

# Case control study of renal function in patients with hypothyroidism attending tertiary care hospital

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## Abstract

**Background:** Thyroid hormones are required for the normal growth, development and function of nearly all tissues, with major effects on oxygen consumption and metabolic rate. Decrease in iodothyronines is associated with reduced blood flow to kidneys and decreased glomerular filtration rate (GFR) along with alteration in tubular reabsorption resulting in decrease in water excretion. In present case control study, renal function of patients with hypothyroidism was compared with healthy adults at a tertiary care hospital. **Material and Methods:** Present study was a case control study. Patients 19-60 years, of either sex, newly diagnosed and confirmed cases of hypothyroidism, attending the medicine outpatient department, willing to participate were considered as cases and healthy age-matched subjects attending OPD for accompanying patients as controls. **Results:** In present study 100 cases and 100 age-matched healthy controls were studied. General characteristics such as age, gender and BMI were comparable in both groups. Out of 100 cases, 31 were overt hypothyroid while 69 were subclinical hypothyroid. A highly significant difference was noted for serum creatinine between cases and controls. Values of serum urea were comparable in both groups. Pearson correlation was significant for values between TSH and serum creatinine while correlation between TSH and serum urea was not significant. **Conclusion:** Hypothyroid state (overt or subclinical) is associated with elevation in the serum creatinine levels, evaluation of renal function should be conducted in newly diagnosed hypothyroid patients.

**Keywords:** Creatinine, hypothyroidism, thyroid-stimulating hormone, renal function

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## INTRODUCTION

Thyroid hormones are required for the normal growth, development and function of nearly all tissues, with major effects on oxygen consumption and metabolic rate. Thyroid Hormone synthesis and secretion is regulated by a negative feedback system that involves the hypothalamus, pituitary and the thyroid gland.<sup>1</sup> Hypothyroidism is a progressive disorder that presents with diverse degrees of thyroid failure and metabolic consequences. An increase in serum thyroid-stimulating hormone (TSH) levels is a very early biochemical marker of impending thyroid failure resulting from the gradual decline of T4 and, at a later stage, of T3. Subclinical hypothyroidism is characterized by increased serum TSH and normal free triiodothyronine

(fT3), free tetraiodothyronine (fT4) levels. Overt is characterized by increased TSH and decreased fT3, fT4 levels.<sup>2</sup> The prevalence and pattern of thyroid disorders depends on sex, age, ethnic, and geographical factors and especially on iodine intake.<sup>3</sup> Decrease in iodothyronines is associated with reduced blood flow to kidneys and decreased glomerular filtration rate (GFR) along with alteration in tubular reabsorption resulting in decrease in water excretion. At the same time, kidneys not only contribute significantly to metabolism and removal of thyroid hormones from the body but also play important role in certain actions of these hormones.<sup>4,5,6</sup> In present case control study, renal function of patients with hypothyroidism was compared with healthy adults at a tertiary care hospital

## MATERIAL AND METHODS

Present study was a case control study conducted in department of medicine, Basaveshwara hospital attached to Mahadevappa Rampure Medical College. Study period was from September 2011 to August 2012 (1 year). Institutional ethical committee approval was taken for present study.

### Inclusion criteria

Cases - Patients 19-60 years, of either sex, newly diagnosed and confirmed cases of hypothyroidism, attending the medicine outpatient department, willing to participate. Control – healthy age-matched subjects attending OPD for accompanying patients

### Exclusion Criteria

Hypertension, cardiovascular disorder, diabetes and impaired glucose tolerance, Malignancy. Previously

## RESULTS

In present study 100 cases and 100 age-matched healthy controls were studied. General characteristics such as age, gender and BMI were comparable in both groups. Out of 100 cases, 31 were overt hypothyroid while 69 were subclinical hypothyroid.

**Table 1:** General characteristics

Characteristics	Cases (n=100)	Controls (n=100)	p-value
Age (in years)	41.6 ± 11.5	43.5 ± 12.2	0.32
Gender (Male/female)	36/64	36/64	0
BMI (kg/m <sup>2</sup> )	24.1 ± 3.5	23.8 ± 4.2	0.69
Thyroid status			
Overt hypothyroid	31	0	
Subclinical hypothyroid	69	0	
Euthyroid	0	100	

We compared serum urea and serum creatinine values between cases and controls. A highly significant difference was noted for serum creatinine between cases and controls. Values of serum urea were comparable in both groups.

**Table 2:** Comparison of levels of fT3, fT4, TSH, Urea and Creatinine

	Cases (n=100)	Controls (n=100)	p-value
Urea (mg/dl)	18.8 ± 4.9	20.01 ± 5.1	0.63
Creatinine (mg/dl)	1.29 ± 0.65	0.81 ± 0.32	<0.001

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

diagnosed renal diseases like nephrotic or nephritic syndrome, nephropathy, urinary tract infection, renal stones, etc. Any 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, i.e., secondary hypothyroidism and hyperthyroidism. 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.

After a thorough history taking and clinical examination, the procedure was explained to the subjects and informed consent was obtained. A sample of 5 ml venous blood was collected and processed for estimation of fT3, fT4, TSH, serum creatinine and serum urea. All samples were processed at our central clinical laboratory. Normal ranges for fT3 (1.2 - 4.1 pg/ml), fT4 (8.9-17.8 pg/ml), TSH (0.45-5.0  $\mu$ IU/ml). Serum creatinine (0.6-1.4 mg/dL) and uric acid (2.7-6.5 mg/dL). Data was collected, entered in Microsoft excel sheet and analysed with help of SPSS version 22. The variables were presented in terms of mean and standard deviation. Student's unpaired 't' test and Pearson's correlation coefficient test was done to see the correlation of serum urea and creatinine levels with the TSH levels. 'p' values <0.05 were considered significant.

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

Cases	P value	Pearson correlation (r value)
TSH vs urea	P=0.893	+ 0.0001
TSH vs creatinine	P<0.001	+ 0.146

## DISCUSSION

Primary hypothyroidism is associated with impaired glomerular filtration which is reversible with treatment in approximately 55% of cases. Long-standing hypothyroidism can cause significant reversible changes in renal function such as a decrease in sodium resorption in the proximal tubules, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in urinary urate excretion, and a decrease in renal blood flow and glomerular filtration rate (GFR).<sup>7,8</sup> In study by Jaiswal N<sup>9</sup>, most patients belong to age group of 31–40 years, similar findings were noted in present study and Chaudhury *et al.*<sup>10</sup> In study by Jaiswal N<sup>9</sup>, mean serum creatinine values of the study and control groups were 0.922 and 0.798 mg/dL, respectively. Mean serum creatinine values were high in the study group than in the control group and the difference was statistically highly significant. Bhutal MB, *et al.*<sup>11</sup> noted a significant increase in mean serum creatinine levels in both subclinical ( $0.95 \pm 0.21$ ) and overt hypothyroid cases ( $1.48 \pm 0.39$ ) in comparison to controls ( $0.67 \pm 0.10$ ). Serum creatinine levels in overt hypothyroid cases were significantly higher in comparison to subclinical cases. Also a significant increase in serum uric acid in both subclinical ( $4.67 \pm 0.70$ ) and overt hypothyroid cases ( $6.53 \pm 0.69$ ) in comparison to controls ( $4.18 \pm 0.65$ ) and serum uric acid levels in overt hypothyroid cases were significantly higher when compared to subclinical cases. In the study by Mamatha BV *et al.*,<sup>12</sup> mean serum creatinine concentrations were significantly increased in cases as compared to controls and significant difference ( $p < 0.001$ ) was found between the groups. A significant positive correlation between TSH and serum creatinine levels with  $p < 0.001$  was noted, but correlation between TSH and serum urea levels was not significant. Similar findings were noted in present study. Thyroid dysfunction causes significant changes in kidney function and the most common kidney derangements associated with hypothyroidism is elevation of serum creatinine levels, reduction in GFR and renal plasma flow. Primary subclinical hypothyroidism is associated with a reversible elevation of serum creatinine in both adults and children.<sup>13</sup> The increase in serum uric acid and creatinine may be either due to increased production or decreased renal clearance due to the generalized hypodynamic circulation in hypothyroid patients. The changes in the metabolic parameters were found to be reversible after thyroxine replacement therapy.<sup>14</sup> Thyroid has negligible effect upon the synthesis of creatine from its precursors. In

hypothyroid state, creatine is retained in the muscle and the stores of both creatine and phosphocreatine are increased; however, the conversion of creatine to creatinine is uncertain.<sup>15</sup> Hypothyroidism results in a reversible elevation in serum creatinine due to the reduction in GFR as well as possible myopathy and rhabdomyolysis. There is a reduction in serum cystatin C levels in hypothyroidism due to reduced production, consequent to reduced cellular metabolism. Both these changes are reversible with treatment of hypothyroidism.<sup>16</sup> Thus renal evaluation is must for patients diagnosed with hypothyroidism and vice a versa. Given the high prevalence of hypothyroidism further research is needed to more accurately define the risks related to renal dysfunction and benefits of treatment with thyroxine on renal functions

## CONCLUSION

Hypothyroid state (overt or subclinical) is associated with elevation in the serum creatinine levels, evaluation of renal function should be conducted in newly diagnosed hypothyroid patients. After treatment with thyroxine, periodic assessment of renal functions is also recommended.

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