



**ASSESSMENT OF RENAL FUNCTIONS IN SUBCLINICAL AND OVERT
HYPOTHYROIDISM IN BHAGALPUR DISTRICT OF BIHAR**

Dr. Anand* and Dr. Rolly Bharty¹

*MBBS. MD (Biochemistry) Tutor, Department of Biochemistry. Jawahar Lal Nehru Medical College Bhagalpur, Bihar. India.

¹MBBS.DGO. MD (Biochemistry) Head, Department of Biochemistry. Jawahar Lal Nehru Medical College Bhagalpur, Bihar. India.

***Corresponding Author: Dr. Anand**

MBBS. MD (Biochemistry) Tutor, Department of Biochemistry. Jawahar Lal Nehru Medical College Bhagalpur, Bihar. India.

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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 concentration 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 300 patients, in the age group of 25-65 years, in the Department of Biochemistry, in collaboration with Department of Internal Medicine, Jawaharlal Nehru Medical College, Bhagalpur Bihar over a period of 09 months. After taking proper universal precaution for sampling of blood and 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. 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. **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 various epidemiological studies in India show a prevalence rate of SCH varying between 9.5% to 11%. 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.^[3] There is lack of data in Indian population. Patients with SCH report more symptoms than euthyroid individuals, but fewer symptoms than overtly hypothyroid patients. There is controversy in management of patients with a serum TSH level <10μIU/L. There is inadequate study 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 growth, development and physiology of the kidney.^[4] Serum Creatinine is elevated and glomerular filtration rate (GFR) values are reversibly reduced in overt hypothyroid patients than in euthyroid subjects.^[5-7] Long standing hypothyroidism can cause significant changes in renal functions such as 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 circulatory system. Hypothyroidism also results in increased glomerular capillary permeability of proteins; the consequent proteinuria often precedes the reduction in GFR in hypothyroidism.^[8]

Very few studies have reported the effect of hypothyroidism on renal function tests especially Creatinine. Some studies have also reported hyperuricemia leading to Gouts in Hypothyroid Subjects. This study was therefore planned to analyze 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 300 patients, in the Department of Biochemistry, in collaboration with Department of Internal Medicine, Jawahar Lal Nehru Medical College, Bhagalpur, Bihar over a period of 09 months, Patients included in the study were in the age group of 25-65 years. Further, out of the 300 patients included in the study, 150 patients were having euthyroid status, i.e. normal TSH, fT3 and fT4 levels, who were taken as controls, while the rest 150 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. 05 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 within the time of 10 minutes in autoanalyser.

Serum urea was calculated by Talke H et al, 1965, defining the principle as: urease specifically hydrolyses urea to form ammonia and carbon dioxide.^[9] 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, defined 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.^[10]

Jaffes method was evaluated by Knapp ML, and Mayne PD, defined the principle as: creatinine in the presence of alkaline medium reacts with picric acid to form reddish yellow colored 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.^[10]

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±9.3 years for euthyroid group and 42.8±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	Control	Sub clinical hypothyroidism	Overt hypothyroidism
TSH	2.44±0.69	7.20±1.04*	45.59±9.31*
fT3	0.99±0.08	0.91±0.08*	0.60±0.29*
fT4	3.19±0.24	2.75±0.17*	1.92±0.42*

*p value vs control: 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 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 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.

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

Tests	Control	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	0.73 ±0.22	0.91± 0.28	<0.001	1.09± 0.29	<0.001
Uric acid	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		F T4		F t3	
	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 v/s control: p<0.05

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

	TSH		F T4		F T3	
	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 v/s controls: p<0.05

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.*^[12]

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, significant correlation with any of the renal function parameters but fT4 and fT3 showed a positive correlation with urea (Table 3). Hypothyroidism can lead to kidney disease or decreased renal function, as also shown by Suher *et al.*^[13]

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.

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

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