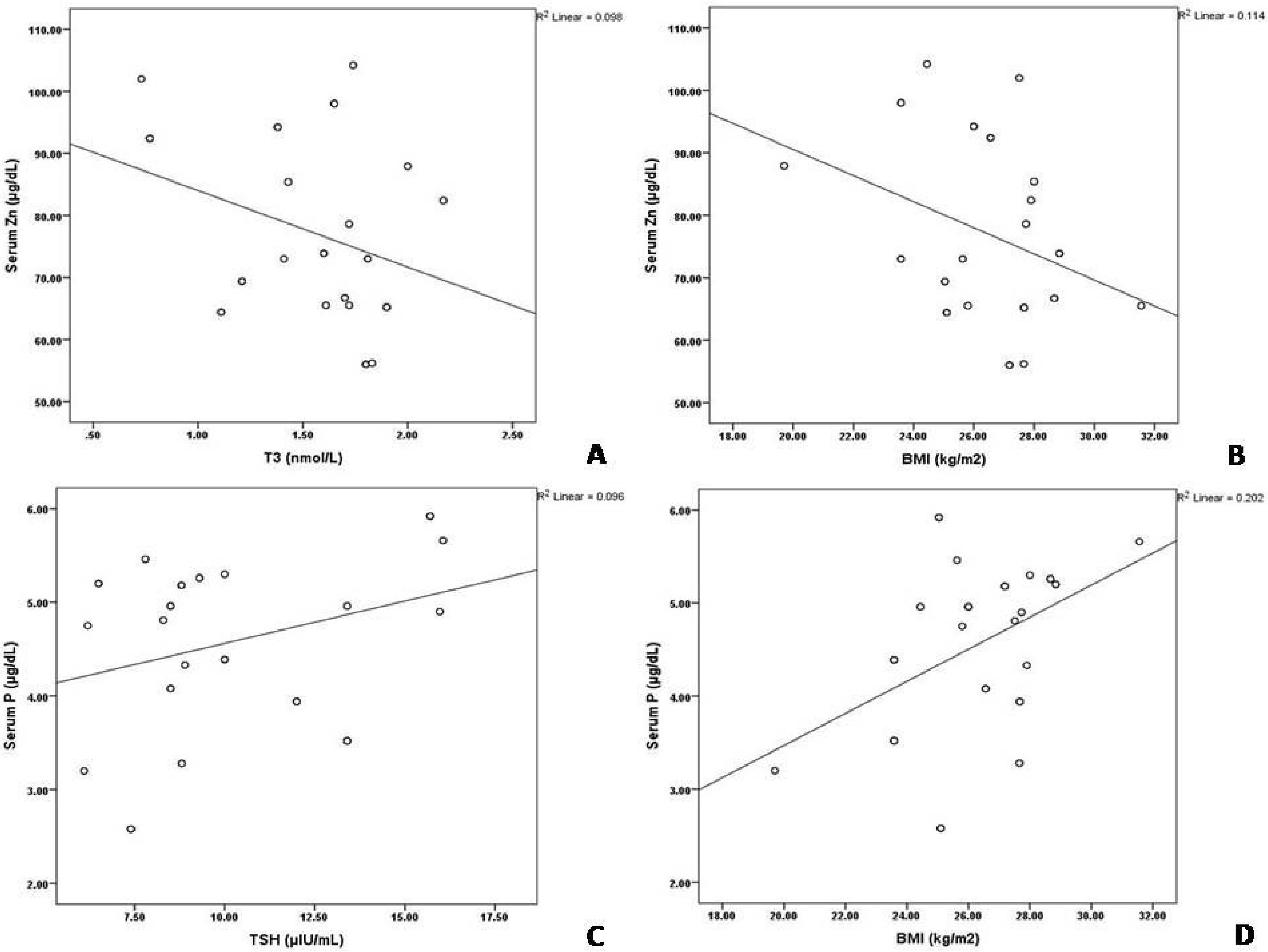

Figure 2

Correlation of Serum Zn and P with T3, TSH, and BMI among cases