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ORIGINAL ARTICLE

Correlation between serum uric acid and thyroid function tests in patients with hypothyroidism

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ABSTRACT

Background: Hypothyroidism has been associated with hyperuricemia due to reduced renal uric acid excretion. This study aimed to determine the correlation between serum uric acid and thyroid function tests in hypothyroid patients.

Methods: This cross-sectional study was performed at the Department of Pathology, Nishtar Hospital Multan, from 22nd January to 21st July 2025. A total of 232 newly diagnosed hypothyroid patients aged 20-70 years were recruited through non-probability consecutive sampling. Individuals with renal, hepatic, or cardiovascular disease, or using anti-hypertensive or hypouricemic agents, were excluded. Serum uric acid and thyroid function tests were analyzed on Cobas c31 chemistry autoanalyzer under standard internal quality control protocols. Data were analyzed using SPSS version 25. Normality was evaluated by Shapiro-Wilk test. Correlation between uric acid and thyroid parameters was determined using Spearman's rho, with $p<0.05$ considered significant.

Results: The median age of participants was 38 years (IQR: 27 to 49.75); 70.7% were female, and 51.3% of the participants were obese. Median serum uric acid, TSH, free T3, and free T4 values were 7.5 mg/dl, 14.05 mU/L 0.31 ng/dl and 0.51 ng/dl, respectively. Serum uric acid showed a strong positive correlation with TSH (r_s=0.81, $p<0.001$) and strong negative correlations with free T3 (r_s= –0.736, $p<0.001$) and free T4 (r_s= –0.779, $p<0.001$). These correlations remain significant after stratification by age gender obesity and smoking status.

Conclusion: Serum uric acid is positively correlated with TSH levels and negatively correlated with T3 and T4 in hypothyroid patients, suggesting that hyperuricemia may serve as a biochemical marker of disease severity and metabolic dysregulation in hypothyroidism.

Key words: Hyperuricemia, Hypothyroidism, Thyroid function tests, Uric acid.

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Introduction

Hypothyroidism is one of the commonest endocrine diseases seen in routine clinical practice. It is due to thyroid hormones deficiency, which disrupts many metabolic functions playing vital roles in the body (1). In Asian population, the prevalence of hypothyroidism varies from 3.8% to 4.6% (2). Two hormones are produced by thyroid gland i.e., T3 and T4. These hormones are needed to maintain adult metabolic homeostasis, to control body temperature, and to promote cell differentiation (3).

There are several connections between thyroid hormones and the kidneys. The physiology and development of the renal system depend heavily on thyroid hormones (4). They have both intrinsic and pre-renal actions, which raise the glomerular filtration rate (GFR) and renal blood flow (5). Hemodynamic alterations produced by hypothyroidism include a reduction in renal plasma flow and GFR, which can lead to a disruption in renal function (6). Additionally, decreased T3 and T4 levels affect purine metabolism, which may alter uric acid (UA) levels (7).

One hundred and fourteen participants were enrolled by Noureen F et al. and split into three equal groups. Patients with overt hypothyroidism were in Group I; those with subclinical hypothyroidism were in Group II; and healthy controls were in Group III. Patients with overt hypothyroidism had significantly higher mean serum UA levels (7.5±0.84 mg/dL) than those in the subclinical hypothyroid and control groups (4.7±0.8, 4.6±1 mg/dL, respectively). Only in group I, there was a statistically significant positive connection between serum uric acid and TSH levels ($r = 0.53$, $p<0.001$) (8).

Helmy MY et al recruited 105 participants and split them up into three equal groups. There were individuals diagnosed with primary hypothyroidism in Group I, with primary hyperthyroidism in Group II, and control subjects in Group III (35 in each group). UA levels varied statistically significantly, with group I having the highest levels (6.6± 1.32 mg/dl, 6.3± 0.8 mg/dl, and 5.4± 0.47 mg/dl, respectively), followed by group II and group III. There was a statistically significant positive connection between UA and FT3 (r=0.54) and FT4 (r=0.48) and a statistically significant negative association between UA and TSH (r -0.733) in hyperthyroid patients (9).

The goal of the current investigation was to determine whether thyroid function tests and serum UA levels were correlated in persons with overt hypothyroidism in our local setting. Serum uric acid levels would act as an early warning sign for possible complications in hypothyroidism patients, enabling prompt action, if a significant association is discovered. It would be beneficial to regularly check uric acid levels in hypothyroid patients to determine their risk of developing cardiovascular illnesses or gout.

Methods

This cross-sectional study was done at Pathology Department of Nishtar Hospital Multan. The study spanned over a period of six months from 22nd January 2025 to 21st July 2025 after approval from the institutional ethics review committee (ERC# 21474/NMU, dated: 09-12-2024). A total of 232 newly diagnosed hypothyroidism patients, 20 – 70 years of age, either male or female gender, **from the outpatient** department of medicine and endocrinology were recruited in the research after obtaining informed consent through non-probability consecutive sampling. Hypothyroidism was labelled if free T3 (ng/dl) < 0.52 (normal 0.52 – 1.9) and serum TSH levels (mU/L) > 5.4 (0.4 – 5.4), measured by chemiluminescence immunoassay (CLIA). Sample size of 232 patients was calculated through PASS 11 software using one sample correlation formula assuming correlation of 0.53 between serum uric acid and TSH (8), power of 80%, significance level of 5% and expected correlation of 0.65. Based on history, clinical examination and medical record review patients with renal or liver dysfunction, cardiovascular disease and on anti-

hypertensive or hypouricemic drugs will be excluded.

Patient characteristics like age, gender, obesity and smoking status were recorded. Thyroid function test – TSH, free T3 and free T4 on diagnosis of hypothyroidism were recorded. The tests were performed by chemiluminescent immunoassay (CLIA). The lab routinely runs two-level control sera (normal and pathological) with every batch or shift to monitor assay precision and accuracy. Instruments were calibrated at manufacturer-recommended intervals using traceable calibrators provided with each reagent lot. After 12 hours overnight fast, all participants underwent aseptic venipuncture and two ml of blood were collected in clot tubes for serum uric acid testing. Serum was separated after centrifugation at 3000 rpm for five minutes. Serum uric acid levels were measured Cobas c311 chemistry autoanalyzer.

The data were analysed through SPSS version 25. Normality of numerical data was evaluated through Shapiro-Wilk test. Age, serum uric acid and thyroid functions being non-normal are documented as median and interquartile range. Categorical variables are documented as frequency and percentages. Correlation between serum UA and thyroid function tests was evaluated through Spearman's (rho) test and p-value <0.05 was taken as significant. Confounding was assessed through stratification on patient characteristics and correlations were measured for each stratified group.

Results

The median age of the study participants was 38 (27.0 – 49.75) years and 53% (n=123) were below 40-years of age. The females constituted 70.7% (n=164) of the study participants. The participants were obese in 51.3% (n=119) of the cases and smoker in 24.6% (n=57) of cases. The median levels of serum uric acid (mg/dl), TSH (mU/L), free T3 (ng/dl), and free T4 (ng/dl) were 7.5 (6.9 – 8.9), 14.05 (7.58 – 49.52), 0.31 (0.21 – 0.38), and 0.51 (0.40 – 0.58) respectively [Table 1].

Table 1: Characteristics of patients newly diagnosed with hypothyroidism (N=232)

Age (years), median (IQR)	38 (27.0 – 49.75)
< 40-years	123 (53)
≥ 40-years	109 (47)
Gender – Male	68 (29.3)
Female	164 (70.7)
Obese – Yes	119 (51.3)
Smokers – Yes	57 (24.6)
Serum Uric Acid (mg/dl), median (IQR)	7.5 (6.9 – 8.9)
TSH (mU/L), median (IQR)	14.05 (7.58 – 49.52)
Free T3 (ng/dl), median (IQR)	0.31 (0.21 – 0.38)
Free T4 (ng/dl), median (IQR)	0.51 (0.40 – 0.58)

Serum uric acid had significant positive correlation with TSH 0.81 (0.76 – 0.85, p-value <0.001), negative correlation with free T3 - 0.736 (-0.79 – -0.671, p-value < 0.001) and free T4 (- 0.779 (-0.827 – 0.721), p-value < 0.001) [Table 2].

Table 2: Correlation of serum uric acid with thyroid functions in patients with hypothyroidism (N=232)

Thyroid functions	Spearman correlation (rho)	p-value
TSH	0.859 (0.819 – 0.890)	< 0.001
Free T3	- 0.794 (-0.838 – -0.739)	< 0.001
Free T4	- 0.779 (-0.827 – 0.721)	< 0.001

After stratification on patient characteristics, correlation of serum uric acid with TSH, free T3 and free T4 remained significant in all stratified groups [Table 3].

Table 3: Effect of demographic characteristics on correlation of serum uric acid with thyroid functions in patients with hypothyroidism (N=232)

Characteristics	TSH	Free T3	Free T4
< 40-years	0.909 (0.872 – 0.936)	-0.860 (-0.901 - -0.803)	-0.839 (-0.885 - -0.775)
p-value	*< 0.001*	*< 0.001*	*< 0.001*
≥ 40-years	0.774 (0.683 – 0.842)	-0.694 (-0.783 - -0.578)	-0.680 (-0.772 - -0.560)
p-value	*<0.001*	*<0.001*	*<0.001*
Male	0.904 (0.847 – 0.941)	-0.815 (-0.884 - -0.712)	-0.810 (-0.880 - -0.704)
p-value	*<0.001*	*<0.001*	*< 0.001*
Female	0.842 (-0.789 – 0.883)	-0.791 (-0.843 - -0.723)	-0.768 (-0.826 - -0.695)
p-value	*<0.001*	*<0.001*	*<0.001*
Obese	0.816 (0.743 – 0.870)	-0.755 (-0.825 - -0.662)	-0.735 (-0.810 - -0.636)
p-value	*<0.001*	*<0.001*	*<0.001*
Non-obese	0.906 (0.865 – 0.935)	-0.839 (-0.887 - -0.772)	-0.823 (-0.876 - -0.750)
p-value	*<0.001*	*<0.001*	*<0.001*
Smoker	0.886 (0.811 – 0.933)	-0.807 (-0.844 - -0.687)	-0.793 (-0.875 - -0.666)
p-value	*<0.001*	*<0.001*	*<0.001*
Non-smoker	0.847 (0.798 – 0.887)	-0.787 (-0.839 - -0.721)	-0.774 (-0.829 - -0.705)
p-value	*<0.001*	*<0.001*	*<0.001*

Discussion

In our study, serum uric acid had significant positive correlation with TSH and negative correlation with free T3 and free T4. In Han population, Wang XJ et al, from China found a negative connection between serum uric acid and FT3 levels (10). This supports lower UA levels with higher thyroid hormone activity and is consistent with our observations of negative FT3–UA relationship.

In 2021, Feng X et al discovered that decreased TSH was linked to an increased risk of hyperuricaemia in type-2 diabetes patients with early kidney disease (i.e., an inverse TSH–UA association in that cohort (11). Their investigation demonstrated that thyroid status is associated with serum UA even though it included diabetic patients with renal problems.

A study on the risk of hyperuricaemia and subclinical thyroid dysfunction was carried out by Xing Y et al. Trends indicated decreased UA with increased FT3/FT4 in some subgroups, but there were inconsistent strong associations and inconsistent results across subtypes (7). Their results showed variation between populations and thyroid states, but these are consistent with our negative FT3/FT4 association with UA levels. Chao G et al, in year 2021, showed intricate connection between metabolic indicators and thyroid hormones. In certain subgroups, they demonstrated inverse correlations between FT3/FT4 and metabolic indicators, such as UA levels (12). The physiological validity of

the negative FT3/FT4–UA association seen in our group is further supported by their findings.

Lu Y et al studied how uric acid metabolism and impaired thyroid sensitivity are related. According to their findings, thyroid functional indices and UA levels are connected (13). This highlights how intermediary factors (insulin resistance, renal handling) affect direction and magnitude, which is consistent with our findings.

In 2024, Boruah P et al studied patients with chronic renal disease. TSH and UA levels were positively correlated (greater TSH → higher UA) (14). This is consistent with our positive association between TSH and UA.

Rafat MN et al examined 50 patients with hypothyroidism (group I), 50 patients with hyperthyroidism (group II), and 50 healthy, normal individuals as a control group (group III). Both hypothyroidism and hyperthyroidism were associated with higher uric acid levels. In hypothyroidism, the elevation was greater (15). The association between subclinical hypothyroidism and UA was discovered by Kaur P et al, who reported higher UA in subclinical hypothyroidism, or a positive TSH–UA correlation (16). Higher UA levels were linked to atrial fibrillation in hyperthyroid individuals, as Chen P et al reported. Their analysis revealed that UA was related to thyroid indices and systemic indicators (17).

The metabolic and renal consequences of hypothyroidism are the main causes of an increase in blood uric acid with increased thyroid-stimulating hormone (TSH) levels. Reduced thyroid hormone activity, or hypothyroidism, is typically indicated by elevated TSH. Reduced hepatic purine metabolism and decreased uric acid breakdown result from lower basal metabolic rate in hypothyroidism (18). Reduced cardiac output and systemic vasoconstriction cause lower blood flow to the kidneys and glomerular filtration rate (GFR) simultaneously, which impairs renal uric acid clearance. Additionally, hypothyroidism causes renal tubular cells' urate transporters to be downregulated, which lowers the excretion of uric acid and rises it in the serum (19).

Furthermore, hypothyroidism-related tissue hypoxia and oxidative stress encourage ATP degradation and purine catabolism, which raises the formation of uric acid (20). By increasing xanthine oxidase activity and decreasing renal urate excretion, altered lipid metabolism and insulin resistance, which are commonly seen in hypothyroid conditions, contribute to hyperuricemia (21).

Strength of The Study

The strengths of our study were that the reliability and statistical strength of correlation estimations were enhanced by the comparatively high sample size (n=232) of the study. The confounding effects of cardiovascular, hepatic, or renal disease on uric acid metabolism were reduced by strict exclusion criteria. Results were more convincing and broadly applicable when stratified by age, gender, obesity, and smoking.

Limitations of The Study

Some of the limitations of our study were that it was a single-centre study, with cross-sectional design, so a causal relationship between thyroid dysfunction and hyperuricemia could not be established. The comparison to normal reference physiology could not be done by the absence of a euthyroid control group. Genetic predispositions and dietary factors that affect uric acid levels were not evaluated.

Future Recommendations

To verify causality, multicenter prospective studies should be carried out in future to evaluate longitudinal changes in uric acid after treating thyroid function impairment. Mechanistic insights would be obtained by measuring renal urate transporter activity and including a euthyroid control group.

Conclusion

The study concluded that serum uric acid showed a strong positive correlation with TSH and negative correlations with free T3 and T4, indicating that impaired thyroid function is closely linked to hyperuricemia. These findings suggest that raised levels of uric acid may reflect both metabolic and renal changes in hypothyroidism, supporting its potential use as a supplementary biochemical marker to predict severity of disease.

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All the authors agree to take responsibility for every facet of the work, making sure that any concerns about its integrity or veracity are thoroughly examined and addressed.	