

## Original Research Article

# Evaluation of renal function in subclinical and overt hypothyroidism

Ashima Badyal<sup>1\*</sup>, Sanjeev Kumar<sup>2</sup>, Kailash Chander<sup>1</sup>

<sup>1</sup>Department of Biochemistry, GMC Jammu, J and K, India

<sup>2</sup>Physician, Sub-District Hospital Hiranagar, Kathua, J and K, India

<sup>3</sup>Department of Medicine, CHC, Bishnah, Jammu, J and K, India

**Received:** 07 April 2019

**Accepted:** 13 April 2019

### \*Correspondence:

Dr. Ashima Badyal,

E-mail: [badyal.ashima@gmail.com](mailto:badyal.ashima@gmail.com)

**Copyright:** © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

### ABSTRACT

**Background:** Thyroid hormones can cause significant changes in renal function such as decrease in sodium re-absorption in the proximal tubules, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in the urinary urate excretion and a decrease in the renal blood flow and glomerular filtration rate (GFR). This study was therefore planned to analyse the changes in biochemical markers of renal function in patients with subclinical and overt hypothyroidism and to correlate these values with the thyroid profile of the patients with an aim to determine whether thyroid dysfunction has deleterious effects on renal function.

**Methods:** Study was conducted on 200 patients, in the age group of 20-70 years, in the Department of Medicine, in collaboration with Department of Biochemistry, GMC Jammu over a period of 6 months. After centrifugation, the serum was divided into 2 aliquots: one for renal function tests and the other for thyroid function tests.

**Results:** Age wise, mean was found to be 33.2±9.3 years for euthyroid group and 42.8±8.7 years for hypothyroid group. Patients with both subclinical hypothyroidism and overt hypothyroidism showed statistically significant rise in TSH levels as compared to controls.

**Conclusions:** It was seen that primary hypothyroidism is associated with a reversible elevation of serum creatinine in adults as well as children. It is believed that renal impairment with hypothyroidism is due to reduced cardiac output and increased systemic and renal vasoconstriction leading to reduced renal blood and plasma flow and decreased GFR.

**Keywords:** Overt hypothyroidism, Renal function tests, Subclinical hypothyroidism, Thyroid function tests

### INTRODUCTION

Thyroid hormones affect renal function by both pre-renal and direct-renal effects. Pre-renal effects are mediated by the influence of thyroid hormones on the cardiovascular system and the renal blood flow. The direct renal effects are mediated by the effect of thyroid hormones on glomerular filtration rate (GFR). Thyroid dysfunction affects renal physiology and development, whereas kidney disease could result in thyroid dysfunction.<sup>1</sup> Subclinical hypothyroidism (SCH) is defined as an elevated serum thyroid-stimulating hormone (TSH) above the defined upper limit of the reference range, with

a serum free thyroxine (fT4) within the reference range. SCH cases present with few or no symptoms or signs of thyroid dysfunction and thus by its very nature SCH is a laboratory diagnosis. The prevalence of SCH in the United States adult population is 4-8.5%.<sup>2</sup> Various epidemiological studies in India show a prevalence rate of SCH varying between 9% and 11.4%. The progression to overt hypothyroidism (OHT) is approximately 2-5% per year. Due to its asymptomatic nature, the SCH cases are not detected clinically and also its relation to the kidney function is not well established.<sup>3</sup> There is paucity of data in Indian population. Patients with SCH report more symptoms than Euthyroid individuals, but fewer

symptoms than overtly hypothyroid participants. There is controversy in management of patients with a serum TSH level  $<10\mu\text{IU/L}$ . There is inadequate literature in this area and statements may often be an expert panel opinion rather than strictly evidence based. There is a well-known interaction between thyroid and kidney functions. Thyroid hormones are involved in the growth, development and physiology of the kidney.<sup>4</sup> Serum creatinine is elevated and glomerular filtration rate (GFR) values are reversibly reduced in overt hypothyroid patients than in euthyroid subjects.<sup>5-7</sup> Long standing hypothyroidism can cause significant changes in renal function such as decrease in sodium re-absorption in the proximal tubules, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in the urinary urate excretion and a decrease in the renal blood flow and glomerular filtration rate (GFR). These renal abnormalities occur because the deficiency of thyroid hormones (TH) reduces the cardiac output leading to generalized hypodynamic state of the circulatory system. Hypothyroidism also results in increased glomerular capillary permeability of proteins; the consequent proteinuria often precedes the reduction in GFR in hypothyroidism.<sup>8</sup>

Very few studies have reported the effect of hypothyroidism on renal function tests especially creatinine. Some studies have also reported hyperuricemia leading to gout in hypothyroid subjects. Not much data is available on the impact of hypothyroidism on renal function tests in this region. This study was therefore planned to analyse the changes in biochemical markers of renal function in patients with subclinical and overt hypothyroidism and to correlate these values with the thyroid profile of the patients.

## METHODS

The present study was conducted on 200 patients, in the Department of Medicine, in collaboration with Department of Biochemistry, GMC Jammu over a period of 6 months, i.e. August 2018 - January 2019. Patients included in the study were in the age group of 20-70 years. Further, out of the 200 patients included in the study, 100 patients were having euthyroid status, i.e. normal TSH, fT3 and fT4 levels, who were taken as controls, while the rest 100 patients with hypothyroidism were taken across all age groups and social backgrounds. Brief clinical history was taken to rule out hypertension, diabetes mellitus or any other clinical condition, which could affect renal function and patients suffering from any such condition were excluded from the study. 6 ml of fasting venous blood sample was taken for analysis. After centrifugation, the serum was divided into 2 aliquots: for renal function tests (urea, creatinine and uric acid) and for thyroid function tests (TSH, fT3, fT4). Both the aliquots were analyzed immediately.

Serum urea was calculated by Talke H et al, in 1965, defining the principle, briefly as: urease specifically

hydrolyses urea to form ammonia and carbon dioxide.<sup>9</sup> The ammonia is used by the enzyme glutamate dehydrogenase to reductively aminate alpha keto glutarate, with simultaneous oxidation of NADH; the change in absorbance at 340nm due to disappearance of NADH is directly proportional to the Blood-Urea-Nitrogen (BUN) concentration in the sample and is measured by using a micromatic rate technique; giving the reference range of serum urea to be 7-18mg/dl.

Uricase method was evaluated by clinical and laboratory standards institute in 2003, defining the principle as: uric acid, which absorbs light at 293nm is converted by uricase to allantoin, which is non-absorbing at 293nm. The change in absorbance at 293nm due to the appearance of uric acid is directly proportional to the concentration of uric acid in the sample and is measured using a bichromatic 293, 700nm; giving the reference range of uric acid as: females 2.6-6.0mg/dl; Males 3.5-7.2mg/dl.<sup>10</sup>

Jaffes method was evaluated by Knapp ML, and Mayne PD, in 1987, defining the principle, briefly as: creatinine in the presence of alkaline medium reacts with picric acid to form reddish yellow coloured complex called as creatine picrate, and measured at 520nm; giving the reference range of serum creatinine for males as 0.7-1.3mg/dl, while for females as 0.6-1.02mg/dl.<sup>11</sup>

## RESULTS

On the first instance, this study showed that the females formed a significant ratio amongst the thyroid cases, with 80% in both hypothyroid and euthyroid groups. Age wise, mean was found to be  $33.2\pm 9.3$  years for euthyroid group and  $42.8\pm 8.7$  years for hypothyroid group ( $p < 0.001$ ) patients with both subclinical hypothyroidism and overt hypothyroidism showed statistically significant rise in TSH levels as compared to controls (Table 1).

**Table 1: comparison between TSH, fT4 and fT3 values obtained in hypothyroid and euthyroid subjects.**

Parameters	Controls	Subclinical hypothyroidism	Overt hypothyroidism
TSH ( $\mu\text{IU/ml}$ )	$2.44\pm 0.69$	$7.20\pm 1.04^{**}$	$45.59\pm 9.31^{**}$
fT4 (ng/dl)	$0.99\pm 0.08$	$0.91\pm 0.08^{**}$	$0.60\pm 0.29^{**}$
fT3 (pg/ml)	$3.19\pm 0.24$	$2.75\pm 0.17^{**}$	$1.92\pm 0.42^{**}$

\*\*p value vs controls:  $p < 0.001$

Besides having significant and positive relation of serum urea and serum creatinine with both subclinical and overt hypothyroidism, the mean levels of uric acid, showed a more significant relation with uric acid values as compared to the controls (Table 2).

Correlation coefficients (r) also showed an association between thyroid function tests and renal function tests. (Table 3, 4) TSH did not demonstrate any statistically

significant correlation with any of the renal function parameters, but fT3 and fT4 showed a positive correlation with urea (Table 3).

**Table 2: Comparison of renal function tests between hypothyroid and euthyroid subjects.**

Tests	Controls	Subclinical hypothyroidism	P value	Overt hypothyroidism	P value
Urea (mg/dl)	19.65±4.28	25.74±7.85	<0.001	29.16±11.08	<0.001
Creatinine (mg/dl)	0.73±0.22	0.91±0.28	<0.001	1.09±0.29	<0.001
Uric Acid (mg/dl)	4.19±0.95	4.39±1.13	>0.001	6.11±1.62	<0.001

**Table 3: Correlation of renal function tests in patients with subclinical hypothyroidism.**

	TSH		fT4		fT3	
	r value	p value	r value	p value	r value	p value
Urea	-0.115	0.433	0.294	0.04*	0.321	0.032*
Creatinine	0.217	0.095	0.163	0.265	0.056	0.701
Uric Acid	0.052	0.775	0.034	0.806	0.085	0.554

\*p value vs controls: p<0.05

**Table 4: Correlation of renal function tests in patients with overt hypothyroidism.**

	TSH		fT4		fT3	
	r value	p value	r value	p value	r value	p value
Urea	0.053	0.663	-0.091	0.551	-0.149	0.212
Creatinine	0.325	0.026*	0.108	0.465	-0.147	0.401
Uric acid	0.044	0.735	-0.063	0.778	-0.081	0.619

\*p value vs controls: p<0.05

Patients with overt hypothyroidism, TSH showed a significant positive correlation with serum creatinine levels, whereas fT4 and fT3 did not show any significant correlation with any of these parameters.

## DISCUSSION

The purpose of the present study was to evaluate the effect of subclinical and overt hypothyroidism on parameters of renal function and to compare it with euthyroid subjects and also to study the correlation of TSH, fT4 and fT3 with urea, creatinine and uric acid.

The study has further shown that there exists a significant relation between the levels of urea and creatinine and hypothyroidism. There is a positive relation between TSH levels and overt hypothyroidism. It was further seen that primary hypothyroidism is associated with a reversible elevation of serum creatinine in adults as well as children. Similar results have also been reported in studies conducted by Rio et al.<sup>12</sup>

It is believed that renal impairment with hypothyroidism is due to reduced cardiac output and increased systemic and renal vasoconstriction leading to reduced renal blood and plasma flow and decreased GFR. Therefore,

hypothyroidism can lead to kidney disease or decreased renal function, as also shown by Suher et al.<sup>13</sup>

Since, statistically significant rise in uric acid levels has been observed in the cases studied, it can be generalized that increasing degree of hypothyroidism is associated with deteriorating renal function. There is probably scope for reversing the decline in renal function among the SCH group. SCH is a common disorder that frequently progresses to OHT. So, it becomes very important for treating clinician to understand the association between renal function and hypothyroidism. It is emphasized here that there should be regular monitoring of renal function in patients of hypothyroidism so that declining renal function may be detected. Given the high prevalence of SCH, treatment with thyroid hormone replacement needs to be addressed in an appropriately powered randomized controlled trial. As per the findings of this study, patients with SCH need to be monitored and treated individually, based on the symptoms and laboratory investigations. It is increasingly important for the treating physician to understand the association between the two, so that a regular monitoring is carried out for the patients with subclinical or overt hypothyroidism. However further studies are needed to completely establish the findings

and to further understand the effects of hypothyroidism on renal function.

*Funding: No funding sources*

*Conflict of interest: None declared*

*Ethical approval: The study was approved by the Institutional Ethics Committee*

## REFERENCES

1. Emmanouel DS, Lindheimer MD, Katz AL. Mechanism of impaired water excretion in the hypothyroid state. *J Clin Invest.* 1974;54:926-34.
2. Surks MI, Ortiz E, Daniels GH, Sawin CT, Col NF, Cobin RH, et al. Subclinical thyroid disease: Scientific review and guidelines for diagnosis and management. *JAMA.* 2004;291:228-38.
3. Deshmukh V, Behl A, Iyer V, Joshi H, Dholye JP, Varthakavi PK, et al. Prevalence, clinical and biochemical profile of subclinical hypothyroidism in normal population in Mumbai. *Indian J Endocrinol Metab.* 2013;17:454-59.
4. Kimmel M, Braun N, Alscher MD. Influence of thyroid function on different kidney function tests. *Kidney Blood Press Res.* 2012;35:9-17.
5. Saini V, Yadav A, Arora MK, Arora S, Singh R, Bhattacharjee J, et al. Correlation of creatinine with TSH levels in overt hypothyroidism-A requirement for monitoring of renal function in hypothyroid patients? *Clin Biochem.* 2012;45:212-45.
6. Iglesias P, Díez JJ. Thyroid dysfunction and kidney disease. *Eur J Endocrinol.* 2009;160:503-15.
7. Iglesias P, Bajo MA, Selgas R, Díez JJ. Thyroid dysfunction and kidney disease: An update. *Rev Endocr Metab Disord.* 2017;18:131-44.
8. Mariani LH, Berns JS. The renal manifestations of thyroid disease. *J Am Soc Nephrol.* 2012;23:22-6.
9. Talke H, Schubert GE. Enzymatic harnstoff bestimmung in blut ans serum in optischen test nach Warburg klin wschr. 1965;41:174.
10. Arkin CF, Bessman JD, Calam RR, Ernst DJ, Parish GT, Szamosi DI. Procedures for the collection of diagnostic blood specimens by venipuncture; approved standard. *Clinical Laboratory Standards Institute.* 2003;23(32):52.
11. Knapp ML, Mayne PD. Development of an automated kinetic jaffe method designed to minimize bilirubin interference in plasma creatinine assays. *Clin Chim Acta.* 1987;168:239-46.
12. Del-Rio CG, Tapia CL, Picazo AB, Ruiz Moreno JA, Hortas Nieto ML, Romero GJ. Renal failure and failure hypothyroidism. *Pediatric Nephrol.* 2003;18(3):290-92.
13. Suher M, Koc E, Ata N, Ensari C. Relation of thyroid dysfunction, thyroid autoantibodies. *Ren Fail.* 2005;27:739-42.

**Cite this article as:** Badyal A, Kumar S, Chander K. Evaluation of renal function in subclinical and overt hypothyroidism. *Int J Res Med Sci* 2019;7:1520-3.