

ORIGINAL RESEARCH

## STUDY OF RENAL FUNCTION IN PATIENTS WITH HYPOTHYROIDISM ATTENDING A TERTIARY CARE HOSPITAL

C.V. Sarada<sup>1</sup>, Md. Masood Ahmed Shareef<sup>2</sup>

<sup>1</sup>Professor, Department of Biochemistry, Government Medical College, Suryapet, Telangana, India.

<sup>2</sup>Assistant Professor, Department of Biochemistry, Kamineni Institute of Medical Sciences, Narketpally, Nalgonda, Telangana, India.

### ABSTRACT

**Background:**Thyroid function has been suggested to have a relationship with kidney function and chronic kidney disease. Present study was aimed to study renal function tests in patients with hypothyroidism attending a tertiary care hospital.

**Materials and Methods:** Present study was hospital based, case-control study, conducted in Cases (Patients 21-60 years, of either sex, newly diagnosed cases of hypothyroidism, attending the medicine outpatient department, willing to participate) & controls (healthy age-matched subjects).

**Results:** In present study 100 cases & 100 case-controlled matches were studied. Age, gender & BMI were comparable among cases & controls, difference was not statistically significant. Among cases 26 had overt hypothyroidism & 74 had subclinical hypothyroidism. We compared T3, T4, TSH, Urea and Creatinine values among cases & controls. TSH and Creatinine levels were more among cases as compared to controls & difference was statistically significant. While T3, T4 & Urea levels were comparable among cases & controls, difference was not statistically significant. Pearson correlation was significant for values between TSH and serum creatinine while correlation between TSH and serum urea was not significant.

**Conclusion:** Subclinical hypothyroid state is associated with a consistent elevation in the serum creatinine levels due to a decrease in the GFR.

**Keywords:** Hypothyroidism, Subclinical Hypothyroid, Serum Creatinine, Renal Function.

**Corresponding Author:**Dr.C.V. Sarada, Professor, Department of Biochemistry, Government Medical College, Suryapet, Telangana, India. Email: cvsarada@hotmail.com

### INTRODUCTION

Thyroid hormones plays a vital role in metabolic and physiologic homeostasis and regulate cardiac output, heart rate, ventilation rate, basal metabolic rate, effects of catecholamines, brain and endometrium development, catabolism of proteins and carbohydrates.<sup>[1]</sup> The functions of thyroid and kidney are interrelated. The thyroid hormones are essential for

growth and development of the kidney and for maintaining electrolyte and water homeostasis. On the other hand, kidney has its vital role in metabolism and elimination of thyroid hormones.<sup>[2]</sup>

Primary hypothyroidism, which is typically identified by biochemical tests including an elevated serum thyrotropin (TSH) level in conjunction with a low or normal thyroxine (T4) level (defined as overt and subclinical hypothyroidism, respectively).<sup>[3]</sup>

Thyroid function has been suggested to have a relationship with kidney function and chronic kidney disease.<sup>[4,5]</sup> It has been hypothesized that hypothyroidism may lead to altered kidney function via effects on cardiac output, intra-renal hemodynamics, and renin angiotensin aldosterone system (RAAS), as well as structural changes including decreased kidney-to-body weight ratio, truncated tubular mass, and altered glomerular architecture.<sup>[6]</sup> Present study was aimed to study renal function tests in patients with hypothyroidism attending a tertiary care hospital.

## **MATERIALS & METHODS**

Present study was hospital based, case-control study, conducted in department of biochemistry with help from department of general medicine, at Government medical college & hospital, Suryapet, Telangana, India. Study duration was of 6 months (July 2021 to December 2021). Study approval was taken from institutional ethical committee.

### **Inclusion criteria**

- Cases - Patients 21-60 years, of either sex, newly diagnosed cases of hypothyroidism, attending the medicine outpatient department, willing to participate.
- Control – healthy age-matched subjects

### **Exclusion Criteria**

- Hypertension, cardiovascular disorder, diabetes and impaired glucose tolerance, Malignancy.
- Previously diagnosed renal diseases like nephrotic or nephritic syndrome, nephropathy, urinary tract infection, renal stones, etc.
- Autoimmune disorders like rheumatoid arthritis, systemic lupus erythematosus, etc. Other endocrine dysfunctions like Cushing syndrome, acromegaly, etc.
- Thyroid dysfunction arising secondary to pituitary or hypothalamus pathology,
- Under treatment with those drugs that affect renal functions like angiotensin converting enzyme inhibitors/angiotensin receptor blockers, diuretics, allopurinol, steroids, etc.
- History of drugs affecting thyroid hormonal status, e.g., Li, amiodarone, phenytoin, carbamazepine, salicylates, beta blockers, rifampicin, cytotoxic drugs, etc.
- Pregnant and lactating women.

Study was explained & a written informed consent was taken from cases & controls to participate in the study. Details such as age, gender, BMI, past medical history was collected & noted in proforma. After 12 hours overnight fasting serum T3, T4, TSH, creatinine and urea levels were estimated.

Plain vacutainer was used. The samples were separated by centrifugation at 2400 rpm. Serum Creatinine (Alkaline picrate Method) and Urea (Urease kinetic Method) were analyzed in DADE Dimension automated system. Thyroid profile (T3,T4,TSH) was estimated by Automated Electro Chemiluminescence (ECLIA) method using commercially available kit by ROCHE Cobas e411 For adequate quality control both normal, abnormal reference control serum solutions and calibrators were run before each batch.

Data was collected and compiled using Microsoft Excel, analysed using SPSS 23.0 version. Frequency, percentage, means and standard deviations (SD) was calculated for the continuous variables, while ratios and proportions were calculated for the categorical variables. Difference of proportions between qualitative variables were tested using chi-square test or Fisher exact test as applicable. P value less than 0.5 was considered as statistically significant.

## RESULTS

In present study 100 cases & 100 case-controlled matches were studied. Age, gender & BMI were comparable among cases & controls, difference was not statistically significant. Among cases 26 had overt hypothyroidism & 74 had subclinical hypothyroidism.

**Table 1: Age and gender distribution**

Characteristics	Cases	Controls	P value
Age (yrs)	42.55 ± 10.33	41.27 ± 11.54	< 0.05
Gender (M/F)	21/79	22/78	< 0.05
BMI (kg/m <sup>2</sup> )	24.1 ± 3.5	23.8 ± 4.2	< 0.05
Thyroid status			
Overt hypothyroid	26	0	
Subclinical hypothyroid	74	0	
Euthyroid	0	100	

We compared T3, T4, TSH, Urea and Creatinine values among cases & controls. TSH and Creatinine levels were more among cases as compared to controls & difference was statistically significant. While T3, T4 & Urea levels were comparable among cases & controls, difference was not statistically significant.

**Table 2: Comparison of levels of T3, T4, TSH, Urea and Creatinine**

Parameter	Cases	Controls	p-value
T3(ng//dl)	101.62 ± 32.5	114.5 ± 43.9	0.22
T4(µg/dl)	8.1 ± 2.4	6.9 ± 3.7	0.064
TSH(µIU/ml)	12.92 ± 6.72	2.7 ± 1.1	< 0.001*
Urea(mg/dl)	22.38 ± 6.63	20.01 ± 9.27	0.078
Creatinine(mg/dl)	0.92 ± 0.15	0.63± 0.12	< 0.001*

\*p<0.001 statistically significant

Pearson correlation was significant for values between TSH and serum creatinine while correlation between TSH and serum urea was not significant.

**Table 3: Correlation of TSH with serum urea and creatinine levels**

Cases	P value	Pearson Correlation (r value)
TSH vs urea	0.078	+ 0.0002
TSH vs creatinine	< 0.001	+ 0.1754

## DISCUSSION

Thyroid hormones (TH) are essential for an adequate growth and development of the kidney. Conversely, the kidney is not only an organ for metabolism and elimination of TH, but also a target organ of some of the iodothyronines' actions. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Hypothyroidism is accompanied by a decrease in glomerular filtration, hyponatremia, and an alteration of the ability for water excretion.<sup>[4,5]</sup>

The GFR is reversibly reduced (by about 40%) in more than 55% of adults with hypothyroidism due to several reasons.<sup>[7]</sup> There is decreased sensitivity to  $\beta$ -adrenergic stimulus and decreased renin release, along with decreased angiotensin II and impaired RAAS activity, resulting in loss of GFR. There is a structural constraint imposed by limited glomerular surface area for filtration due to renal parenchymal growth retardation in hypothyroidism.<sup>[8]</sup>

In a cross-sectional analysis of 461,607 US veterans who underwent repeated measures of serum TSH and creatinine testing at identical time points, each 10 ml/min/1.73m<sup>2</sup> decrement in eGFR was associated with an 18% higher risk of hypothyroidism, independent of socio-demographics and comorbidities.<sup>[9]</sup>

Sowjanya Y,<sup>[10]</sup> conducted a study on RFTs in newly diagnosed 40 hypothyroidism patients attended OPD and 40 age and sex matched healthy controls was done. The statistical analysis of serum T3 (P<0.001), T4 (P<0.001), TSH (P<0.001), Urea (P<0.001) and serum creatinine (P<0.001) were highly significant indicating significant association between kidney dysfunction and thyroid profile. There is a consistent and reversible increase of serum creatinine and Urea levels in the hypothyroid state.

Devika T et al,<sup>[11]</sup> studied Thyroid function tests (T3, T4 and TSH levels) in 385 subjects. Based on TSH levels, subjects were classified as euthyroid (n=198), sub-clinical hypothyroid (n=98; TSH 6.1 to 19.9  $\mu$ IU/ml) and overt hypothyroid (n=89; TSH  $\geq$  20  $\mu$ IU/ml, abnormally low T4 levels). 48 hypothyroid patients were re-evaluated after 3 months of thyroxine replacement therapy. Renal function tests were carried out in all subjects and statistically analyzed. Serum creatinine was significantly increased in subclinical and overt hypothyroid groups as compared to euthyroid subjects. Serum creatinine showed a significant negative correlation with T3 & T4 levels in overt group (r = -0.372 and r = - 0.371), whereas a positive correlation was observed with TSH (r=0.283). Uric acid levels were significantly increased in the overt group as compared to euthyroid subjects. Uric acid levels showed a significant negative correlation with T3 levels in the overt group (r= -0.298).

Manoj KM et al,<sup>[12]</sup> conducted clinical & diagnostic evaluation and follow up in 100 newly diagnosed patient of primary hypothyroidism Mean serum TSH value before treatment was 44.70 $\pm$ 31.59 and after treatment was 2.69 $\pm$ 1.06, difference was significant (p=0.000). Mean

serum creatinine value before and after treatment were  $0.95 \pm 0.24$  and  $0.83 \pm 0.18$  respectively, which was significant ( $p=0.000$ ). Mean creatinine clearance level before and after therapy were  $77.62 \pm 7.01$  and  $87.45 \pm 6.61$ , difference before and after therapy was significant ( $p=0.0001$ ).

Saha S et al,<sup>[13]</sup> noted that mean values of serum creatinine, urea, and ACR are significantly increased among untreated patients with primary hypothyroidism, with the decrease in the eGFR, in comparison to healthy control group ( $p < 0.001$ ); whereas patients on treatment for hypothyroidism show fall in serum creatinine, serum urea, and ACR level, with increase in eGFR values compared with drug naïve primary hypothyroid patients ( $p < 0.001$ ). In addition, the results of eGFR and ACR are significantly correlated with thyroid-stimulating hormone (TSH) values.

Primary hypothyroidism is associated with a reversible elevation of serum creatinine in both adults and children.<sup>[14-16]</sup> This increase is observed in more than half (~55%) of adults with hypothyroidism. Moreover, some authors have reported an elevation of serum creatinine associated with subclinical hypothyroidism.<sup>[17]</sup>

In patients with unexplained abnormal renal function should be screened for thyroid disorders, especially for primary hypothyroidism. But it is still not certain about the possible outcome of the deranged renal function among the untreated patients with hypothyroidism in the long run. Also, it should be recommended to check for alteration in renal functions among untreated hypothyroid patients and take necessary actions in the form of hormone replacement therapy to abort any possibility of future nephropathy.

## CONCLUSION

Subclinical hypothyroid state is associated with a consistent elevation in the serum creatinine levels due to a decrease in the GFR. Assessment of renal function is recommended in thyroid abnormalities & thyroid function in patients presenting with deranged renal function.

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