

Correlation of serum uric acid and serum creatinine in hypothyroidism

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ABSTRACT


Background: Hypothyroidism is a progressive disorder that presents with diverse degrees of thyroid failure and metabolic consequences. Purine metabolism can be affected by disturbance in thyroid hormones, which leads to alteration in the uric acid levels, leading to hyperuricemia and subsequently causing gout. Also, hemodynamic changes occur in hypothyroidism that leads to reduction in renal plasma flow and glomerular filtration rate, which also causes increase in the levels of serum uric acid and serum creatinine. **Aims and Objective:** To determine whether thyroid dysfunction, subclinical and overt, has deleterious effects on renal function. **Materials and Methods:** This was a cross-sectional study that comprised 108 individuals (56 cases and 52 controls; 52 men and 56 women) aged between 20 and 60 years. Case group comprised suspected cases of hypothyroidism. Serum TSH, T4, T3, uric acid, and creatinine were estimated after applying inclusion and exclusion criteria. **Result:** Uric acid and creatinine levels were significantly elevated in case group as compared to control group (7.09 ± 0.45 and 1.52 ± 0.16 mg/dL versus 4.08 ± 0.25 and 0.62 ± 0.05 mg/dL, respectively; $p < 0.001$). There was insignificant correlation between serum uric acid and creatinine levels with hypothyroidism ($r = 0.185$, $p = 0.172$ and $r = 0.082$, $p = 0.550$). Also, there was no significant correlation between serum uric acid and creatinine levels with the age in hypothyroidism ($r = 0.143$; $p = 0.292$ and $r = -0.154$; $p = 0.257$, respectively). **Conclusion:** Hypothyroidism causes significant increase in serum uric acid and creatinine levels. Therefore, we would emphasize the importance of the routine evaluation of serum uric acid and creatinine levels in patients with hypothyroidism.

KEY WORDS: Uric Acid; Creatinine; Hypothyroidism

INTRODUCTION

Thyroid gland is one of the largest endocrine glands in the body, which secretes thyroxine (T4) and triiodothyronine (T3). The production of T4 and T3 in the thyroid gland is regulated by the hypothalamus and pituitary gland. Hypothyroidism is a progressive disorder that presents with diverse degrees of thyroid failure and metabolic consequences. An increase in serum thyroid-stimulating hormone (TSH) levels is a very early biochemical marker of

impending thyroid failure resulting from the gradual decline of T4 and, at a later stage, of T3. Hypothyroidism is a clinical syndrome caused by the deficiency of thyroid hormones that cause a generalized slowing of metabolic processes.^[1] Thyroid hormones (T4 and T3) regulate the rate of metabolism, affect growth, and modulate energy utilization by increasing the basal metabolic rate, increasing oxygen consumption, and facilitating heat production.^[2] Physiological interactions exist between thyroid hormones and uric acid synthesis and excretion and even minor degree of hypothyroidism leads to adverse effects in various tissues, even though clinically the patients are euthyroid. Furthermore, these hormones affect most of the metabolic pathways in the body—purine metabolism is one of these metabolic pathways can be affected by disturbance in thyroid hormones. This leads to alteration in the uric acid levels, causing hyperuricemia and subsequently gout.^[3] Also, hemodynamic changes occur in hypothyroidism that leads to reduction in renal plasma flow and glomerular filtration rate, which also causes increase in the levels of serum uric acid and

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serum creatinine.^[4,5] Thus, hypothyroidism is associated with many biochemical abnormalities such as increased serum creatinine and uric acid levels.^[6,7] This study was conducted to determine whether thyroid dysfunction, subclinical and overt, has deleterious effects on renal function.

MATERIALS AND METHODS

This was a retrospective, cross-sectional study conducted in a 550-bedded, rural-based tertiary-care hospital. A study protocol was designed before undertaking this study, which was approved by the human research ethics committee. Serum TSH, T4, T3, uric acid, and creatinine data of the patients were collected after applying inclusion and exclusion criteria. Because no extra samples were collected and patients' details were not disclosed, the consent forms were waived off. The study included 108 individuals who visited the Health-check and routine OPDs. Men and women between the age group of 20–70 years were included in this study and were divided into cases and controls. Controls included individuals without any thyroid disorder whereas cases comprised patients diagnosed with hypothyroidism.

The diagnosis was based on decreased serum T3 and T4 levels associated with increased TSH levels. All patients with hypothyroidism were diagnosed based on T3 (normal: 1.3–3.1 nmol/L), T4 (normal: 66–181 nmol/L), and TSH (normal: 0.5–4.2 mIU/L) levels of the patients.

Patients who were known cases of diabetes, hypertension, renal failure (acute and chronic), hepatic disorders, bone disorders, malignancies, or were on chemotherapy or radiotherapy, were pregnant were excluded from the study. Serum TSH, T4, and T3 levels were estimated using Cobas e411, which is based on electrochemiluminescence (ECL) technology. T4 and T3 levels were estimated by competitive method of ECL whereas TSH was estimated by sandwich method. Serum uric acid and creatinine levels were estimated using colorimetric method on Cobas Integra 400 plus. Uric acid level was estimated using uricase enzymatic method whereas creatinine level was estimated using buffered kinetic Jaffé reaction method.

Statistical Analysis

Demographic data analysis was performed and unpaired *t*-test was used to show the significance of TSH, T4, T3, uric acid, and creatinine levels between cases and controls. The entire data were analyzed using the software MedCalc, version 12.5. A *p*-value of < 0.05 was considered to be statistically significant.

RESULTS

This study comprised 108 individuals (56 cases and 52 controls) with mean age of 44.57 ± 10.97 years. Among 108 individuals, 52 were men and 56 were women [Table 1]. Case group had a mean age of 45.27 ± 11.88 years; of which, 27 were men and 29 were women. However in control group, 52 individuals had

Table 1: Demographic data of all individuals included in study groups (n = 108)

Age (years)	Gender		Total (%)
	Female (%)	Male (%)	
21–30	8 (7.41)	3 (2.77)	11 (10.18)
31–40	17 (15.75)	15 (13.89)	32 (29.64)
41–50	11 (10.18)	18 (16.67)	29 (26.85)
51–60	15 (13.89)	14 (12.96)	29 (26.85)
61–70	5 (4.63)	2 (1.85)	7 (6.48)
Total (%)	56 (51.85)	52 (48.15)	108 (100)

Table 2: Descriptive statistic of plasma levels of uric acid, creatinine, T3, T4, and TSH in cases and controls

Variable	Cases (mean ± SD) n = 56	Controls (mean ± SD) n = 52	p-value	Degree of freedom
Serum T3 (nmol/L)	1.23 ± 0.07	1.81 ± 0.11	<0.0001	106
Serum T4 (nmol/L)	68.77 ± 6.72	105.4 ± 5.74	<0.0001	106
Serum TSH (mIU/L)	8.00 ± 1.06	2.20 ± 0.25	<0.0001	106
Serum uric acid (mg/dL)	7.09 ± 0.45	4.08 ± 0.25	<0.0001	106
Serum creatinine (mg/dL)	1.52 ± 0.16	0.62 ± 0.05	<0.0001	106

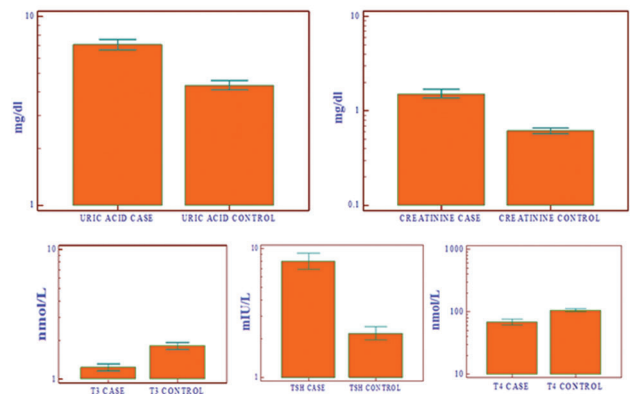


Figure 1: Box and whisker plot showing comparison of different parameters between case and control group.

mean age of 43.83 ± 9.96 years; of which, 25 were men and 27 were women. Table 2 shows plasma levels of uric acid, creatinine, T3, T4, and TSH in cases and controls with significant difference [Figure 1]. Uric acid and creatinine levels were significantly increased in patients with hypothyroidism (7.09 ± 0.45 and 1.52 ± 0.16 mg/dL, respectively; *p* < 0.001)

Table 3: Correlation between serum uric acid and creatinine levels with duration of disease and ages in patients with hypothyroid

Variable	Statistic	Ages (years)	Duration
Serum uric acid (mg/dL)	Pearson correlation (<i>r</i>)	0.143	0.185
Significance (<i>p</i>)	0.292	0.172	
Serum creatinine (mg/dL)	Pearson correlation (<i>r</i>)	-0.154	0.082
Significance (<i>p</i>)	0.257	0.550	

as compared to control group (4.08 ± 0.25 and 0.62 ± 0.05 mg/dL, respectively; $p < 0.001$). Table 3 shows an insignificant correlation exists between serum uric acid and creatinine levels with duration of hypothyroidism ($r = 0.185$, $p = 0.172$ and $r = 0.082$, $p = 0.550$), respectively. Also, there is no significant correlation between serum uric acid and creatinine levels with the age in patients with hypothyroidism ($r = -0.143$, $p = 0.292$ and $r = -0.154$, $p = 0.257$), respectively.

DISCUSSION

Hypothyroidism and Hyperuricemia

Our study evaluated the possible interrelationship between purine nucleotide metabolism and thyroid endocrine disorders, mainly primary hypothyroidism. Significant increase in uric acid levels was found in the patients with hypothyroidism. Moreover, our study showed that hyperuricemia in hypothyroidism is associated with increased serum creatinine levels. This fact suggests that hypothyroid hyperuricemia is secondary to reduction in renal plasma flow and glomerular filtration.

Giordano et al.^[8] conducted a study among 28 patients with primary hypothyroidism and showed 33.3% prevalence of hyperuricemia in patients with hypothyroidism. Similar studies were conducted by Erickson et al.,^[9] Dariyerli et al.,^[10] and Yokogoshi and Saito^[11] and found hyperuricemia in patients with hypothyroidism. The results of our study were in agreement with the earlier mentioned studies.

Hypothyroidism and Hypercreatininemia

The authors concluded that the hypothyroid state is associated with a consistent elevation in the serum creatinine level, presumably related to a decrease in the GFR. The changes in serum creatinine levels develop rapidly and appear to be reversible. It may be clinically relevant to know of this association and the fact that it could account for creatinine elevation in a patient with hypothyroidism. It should also alert the clinician to consider evaluation of thyroid function in a patient who has a modest, serum creatinine and uric acid elevation but whose thyroid status is unknown.

Kreisman and Hennessey^[12] evaluated serum creatinine levels in 24 consecutive patients with iatrogenically induced hypothyroidism in conjunction with treatment of thyroid carcinoma. The creatinine values were obtained in a subgroup of 15 patients during

the euthyroid state (before induction of hypothyroidism). The mean creatinine values were significantly higher (increased by 34.4%) in 90% of this group during hypothyroidism than during the euthyroid state. The mean hypothyroid creatinine values were significantly higher during hypothyroidism than during the euthyroid state. Creatinine values increased by 34.4% after induction of hypothyroidism. In another study conducted by Schmid et al.^[13] among 14 newly diagnosed patients with hypothyroidism, mean serum creatinine level was found to be elevated and decreased after thyroxine replacement therapy.

Merla et al.^[14] conducted a study on 30 patients with hypothyroidism with heart failure and observed that heart failure patients with insufficiently treated hypothyroidism have worse renal function than the patients whose thyroid function is normal or whose hypothyroidism is effectively treated.

Nakahama et al.^[15] conducted a study in which treatment of hypothyroidism resulted in a significant reduction of serum creatinine levels in two cases indicating that TSH should be considered in screening procedures of patients with chronic renal failure presenting with recent accelerated aggravation of renal function. The results of our study were in agreement with the earlier mentioned studies.

CONCLUSION

This study indicates the profound influence of thyroid hormone on renal function. This information would avoid unnecessary investigations, treatment cost, and worry in patients presenting with either increased creatinine or gout with undetermined thyroid status. Moreover, hypothyroid-induced renal dysfunction may lead to adverse clinical consequences, especially among patients on medications cleared by the kidneys. The thyroid function should, therefore, be routinely assessed for evaluation of patients presenting with deranged renal function and vice versa. Therefore, we would emphasize the importance of the routine evaluation of serum uric acid and creatinine levels in patients with hypothyroidism.

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