

## Evaluation of Serum Uric Acid in Hypothyroidism

Indu Prasad<sup>1</sup>, Vaidehi<sup>2</sup>, Usha Kumari<sup>3</sup>, Rashmi Kumari<sup>4</sup>

<sup>1</sup>Associate Professor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

<sup>2</sup>Tutor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

<sup>3</sup>Professor, Department of Biochemistry, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

<sup>4</sup>Professor, Department of Medicine, Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, Bihar, India

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Corresponding Author: Indu Prasad

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### Abstract:

Hypothyroidism is the most common thyroid ailment, affecting 2% to 15% of the population. Cases of hypothyroidism are often linked to higher levels of blood creatinine and uric acid. The retrospective case-control study was performed in the Clinical Biochemistry department at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri, Nalanda, involving 50 newly diagnosed hypothyroidism cases aged 20 to 60 years, of both sexes, and 50 controls of the same age and sex. There was a substantial increase in blood uric acid and serum creatinine levels among the hypothyroid individuals ( $p < 0.001$ , respectively). The use of Pearson's correlation coefficient demonstrated a strong link between TSH and uric acid, while indicating a non-significant correlation with serum creatinine. The study underscores the clinical importance of routinely conducting thyroid function tests in individuals with impaired renal function and vice versa.

**Keywords:** Hypothyroidism, Serum Uric Acid, Hyperuricaemia, Creatinine.

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### Introduction

Thyroid hormones elicit crucial role in growth, development and metabolism. Abnormalities in the function and anatomy of the thyroid gland constitutes one of the commonest endocrine disorders Hypothyroidism is the most common thyroid ailment. It is caused by a lack of thyroid hormones, which can show up in mild or severe forms and impact 2% to 15% of the population.

Hypothyroidism is a clinical disorder characterised by a generalised deceleration of metabolic processes. The diagnosis can be made quickly, verified or ruled out, and therapy is simple with a good chance of success [1].

The liver makes most of the uric acid, which is an antioxidant that dissolves in water [2]. Research has demonstrated that uric acid directly inhibits free radicals injury from hurting cells protecting cell membranes and DNA [3]. Uric acid is a heterocyclic molecule made up of hydrogen, carbon, oxygen, and nitrogen [4]. Serum UA levels indicate an equilibrium between the metabolic degradation of purine nucleotides and UA elimination [5]. Serum UA levels have been regarded as an autonomous predictive indicator for metabolic syndrome [6,7].

The rise in uric acid levels is believed to be an inflammation mediating element in adipose tissue, regulating endocrine diseases. These substances induce inflammation and may significantly contribute to dyslipidaemia in thyroid disorders [6]. Hypothyroidism is a common cause of hyperuricemia. which may be due to renal dysfunction. Changes in thyroid hormone levels also affect purine metabolism, which leads to alteration in levels of uric acid causing hyperuricemia. These data elucidate the interplay between the variables, highlighting the adverse impact of a hypothyroid condition on renal function.[1].

Creatinine is produced from creatine phosphate in muscles by irreversible non-enzymatic breakdown and phosphate loss. In skeletal muscle and the brain, creatine phosphate is the high-energy buffer. Creatinine phosphate stops ATP from running out too quickly by giving it a high-energy phosphate that can be used to make ATP from ADP. Hypothyroidism is often linked to higher levels of creatinine and uric acid in the blood [10].

Currently, some studies have pointed out the correlation between thyroid hormone and uric acid

levels [10]. A recent study indicates that thyroid hormones influence uric acid levels in subclinical hypothyroidism by modulating insulin resistance [11]. Men with hypothyroidism were at a greater risk for hyperuricaemia compared to women with hypothyroidism [12].

Consequently, the assessment of serum uric acid in hypothyroidism at the time of diagnosis is essential. However, the relationship between thyroid function and uric acid is still controversial and requires further elucidation. Consequently, this study employs a retrospective examination of specific laboratory data to determine the association between uric acid and thyroid hormones.

**Aim and objective**

- To compare the serum uric acid levels among the study and control group.
- To compare the serum creatinine levels among the study and control group.
- To find the correlation between Thyroid profile (T<sub>3</sub>, T<sub>4</sub>, TSH) and serum uric acid, serum creatinine.

**Material and Method**

The retrospective case control study was conducted in the department of Clinical Biochemistry at Bhagwan Mahavir Institute of Medical Sciences, Pawapuri Nalanda. It consisted of 50 cases of newly diagnosed cases of hypothyroidism (subclinical, overt) of the age group 20 – 60 years of both the sexes and 50 controls (euthyroid cases) of the same age and sex. Fasting (10-12 hours) blood samples were collected from anticubital veins of patients attending the MOPD of our institution. These were

analysed for T<sub>3</sub>, T<sub>4</sub>, TSH, serum uric acid and serum creatinine. Estimation of T<sub>3</sub>, T<sub>4</sub>, TSH was done by Quanti microlisa method. Serum uric acid (Uricase Trinder-Enzymatic method) and serum creatinine (Modified Jaffe’s method) were analysed on Erba 200 automated Jaffe analyser in the Dept. of Clinical Biochemistry.

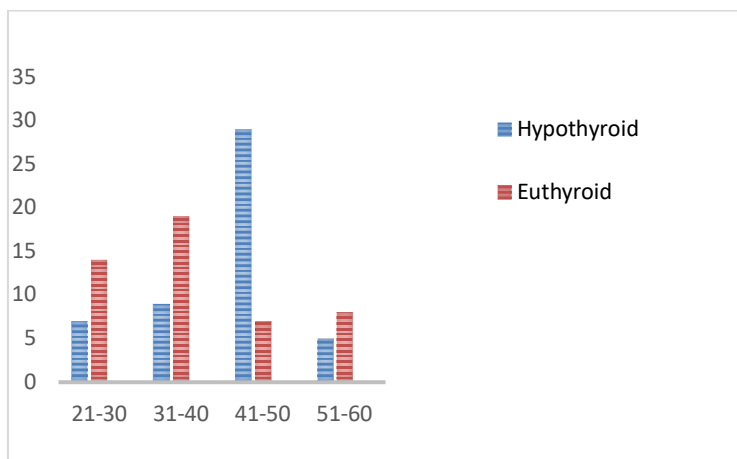
**Inclusion Criteria:** Newly diagnosed case of hypothyroidism

**Exclusion Criteria:**

- Patients with severe heart, liver, and kidney dysfunction
- Individuals with a history of thyroid disease, including those previously diagnosed with apparent hypothyroidism or hyperthyroidism, thyroid cancer or thyroid nodules, thyroid hormone/antithyroid drug intake history, or previous thyroid surgery or radioactive iodine intake
- Patients with hyperuricemia or gout who continue to receive medication.
- Pregnancy, critical illness

**Statistical Analysis:** Categorical variables were expressed as percentage (%). Continuous variables were expressed as mean, median, interquartile ranges (IQRs.). Mann-Whitney U test was applied to find difference between the categorial values. Pearson’s correlation ‘r’ was used to analyse the relationship of T<sub>3</sub>, T<sub>4</sub>, TSH with serum uric acid and serum creatinine. Statistical analysis was done on SPSS version.

**Result**



**Figure 1: Age wise distribution of patients**

The above figure shows maximum number of hypothyroid patients were in the age group 41-50 years (29) while maximum number o

f patients in the euthyroid group (19) belonged to the age group 31-40 years.

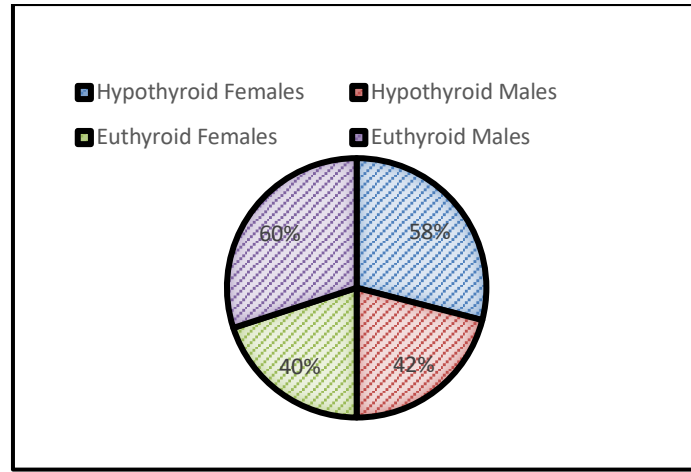


Figure 2: Sexwise distribution of patients

Table 1: Mann-Whitney U test performed to evaluate TSH levels between Hypothyroidism & Euthyroid

| Parameters             | Gr Group    | N  | Mean | Median | SE    | U   | Mean difference | P       |
|------------------------|-------------|----|------|--------|-------|-----|-----------------|---------|
| TSH ( $\mu$ IU/L)      | Hypothyroid | 50 | 9.00 | 7.42   | 0.998 | 402 | 3.84            | <0.001  |
|                        | Euthyroid   | 50 | 3.50 | 3.54   | 0.208 |     |                 |         |
| T <sub>4</sub> (ng/dL) | Hypothyroid | 50 | 6.91 | 7.06   | 0.55  | 924 | 2.05            | 0.025   |
|                        | Euthyroid   | 50 | 8.96 | 8.95   | 0.38  |     |                 |         |
| T <sub>3</sub> (ng/ml) | Hypothyroid | 50 | 0.85 | 0.96   | 0.91  | 573 | 0.57            | <0.0001 |
|                        | Euthyroid   | 50 | 1.42 | 1.41   | 0.05  |     |                 |         |

Mann-Whitney U test indicated that individuals with hypothyroidism had significantly higher TSH, T<sub>4</sub> and T<sub>3</sub> ( $p < 0.001$ ,  $0.025$ ,  $< 0.0001$ ;  $U = 402, 924$  and

573 respectively) with mean difference of 3.84, 2.05 and 0.57 respectively.

Table 2: Student's t- test to compare the values in both groups

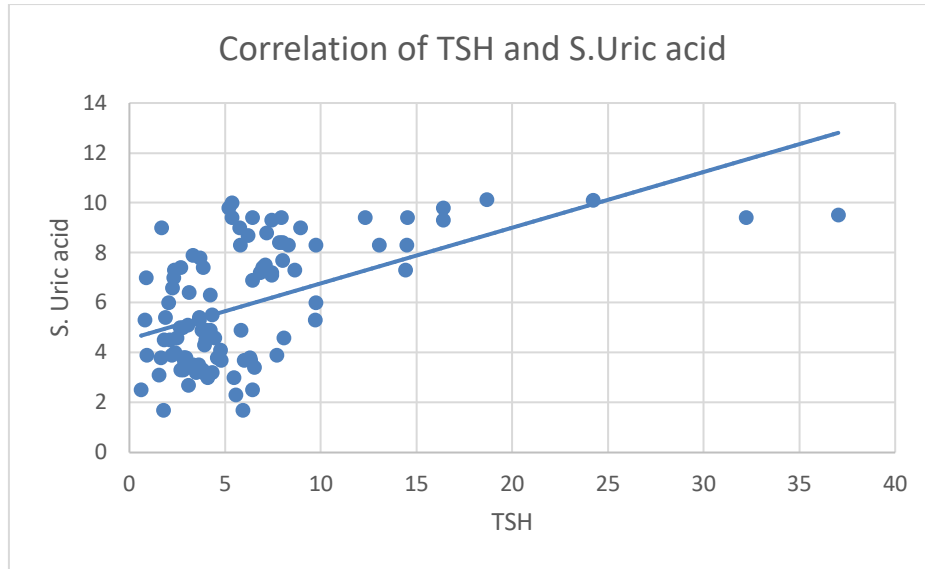
| Parameters            | Group       | N  | Mean | Median | SE    | Mean difference | p      |
|-----------------------|-------------|----|------|--------|-------|-----------------|--------|
| S. Uric acid (mg/dl)  | Hypothyroid | 50 | 7.53 | 2.07   | 0.30  | 3.19            | <0.001 |
|                       | Euthyroid   | 50 | 4.34 | 1.45   | 0.20  |                 |        |
| S. Creatinine (mg/dl) | Hypothyroid | 50 | 1.98 | 0.60   | 0.085 | 0.94            | <0.001 |
|                       | Euthyroid   | 50 | 1.04 | 0.55   | 0.078 |                 |        |

Student's t-test performed to evaluate significant difference ( $p < 0.001$  resp.) of serum uric acid and

serum creatinine values between the groups, with mean difference of 3.19 and 0.94 respectively.

Table 3: Correlation between Serum TSH, T<sub>3</sub>, T<sub>4</sub> and Serum Uric Acid Levels

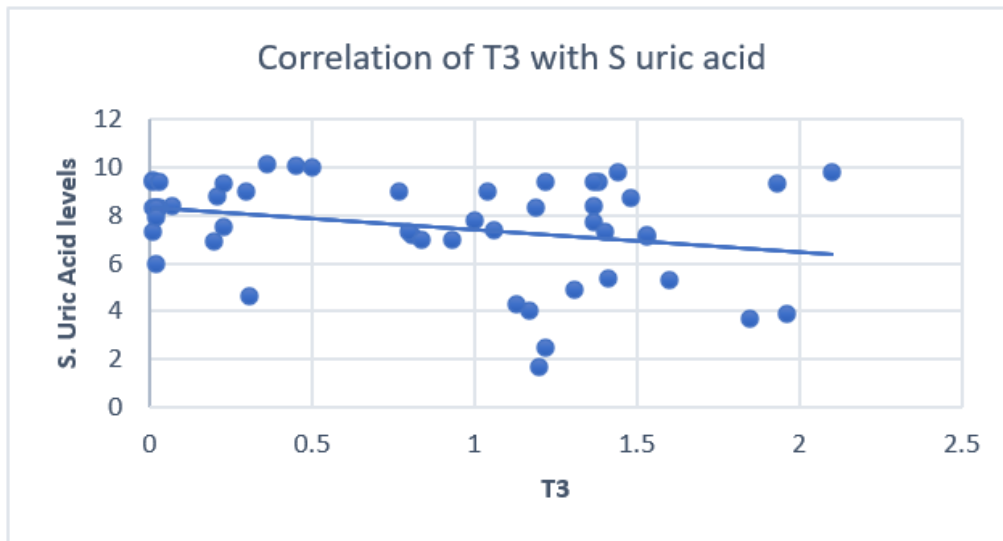
| Variables                         | Spearman's rho( $\rho$ ) | P value |
|-----------------------------------|--------------------------|---------|
| S. TSH vs S. Uric Acid            | 0.514                    | <0.001  |
| S. T <sub>3</sub> vs S. Uric Acid | -0.208                   | 0.147   |
| S. T <sub>4</sub> vs S. Uric Acid | -0.090                   | 0.532   |



**Figure 3: Correlation between Serum TSH Level and Serum Uric Acid Levels**

**Interpretation:** A Pearson's product-moment correlation showed a moderate significant, positive correlation between TSH level and Serum Uric Acid

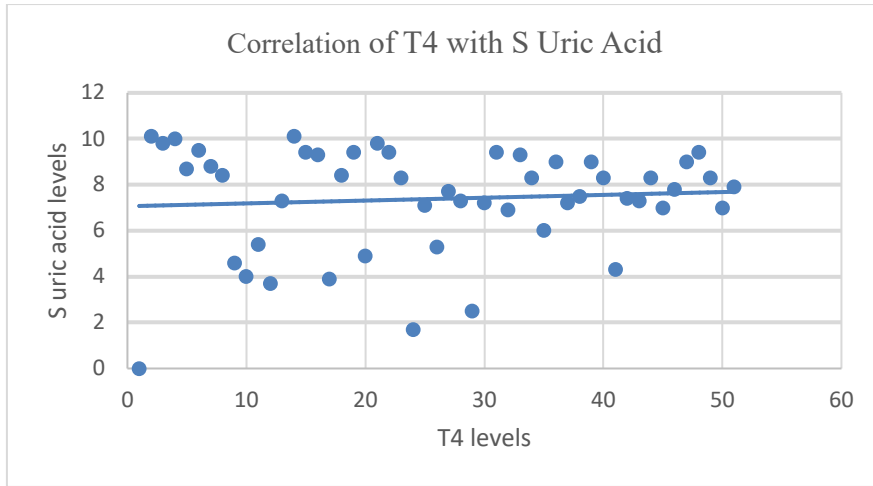
levels,  $\rho = 0.514$ ,  $p < 0.001$ , with TSH explaining 28.9% (coefficient of determination) of the variation in Serum Uric Acid levels.



**Figure 4: Correlation between Serum T3 Level and Serum Uric Acid Levels**

**Interpretation:** A Spearman's rank-order correlation demonstrates a statistically non-significant, very weak, negative correlation between

T3 level and Serum Uric Acid levels, which was,  $\rho = -0.208$ ,  $p = 0.147$ .

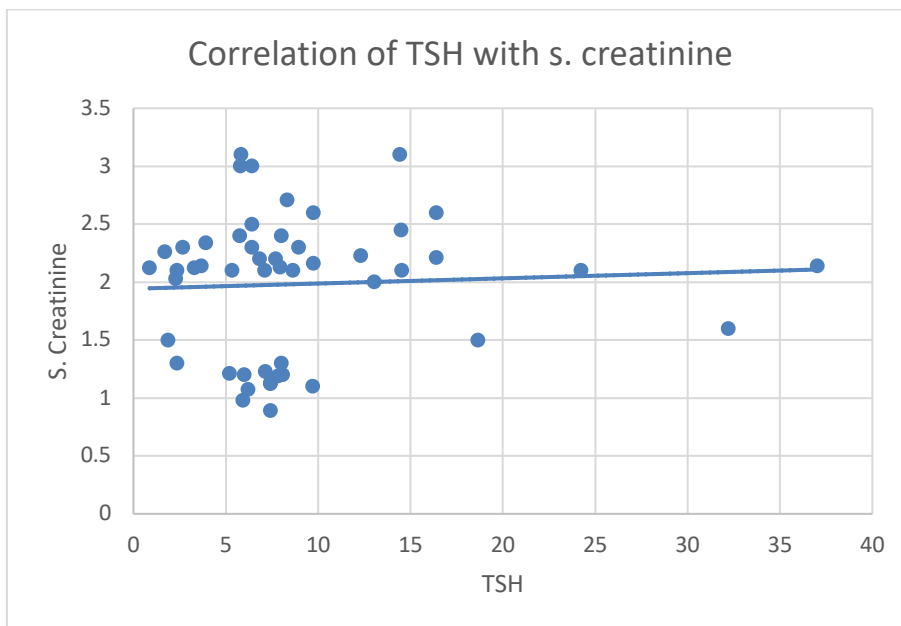


**Figure 5: Correlation between Serum T4 Level and Serum Uric Acid Levels**

**Interpretation:** A Spearman's rank-order correlation again shows a very weak, non-significant negative correlation between T<sub>4</sub> level and Serum Uric Acid levels, with  $\rho = -0.090$ ,  $p = 0.532$ .

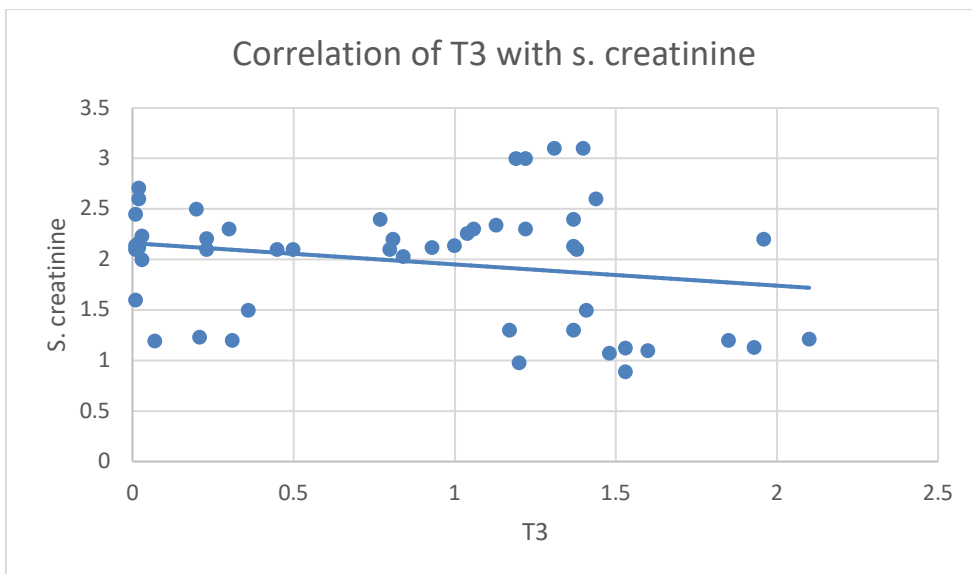
**Table 4: Correlation between Serum TSH, T<sub>3</sub>, T<sub>4</sub> and Serum Creatinine Levels**

| Variables                          | Spearman's rho( $\rho$ ) | p value |
|------------------------------------|--------------------------|---------|
| S. TSH vs S. Creatinine            | 0.0657                   | 0.650   |
| S. T <sub>3</sub> vs S. Creatinine | -0.236                   | 0.100   |
| S. T <sub>4</sub> vs S. Creatinine | -0.142                   | 0.323   |



**Figure 6: Correlation between Serum TSH and Serum Creatinine Levels**

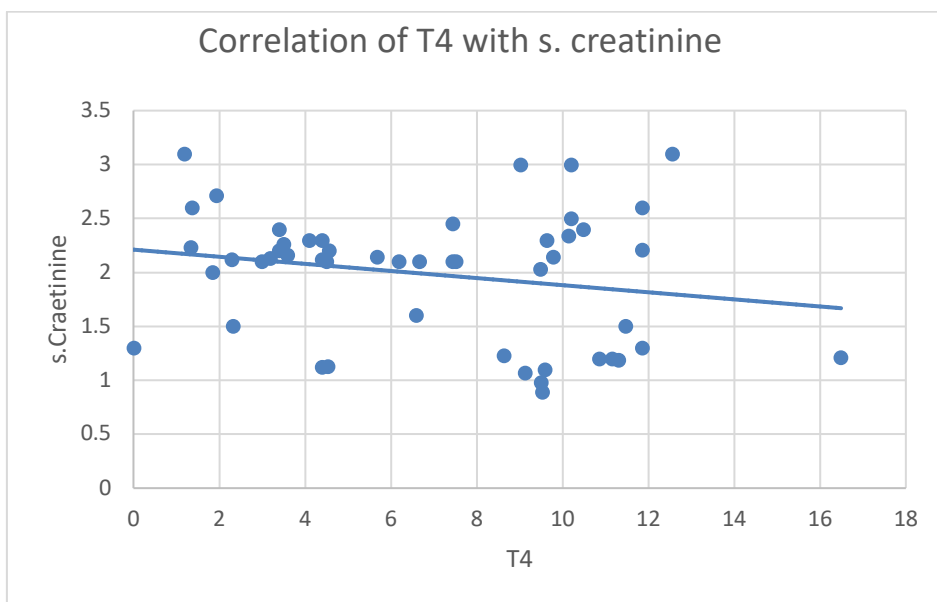
A Spearman's rank-order correlation shows statistically non-significant,  $\rho = 0.0657$ ,  $p = 0.650$ . variation in serum creatinine levels with TSH.



**Figure 7: Correlation between Serum T<sub>3</sub> and Serum Creatinine Levels**

A Spearman's rank-order correlation shows weak and non-significant relation,  $\rho = -0.236$ ,  $p = 0.100$ .

This shows T<sub>3</sub> level do not significantly explain the variation in serum creatinine levels.



**Figure 8: Correlation between Serum T<sub>4</sub> and Serum Creatinine Levels**

A Spearman's rank-order correlation was run to assess the relationship between T<sub>4</sub> level and serum Creatinine levels which was statistically non-significant,  $\rho = -0.142$ ,  $p = 0.323$ . This indicates that changes in T<sub>4</sub> level do not significantly explain the variation in serum creatinine levels.

**Discussion**

This retrospective case-control study aims to investigate the correlation between uric acid and thyroid hormones in patients with primary thyroid disease, along with serum creatinine levels. The current study assessed the impact of hypothyroidism on renal function and compared it them with

euthyroid subjects, and examined the correlation of TSH, T<sub>4</sub>, and T<sub>3</sub> with uric acid and creatinine levels.

In our study, the majority of patients were aged 41-50 years, which is comparable to several other studies.[13]

Like our study, other studies [10,13,14] likewise had a higher percentage of females than males. The elevated production of TBG in females, is likely influenced by oestrogen, resulting in this gender disparity [15,16].

The markedly elevated mean TSH readings for hypothyroid individuals were consistent with several analogous investigations [10,17,18].

Indrajith et al. [20] likewise observed a large disparity between the levels of T3 and T4. Our investigation identified a substantial comparative difference in uric acid and creatinine levels across the groups. This result was consistent with that of Srivastva S. et al. [10]. Nevertheless, Bhagyashree et al. [21] did not identify any significant comparable differences between the groups. Conversely, the study by Abebe et al. [22] indicated reduced serum UA levels in hypothyroid individuals.

Numerous research has been suggested to support the association of hyperuricemia and hypothyroidism. In hypothyroidism, ADP levels will be higher than ATP levels because as of low metabolic profile. The xanthine oxidase system will turn the extra adenine into additional uric acid.[23]

Hypothyroid hyperuricemia may also result from diminished renal plasma flow and glomerular filtration secondary to thyroid hormone deficit, resulting in decreased uric acid clearance and elevated uric acid concentration.[17]

The current investigation demonstrated a robust positive connection between uric acid and TSH. Various investigations [17, 18, 21] reported analogous findings. Nonetheless, a few investigations, including that of Srivastva S. et al. [10], identified a slight positive correlation. Lai-Chu See et al. examined the lack of a significant association between TSH and blood uric acid levels.[24]. In the study by Jia D et al. (2015), TSH exhibited no connection with serum uric acid levels.[25]

Conversely, uric acid exhibited a negative connection with T3 and T4 readings. The study was akin to that of Srivastva S. et al. [10]

In the study conducted by Tayal et al. [19], uric acid exhibited a substantial negative connection solely with T3 levels in the overt hypothyroid group, alongside a weak negative correlation with T4 and a positive correlation with TSH.

The current study, similar to Tayal D et al. [19], found no instances of gout despite the occurrence of hyperuricemia in hypothyroid patients. Conversely, Giordano et al. [26] identified a notable rise in the prevalence of hyperuricaemia concomitant with gout in hypothyroid individuals.

The study also revealed a significant elevation in serum creatinine levels in persons with hypothyroidism, paralleling findings related to serum uric acid, which has been consistently linked to hypothyroidism in previous research [27, 28, 29]. Kreisman SH et al. [28] documented markedly elevated mean creatinine levels in hypothyroidism, underscoring the influence of thyroid disease on renal function.

A limited number of research [10,29] demonstrated a positive association between TSH and creatinine, although Jia D et al. [25] indicated a mild negative link between both variables. We found that creatinine levels were negatively correlated with T3 and T4. Srivastva S. et al. [10] discovered findings that were contradictory. In this investigation, serum creatinine exhibited a positive connection with T3 and TSH, and a negative correlation with T4. But all of them were weak and didn't matter statistically. In the study by Jia D et al., FT3 and FT4 exhibited a strong negative connection with creatinine [25]. Hajfa Eranhikkal et al. [17] demonstrated an insignificant negative correlation between FT3 and creatinine, as well as a lack of meaningful link between FT4 and creatinine.

Subsequent studies [14,16,29] yielded analogous results. They elucidated physiological consequences such as modifications in renal haemodynamics, a reduction in GFR, and reduced creatinine clearance, leading to elevated serum creatinine levels in hypothyroid individuals. Some people said that hypothyroid myopathy might also raise the level of creatinine in the blood [16].

A reduced cardiac output, increased systemic and renal vasoconstriction, less blood and plasma flow to the kidneys, and a lower GFR could all be the possible causes of kidney damage. Hypothyroid myopathy may also lead to elevated blood creatinine levels [11]. Thus, hypothyroidism must be excluded in people exhibiting acute renal failure and elevated muscle enzymes.

Furthermore, Mooraki et al. [29] emphasised the critical importance of early identification and efficient thyroid hormone replacement therapy in reducing blood creatinine levels, suggesting the potential for reversible renal impairment in hypothyroid patients. Altered purine nucleotide metabolism and renal function, in conjunction with hypothyroidism, may exacerbate uric acid levels and gout in the future. Consequently, in individuals with hyperuricaemia, assessment of thyroid hormones is crucial.

The findings of the current study highlight the clinical importance of assessing renal function in hypothyroid individuals. The observed findings further indicate the necessity to monitor thyroid function in individuals with aberrant renal function, and conversely.

Some drawbacks of the study were that there were no follow-up and no information about how diet affected thyroid function. The study exclusively focused on hypothyroidism, neglecting other variances seen in different thyroid conditions.

## Conclusion

The study highlights the clinical significance of thyroid function test in those with abnormal renal function. Gender predominance observed among hypothyroid patients is also a possible considerable alteration in thyroid function measures. The thyroid function should, therefore, be routinely assessed screening of patients presenting with deranged renal function and vice versa.

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