

## Study of Thyroid Stimulating Hormone, Serum Creatinine and Uric Acid Levels in Patients with Hypothyroidism

Nagarajappa K\*, Sushma B. J. and Shweta R. Hebbar

Department of Biochemistry, S. S. Institute of Medical Sciences and Research Centre, Davangere

\*Corresponding Author E-mail: [sushmabj1983@gmail.com](mailto:sushmabj1983@gmail.com)

### ABSTRACT

*Background:* Hypothyroidism is the most common endocrine disorder especially in women. It is associated with increased risk for atherosclerosis and other complications. The frank development of hypothyroidism is associated with metabolic derangements including dyslipidemia- which is an etiopathologic factor for development of renal impairment. This study was to evaluate whether hypothyroidism is associated with impaired renal function by measuring serum uric acid and creatinine levels. *Aim of the study:* To estimate and compare serum creatinine and uric acid in healthy controls and hypothyroid patients. *Materials and Methods:* A cross sectional analytical study of 40 newly diagnosed and untreated cases of hypothyroidism and 40 healthy controls in the age group of 18 - 60 years were included in whom 5mL of fasting blood sample was drawn to estimate serum levels of T<sub>3</sub>, T<sub>4</sub>, TSH by Chemiluminiscence immuno assay. Uric acid, Creatinine and lipid profile parameters were measured using automated clinical chemistry analyzer according to manufacturer's protocol. *Results:* There was significant increase in the levels of serum creatinine and uric acid found in hypothyroid patients compare to healthy controls.

**Key words:** Hypothyroidism, Thyroid stimulating hormone, Creatinine and Uric acid.

### INTRODUCTION

The thyroid gland produces two related hormones, thyroxin (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>). Acting through thyroid hormone receptors  $\alpha$  and  $\beta$ , these hormones play a critical role in cell differentiation during development and help maintain thermogenic and metabolic homeostasis in the adult<sup>1</sup>.

Thyroid hormones are necessary for growth and development of the kidney and for the maintenance of water and electrolyte homeostasis. On the other hand, kidney is involved in the metabolism and elimination of thyroid hormones. Moreover, the decline of kidney function is accompanied by changes in the synthesis, secretion, metabolism, and elimination of thyroid hormones. On the other hand, the different treatments used in the management of patients with kidney and thyroid diseases may be accompanied by changes or adverse events that affect thyroid and kidney function respectively<sup>2</sup>. Hypothyroidism is a clinical syndrome caused by deficiency of thyroid hormones (below reference range) that causes a generalized slowing of metabolic process<sup>3,4</sup>. Primary hypothyroidism is frequent syndrome, whose prevalence is 0.5–2.0% among women and around 0.2% among men. According to several authors, recently the number of patients with autoimmune diseases with hypothyroidism increased by 2.1%<sup>5</sup>.

Certain effects of the hypothyroid state on the kidney are well established. Physiological effects include changes in water and electrolyte metabolism and reliable alterations of renal hemodynamics, including decrements in renal blood flow, renal plasma flow, glomerular filtration rate (GFR), and single nephron GFR. The cause of the decreased renal plasma flow and GFR observed is believed to be principally due to the generalized hypodynamic state of the circulatory system in hypothyroidism<sup>6,7</sup>.

Hypothyroidism is associated with many biochemical abnormalities including serum creatinine and uric acid levels. Creatinine is the cyclic anhydride of creatine that is produced as the final product of

decomposition of phosphocreatine. It is excreted in urine. Measurement of plasma creatinine and its renal clearance are used as diagnostic indicators of kidney function.

Uric acid is a nitrogenous compound present as principal nitrogenous component of excrement of reptiles and birds. It is the major product of catabolism of purine nucleosides. Measurement of plasma uric acid is predominantly used in the investigation of gout, either as a result of primary hyperuricemia or caused by other conditions or treatments that give rise to secondary hyperuricemia<sup>8</sup>.

Even though thyroid disorders are most common and prevalent conditions, the effect of hypothyroidism on serum creatinine and uric acid levels has not been well documented in Indian population<sup>7</sup>.

Previous studies indicate the profound influence of thyroid hormone on renal function. Knowledge of reversible association between hypothyroidism and elevated serum creatinine and uric acid is very important. Hence the present study has been undertaken to study the serum creatinine and uric acid levels in hypothyroid patients.

## MATERIALS AND METHODS

### *Source of data:*

Hospital based study on “**Study of thyroid stimulating hormone, serum creatinine and uric acid levels in patients with Hypothyroidism**” was conducted at S. S Hospital, Davangere (attached teaching hospital for S.S Institute of Medical Sciences & Research Centre, Davangere) between July 2013-December 2013. We included 40 newly diagnosed and untreated cases of hypothyroidism and 40 healthy controls in the age group of 18 - 60 years.

The study was approved by the ethical and research committee of S.S Institute of Medical Sciences and Research Centre, Davangere, to use human subjects in the research study. Written informed consent was taken from the study subjects. Hypothyroid subjects and controls participated voluntarily in the study. Detailed medical history and relevant clinical examinations were carried out in both cases and controls. Based on inclusion and exclusion criteria, about 40 cases of Hypothyroidism and 40 age matched healthy controls were included.

### *Inclusion criteria:*

The study subjects were divided into two groups of which include:

**Group 1:** Comprised of 40 newly diagnosed and untreated cases of hypothyroidism. The diagnosis will be based on decreased serum T3 and T4 levels associated with increased TSH levels. All patients suffering from hypothyroidism will be diagnosed and confirmed by the physician based on T3 (Normal: 0.7- 2.0 ng/ml), T4 (Normal: 4.5-11.0 µg/ dl) and TSH (Normal: 0.4- 4.2 µIU/ ml) levels of the patients.

**Group 2:** Comprised of 40 healthy controls in the similar age group having normal thyroid profile.

### *Exclusion criteria were:*

- a) Pregnancy
- b) Paediatric age group (<18 yrs).
- c) Elderly age group (> 60 yrs).
- d) Renal disorders.
- e) Hepatic disorders.
- f) Bone disorders.
- g) Diabetes, hypertension or any other systemic illness that may affect the renal function.
- h) Patients on drugs for treatment of thyroid disorders or any other medications that might affect renal function.

### *Source of data:*

A cross sectional study was carried out between July 2013 - December 2013. The study group will be selected from patients attending Medicine OPD of S.S. Hospital attached to SSIMS & RC, Davangere. Both cases and controls will be interviewed to obtain relevant data after taking informed written consent.

### *Method of sample collection:*

About 3 ml of venous blood will be drawn using a disposable syringe under aseptic conditions in a sterile bulb from selected subjects by the investigator. Blood will be allowed to clot and serum will be separated

after 30-45 min by Remicentrifuge machine at 3000 rpm, serial no: LMC-9375. The serum will be used for the analysis of creatinine and uric acid. Parameters will be estimated by following methods:

- Estimation of serum creatinine by modified Jaffe's method<sup>8,9</sup>.
- Estimation of serum uric acid by modified Trinder peroxidase method using 2, 4, 6- Tribromo-3-hydroxy benzoic acid<sup>8,10</sup>.

### Statistical analysis

The variables will be presented in terms of mean and standard deviation. The data was analyzed using student's unpaired 't' test.

## RESULTS AND DISCUSSION

A total of 40 cases and 40 controls in the age group of 18- 60 years were studied. Table 1: shows age and sex distribution in cases and healthy controls. The mean  $\pm$  SDs of age in years was  $35.4 \pm 11.0$  in cases and  $37.3 \pm 10.7$  in healthy controls. Among cases 8 were males and 32 were females and in healthy controls 10 were males and 30 were females. Table 2: shows Comparison of levels of T3, T4, TSH, Creatinine and Uric acid between cases and controls. As shown in Table 2: the mean  $\pm$  SDs of T3 (ng/ml), T4 ( $\mu$ g/dl), TSH ( $\mu$ IU/ml), Creatinine (mg/dl) and Uric acid (mg/dl) in cases are in the range of  $0.79 \pm 0.39$ ,  $4.73 \pm 2.5$ ,  $28.58 \pm 24.96$ ,  $1.8 \pm 0.03$  and  $6.92 \pm 0.47$ , respectively. It is observed that the mean  $\pm$  SDs of T3 (ng/ml), T4 ( $\mu$ g/dl), TSH ( $\mu$ IU/ml), Creatinine (mg/dl) and Uric acid (mg/dl) in controls are in the range of  $1.13 \pm 0.31$ ,  $8.89 \pm 2.03$ ,  $2.39 \pm 1.06$ ,  $0.86 \pm 0.24$  and  $5.78 \pm 0.60$ , respectively. It is evident that T3 and T4 levels are decreased in cases as compared to controls and TSH, Creatinine and Uric acid levels are increased in cases as compared to controls and the increase is statistically highly significant ( $p < 0.001$ ).

Most of the studies done in hypothyroid patients have shown increased serum creatinine levels<sup>4, 6,7</sup>. Studies say that the elevated serum creatinine levels in hypothyroid patients are due to reduction in glomerular filtration rate and renal plasma flow because of hemodynamic changes in severe hypothyroidism<sup>2,4,6,11,12</sup>. Thyroid hormone deficiency decreases myocardial contractility and cardiac output. On the other hand, an impaired endothelial-mediated vasodilatation in hypothyroidism increases peripheral and renal plasma flow and GFR, resulting in free water overload and decrease in creatinine clearance. Consequently, an elevation of plasma creatinine levels might result<sup>13,14</sup>.

Serum creatinine level may also be increased due to hypothyroid myopathy. In hypothyroidism, associated autoimmune diseases may also play role in modifying the underlying renal problem<sup>4</sup>.

Studies done in hypothyroid patients reported hyperuricemia. In comparison to the prevalence reported in the general population, a significant increase of both hyperuricemia and gout was found in the hypothyroid patients<sup>4</sup>.

In hypothyroidism, the hyperuricemia is secondary to decreased renal plasma flow and urate excretion<sup>3,4,6</sup>. Some studies concluded that it could be due to increased production due to myopathy associated with hypothyroidism.

**Table 1: Shows Age and sex distribution in cases and healthy controls**

Variable	Hypothyroid	Controls
Age (Yrs)	$35.4 \pm 11.0$	$37.3 \pm 10.7$
Gender (M/F)	08/32	10/30

**Table 2: Comparison of levels of T3, T4, TSH, Creatinine and Uric acid between cases and controls**

	Group 1 (N=40) Hypothyroid	Group 2 (N= 40) Healthy controls
T3 (ng/ml)	$0.79 \pm 0.39^{**}$	$1.13 \pm 0.31$
T4 ( $\mu$ g/dl)	$4.73 \pm 2.51^{**}$	$8.89 \pm 2.03$
TSH ( $\mu$ IU/ml)	$28.58 \pm 24.96^{**}$	$2.39 \pm 1.06$
Creatinine (mg/dl)	$1.8 \pm 0.03$	$0.86 \pm 0.24$
Uric acid (mg/dl)	$6.92 \pm 0.47$	$5.78 \pm 0.60$

**Table 3: Comparison of levels Total cholesterol, HDL, LDL and Triglycerides between cases and controls**

	<b>Group 1 (N=40) Hypothyroid</b>	<b>Group 2 (N= 40) Healthy controls</b>
<b>TC (mg/dL)</b>	245.6 ± 45.54**	154.7 ± 13.67
<b>HDL (mg/dL)</b>	42.56 ± 2.51 *	48.89 ± 2.03
<b>LDL (mg/dL)</b>	134.56 ± 24.96 **	97.23 ± 12.06
<b>Triglycerides (mg/dL)</b>	167.8 ± 12.34**	132.6 ± 9.24

\* p &lt;0.05

\*\*p &lt;0.001

### CONCLUSION

The present 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 in patients taking medications cleared by the kidneys. The assessment of thyroid function should therefore be routinely carried out for evaluation of patients presenting with deranged renal function and vice versa.

### ACKNOWLEDGEMENT

I thank all the subjects included in our study for their kind co-operation. I thank all the lab technicians who were involved in the sample collection, storage and analysis throughout during our study.

### REFERENCES

1. Jameson J. L, Weetman A.P. Disorders of the thyroid gland. In: Fauci A S, Longo D L, Kasper D L, Hauser S L, Jameson J L, Loscalzo J, editors. Harrison's principles of internal medicine. 18<sup>th</sup>ed. New York: McGraw Hill; 2008. p. 2911.
2. Iglesias P, Diez J J. Thyroid dysfunction and kidney disease. *Eur J Endocrinol.* **160**: 503-15 (2009)
3. Wedaatalla M A, Abdella A M. Assessment of plasma uric acid level among Sudanese female with thyroid dysfunction. *Sudanese Journal Of Public Health.* **7(3)**: 89-92 (2012)
4. Khan A H, Majumder I. Serum creatinine and uric acid levels of hypothyroid patients. *Bangladesh J Med Biochem.* **3(2)**: 61-63 (2010)
5. Orlova M M, Rodionova T I. Functional state of kidneys in patients with clinical manifestations of hypothyroidism. *Russian Open Medical Journal.* **2**: 1-5 (2013)
6. Chaudhury H S, Raihan K K, Uddin M N, Ansari S M, Hasan M, Ahmed M, et al. Renal function impairment in hypothyroidism. *Bangladesh J Med Biochem.* **6(1)**: 19-25 (2013)
7. Tayal D, Chawla R, Arora S, Gupta V K, Sohi J S, Mallika V. Dynamic changes in biochemical markers of renal function with thyroid status- a study in Indian population. *Internet Journal Of Medical Update.* **4(2)**: 36-41 (2009)
8. Lamb E J, Price C P. Creatinine, urea and uric acid. In: Burtis A C, Ashwood E R, editors. Teitz Fundamentals of clinical chemistry. 5<sup>th</sup> ed. Philadelphia: W B Saunder's; 2001. p. 363, 365, 371.
9. Erba diagnostics Mannheim. Creatinine (CRE) Jaffe's Method, Initial Rate (Pamplet). Germany: Erba Diagnostics Mannheim; 2009.
10. Erba diagnostics Mannheim. Uric Acid Des Modified Trinder Method, End Point (Pamplet). Germany: Erba Diagnostics Mannheim; 2008.
11. Goede DL et al. Effects of thyroxine replacement on serum creatinine and Cystatin C in patients with primary and central hypothyroidism. *SWISS MED WKLY.* **139**: 339-344 (2009)
12. Kreisman SH, James V. Consistent reversible elevations of serum creatinine levels in severe hypothyroidism. *Arch Intern Med* 1999; **159**: 79-82
13. Dragovic T. Reversal deterioration of renal function accompanied with primary hypothyroidism. *Vojnosanitetski Pregled.* **69(2)**: 205-208 (2012)
14. Paula S. Kidney failure in the elderly due to hypothyroidism: a case report. *Sao Paulo Med J;* **126(5)**: 291-293 (2008)