

Circulating thyroid hormones with serum uric acid and creatinine in hypo and hyperthyroidism

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Abstract

Introduction: Thyroid dysfunction is related to damaging effect on glomerular and tubular functions. In recent studies it was found that hypo and hyperthyroidism was accompanied with renal derangement resulting in abnormal levels of serum creatinine and uric acid. So this study was conducted for estimation of serum non-protein nitrogenous constituents in hypo and hyperthyroidism.

Materials and Method: 60 patients, with 30 hypothyroid and 30 hyperthyroid patients were included in this study along with 30 controls. Thyroid hormones (T3, T4, and TSH) were estimated by Beckman coulter Access-2 immunoassay analyser. Uric acid, creatinine and urea parameters were measured using fully automated Beckman coulter clinical chemistry analyser AU480. Analysis of Statistical data was done by SPSS 20.

Results: There was a significant increase in the levels of serum uric acid and ($p < 0.0001$) in hypothyroid patients and hyperthyroid patients showed significant decrease in serum creatinine levels ($p < 0.0001$). When correlated with TSH, Serum creatinine showed positive correlation, whereas it was negative for serum uric acid in hypothyroidism, in hyperthyroid patients, there was a negative for serum creatinine and uric acid levels.

Conclusion: The results of this study indicate that the non-protein nitrogenous constituent's mainly uric acid and creatinine were significantly altered in hypothyroid and hyperthyroid patients. Therefore, we have emphasize and the importance of the routine evaluation of these biochemical parameters in hypo and hyperthyroid patients.

Keywords: Hypothyroidism, Hyperthyroidism, Thyroid Stimulating Hormone (TSH), Creatinine, Uric Acid.

Introduction

Among many known non-protein nitrogenous substances, the commonly and routinely used parameters in clinical chemistry for diagnosis are Urea, Creatinine and Uric acid. In present study, we tried to assess these three NPN's in hypo and hyperthyroidism. Thyroid abnormalities are the most common disorders among other endocrine gland. Thyroid dysfunction affects renal function.⁽¹⁾ Hypothyroidism is the most common thyroid disorder among the endocrine disorders.⁽²⁾ Hypothyroidism is a clinical condition arises due to the deficiency of thyroid hormones which hinders the metabolic pathways.^(3,4) The effects of hypothyroid state on the kidney are well established. Physiological effects include water and electrolyte imbalance and changes in renal function.^(5,6) The renal biochemical effects associated with hypothyroidism affects serum creatinine and uric acid levels, so there might be a decrease in GFR.^(7,8)

Hyperthyroidism is a thyroid disorder characterized by decrease in TSH level. Very few studies show the effect of hyperthyroidism on renal function. Hyperthyroidism is mainly associated with decreased serum creatinine levels due to elevated renal plasma flow and GFR.^(9,10)

Very few studies on Indian population show that hypo and hyperthyroidism alter NPN's like creatinine, urea and uric acid levels. Hence the present study was undertaken to study these non-protein nitrogenous substances in hypothyroid and hyperthyroid patients.

Materials and Methods

Total 60 clinically diagnosed, 30 hypothyroid and 30 hyperthyroid female patients along with 30 female controls of 18-75 years were included in this study. The study was conducted in BMC&RI, attached to victoria hospital, Bengaluru. Patients on thyroid drugs and history of hypertension, diabetes mellitus, obesity, renal disorders and hepatic disorders were excluded from the study.

Method of Analysis: After obtaining written informed consent, 5ml of venous blood was obtained by venepuncture under aseptic conditions, Samples were centrifuged and separated serum was used for estimation of thyroid hormones, urea, creatinine and uric acid. Thyroid hormones were measured by Chemiluminescence Imunnoassay method on Beckman Coulter Access-2 auto-analyzer. The fully automated clinical chemistry analyser Beckman Coulter AU480 was used to analyse serum urea, uric acid and creatinine levels. The results were tabulated. Results on continuous measurements are presented on Mean \pm SD. The Statistical analysis of data was done by using software namely SAS 9.2, SPSS 20.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R env ver.2.1.1.

The results of cases and controls were compared by student 't' test. A 'p' value of < 0.05 was considered significant. A 'p' value of < 0.0001 was considered as highly significant. All three parameters were compared with TSH levels. Pearson's correlation and t test of coefficient were calculated.

Results

Table 1: Comparison between Controls and Hypothyroid patients

Lab variables	Controls	Patients	p value
T3(ng/ml)	1.22±0.21	0.94±0.15	<0.0001
T4(µg/dl)	9.68±1.21	4.85±1.07	<0.0001
TSH (µIU/ml)	2.16±0.94	44.46±29.42	<0.0001
Urea(mg/dl)	25.06±3.26	25.66±3.48	<0.4945
Creatinine(mg/dl)	0.81±0.03	1.34±0.18	<0.0001
Uric acid (mg/dl)	5.54±0.25	6.46±0.31	<0.0001

Table 2: Comparison between Controls and Hyperthyroid patients

Lab variables	Controls	Patients	p value
T3(ng/ml)	1.22±0.21	1.85±0.73	<0.0001
T4(µg/dl)	9.68±1.21	16.35±2.43	<0.0001
TSH (µIU/ml)	2.16±0.94	0.26±0.24	<0.0001
Urea(mg/dl)	25.06±3.26	25.8±2.55	<0.3368
Creatinine(mg/dl)	0.81±0.03	0.70±0.02	<0.0001
Uric acid (mg/dl)	5.54±0.25	5.43±0.26	<0.1058

Table 3: Pearson's correlation coefficient (r) between NPN's and TSH

TSH	Correlation coefficient (Hypothyroidism)	Correlation coefficient (Hyperthyroidism)
Urea(mg/dl)	0.3562	-0.0812
Creatinine(mg/dl)	0.2144	-0.3461
Uric acid (mg/dl)	-0.0435	-0.1731

Discussion

The abnormalities in thyroid gland alter renal function. Both hypothyroidism and hyperthyroidism affect renal blood flow, GFR, tubular function and also water and electrolyte balance.⁽¹¹⁾

The Table 1, our study shows that the levels of serum creatinine and uric acid significantly increased in hypothyroid patients compared to controls ($p < 0.0001$), with no significant difference in the level of urea. The Table 2, showed that in hyperthyroid patients, the serum creatinine level was decreased as compared to controls ($p < 0.0001$). However, there was no significant difference in the levels of urea and uric acid.

Kreisman and Hennessey in their study found that serum creatinine levels in hypothyroid cases were significantly higher in compared to controls.⁽¹²⁾ Various etiologies have been put for the pathophysiology of renal dysfunction in hypothyroidism. In hypothyroid state, hypovolemia occurs due to decreased cardiac output resulting in a fall in renal blood flow. Thyroxine leads to an increase in systemic and renal vasoconstriction and finally leading to reduced renal blood flow.⁽¹³⁾ Thyroxine has been postulated for increasing creatinine reabsorption and in blood by affecting its urinary excretion.⁽¹⁴⁾ Thyroxine may fluctuate transcription in the sarcoplasmic reticulum, affecting the $\text{Na}^+/\text{Ca}^{2+}$ exchanger and the Na^+/K^+ -ATPase activity in the kidneys and these developments are related to increase in creatinine level.⁽¹⁵⁾

In hypothyroid patients, myopathy is associated with increased serum creatinine phosphokinase and rhabdomyolysis may also occur. Increased release of creatinine may lead to reversible renal damage⁽¹⁶⁾ and Kreisman et al found that there was privation of obvious association between levels of creatine kinase and degree of renal failure.

Hyperuricemia in hypothyroid patients was due to increase urate reabsorption and decreased renal plasma flow or due to hypothyroidmyopathy.^(17,18) In our study the creatinine and uric acid levels were showed positive correlation with TSH as depicted in Table 3.

There are only few studies explaining the effect of hyperthyroidism on renal function. It may be due to an increase in renal plasma flow and GFR resulting in a reduction of serum creatinine levels, whereas uric acid levels are within normal range in this study. The creatinine and uric acid levels negatively correlated with TSH as depicted in Table 3.

Another possible mechanism of action of thyroid hormone on renal function could be explained by its influence on maturation of the renin-angiotensin system (RAAS). Plasma renin activity and plasma levels of angiotensinogen, angiotensin II and aldosterone are directly associated to plasma levels of thyroid hormones.⁽¹⁹⁾ Hypothyroidism is associated with low plasma renin, which may cause an increase in creatinine and uric acid levels.⁽²⁰⁾ In contrast, hyperthyroidism is accompanied by hyperactivity of the RAAS.⁽²¹⁾ T_3 also induces relaxation of blood vessel resulting in a

reduction in vascular resistance and increases serum levels of renin activity and angiotensinogen concentration.⁽²²⁾ This leads to decrease in TSH with increase in T₃ and T₄ and decreased creatinine levels without much effect on uric acid levels.⁽²²⁾

Conclusion

This study was deliberated to evaluate the role of non-protein nitrogenous substances in hypo and hyperthyroidism and correlate the changes with TSH. Our study confirms that hypothyroidism is associated with increased creatinine and uric acid levels and decreased creatinine levels in hyperthyroidism. Therefore, in case of deranged renal function, our study concludes that thyroid function tests should be carried out routinely to know the status of thyroid gland and viceversa.

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