

INTER- RELATIONSHIP BETWEEN THYROID AND RENAL PROFILE IN OVERT HYPOTHYROIDISM

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ABSTRACT: BACKGROUND: Renal function is altered by thyroid status. Therefore, this study was done to determine the relationship between thyroid and renal parameters in overt type of thyroid dysfunction.

AIM: The aims of this study were to correlate parameters of serum creatinine, creatinine clearance, with serum T₃, T₄ and TSH in overt hypothyroid cases.

MATERIALS AND METHODS: This Case control study included fifty diagnosed cases of hypothyroidism in the department of Endocrinology, Medicine and Surgery of A J Institute of Medical Sciences & Research Centre, Mangaluru, of age group 15-75 years. Based on TSH levels, subjects were classified as subclinical hypothyroids and overt hypothyroids. Results were compared with age and sex matched twenty five euthyroids. Serum T₃, T₄ and TSH; Serum creatinine; and Creatinine clearance were estimated and analysed.

RESULTS: The results of the present study were obtained from 75 subjects out of whom 25 were controls, 22 were subclinical hypothyroids and 28 were overt hypothyroids. Age distribution of study subjects shows that the mean age was 39.56±13.019 for overt hypothyroids. Sex distribution of study subjects shows that majority of overt hypothyroids (78.6%) were females. Percentage of individuals with altered serum creatinine, and creatinine clearance among overt hypothyroids shows that there were more cases of overt hypothyroids with increased serum creatinine. Hypothyroid cases had decreased renal function. Overt hypothyroids showed statistically significant difference in the levels of serum creatinine, but they did not differ in the levels of creatinine clearance.

CONCLUSION: Hypothyroidism is linked with considerable derangement in biochemical parameters of renal function, necessitating regular monitoring of renal parameters in hypothyroid patients.

KEYWORDS: Creatinine; Creatinine Clearance; Overt Hypothyroidism; Thyroid Hormones.

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INTRODUCTION: Long standing hypothyroidism causes significant reversible changes in renal function such as decrease in sodium resorption in the proximal tubules, impairment in the concentrating and diluting capacities of the distal tubules, a decrease in urate concentration, and a decrease in renal blood flow and GFR. This is because of hypodynamic state that occurs in hypothyroidism. The altered thyroid function induces a decrease in myocardial contractility and cardiac output. There is increase in peripheral resistance leading to systemic and renal vasoconstriction. This results in decreased renal blood flow causing decrease in GFR, increase in creatinine and a decrease in creatinine clearance.

There is thickening of basement membrane which again causes reduced blood flow to the kidneys, so there is decreased creatinine clearance.¹ this study intends to correlate parameters of serum creatinine, creatinine clearance, with serum T₃, T₄ and TSH in overt hypothyroid cases.

MATERIALS AND METHODS: This Case control study included fifty diagnosed cases of hypothyroidism in the department of Endocrinology, Medicine and Surgery of A J Institute of Medical Sciences & Research Centre, Mangalore, of age group 15-75 years after Ethical clearance from Institutional Ethical Committee. Based on TSH levels, subjects were classified as subclinical hypothyroids (TSH 6.1-19.9 µU/ml) and overt hypothyroids (TSH ≥20 µU/ml).

Results were compared with age and sex matched twenty five euthyroids. Diagnosed cases of hypothyroidism of age group 15-75 years (50) were included in the study. Age and sex matched euthyroids (25) taken as control subjects. Patients with acute infections, hepatobiliary diseases, renal diseases, diabetes mellitus, heart diseases, myopathies, pregnant females were excluded from the study.

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In all selected individuals about 5ml of blood was collected in plain tube from large peripheral vein with aseptic precautions after obtaining informed consent. Serum was separated after centrifugation at 3000rpm for 10min and following parameters were estimated: Serum T₃, T₄ and TSH measured by Chemiluminescence method in Immulite 1000 autoanalyzer.^{2,3,4} Serum creatinine measured by Modified Jaffe's method in semiautoanalyzer using commercially available kit.⁵ Creatinine clearance measured using Cockcroft-Gault formula.⁶

$$\text{Creatinine clearance (ml/min/1.73m}^2\text{)} = \frac{[(140 - \text{age (years)}) \times \text{weight (kg)}]}{72 \times \text{plasma creatinine (mg/dL)}}$$

Correction factor of 0.85 is recommended for females.

Data was analyzed using Analysis of Variance, Bonferroni test, Kruskal Wallis test, Mann Whitney test, Karl Pearson's correlation and Chi square test. $P < 0.05$ was considered to be statistically significant.

RESULTS: The results of the present study were obtained from 75 subjects out of whom 25 were controls, 22 were subclinical hypothyroids and 28 were overt hypothyroids. Age distribution of study subjects shows that the mean age was 39.56 ± 13.019 for overt hypothyroids. Sex distribution of study subjects shows that majority of overt hypothyroids (78.6%) were females. Percentage of individuals with altered serum creatinine, and creatinine clearance among overt hypothyroids shows that there were more cases of overt hypothyroids with increased serum creatinine (14.8%) as illustrated in Table 1.

Correlation of T₃, T₄ and TSH with other parameters in hypothyroids shows positive correlation between T₃ and creatinine clearance ($r=0.361$) in hypothyroids. It shows negative correlation with serum Creatinine ($r=-0.406$). The table shows positive correlation of T₄ with creatinine clearance ($r=0.429$) and negative correlation with serum creatinine ($r=-0.484$). Study also shows positive correlation of TSH with serum creatinine ($r=0.510$) and negative correlation of creatinine clearance ($r=-0.451$) with TSH. All correlations were statistically significant with p value < 0.05 as depicted in Table 2.

Correlation of serum creatinine, and creatinine clearance in the study groups shows that there was negative correlation of T₃ with serum creatinine ($r=-0.552$), and with creatinine clearance ($r=0.396$). This correlation was statistically significant. The negative correlation of T₄ with serum creatinine ($r=-0.596$) was statistically significant with p value of 0.001. The positive correlation between T₄ with creatinine clearance ($r=0.377$) was not statistically significant in overt hypothyroids. The positive correlation of TSH with serum creatinine ($r=0.351$) was not statistically significant. The negative correlation of TSH with creatinine clearance ($r=-0.264$) was not statistically significant in overt hypothyroids as elaborated in Table 3; Fig. No. 1, 2, and 3.

DISCUSSION: Hypothyroidism is a graded phenomenon, ranging from very mild cases in which biochemical abnormalities are present but the individual hardly notices

symptoms and signs of thyroid hormone deficiency, to very serious cases of life threatening myxedema coma. The transition from the euthyroid to the hypothyroid state is first detected by a slightly elevated serum TSH, caused by a minor decrease in thyroidal secretion of T₄ which does not give rise to subnormal serum T₄ concentration.

A further decline in T₄ secretion results in T₄ value below the lower normal limit and even higher TSH, but serum T₃ concentrations remain within the reference range. It is only in the last stage that subnormal serum T₃ concentrations are found, when serum T₄ has fallen to very low levels associated with markedly elevated serum TSH concentrations. In hypothyroidism, the first stage of subclinical hypothyroidism may progress towards overt hypothyroidism.

This study showed that the mean age group of overt hypothyroids was 39.56 ± 13.019 . This is in accordance with a study done by Tayal D et al which showed the age group of patients in the study group as 43.4 ± 2.67 years and in the control group as 44.1 ± 3.2 years.⁷ Prevalence of overt hypothyroidism was high in females with 78.6% under overt hypothyroidism. This is in accordance with studies done with Sheikh BA et al and Ali M N et al.^{8,9}

The study showed statistically significant negative correlation between T₃ and T₄ and serum creatinine with $r = -0.406$ and $r = -0.484$ respectively and a positive correlation between TSH and serum creatinine ($r=0.510$) among hypothyroids which is in accordance with the study of Tayal D⁷ and Prakash A et al¹⁰. The negative correlation between T₃ and T₄ and serum creatinine with $r=-0.552$ and $r=-0.596$ respectively were statistically significant in overt hypothyroids ($p < 0.05$) as the hypodynamic state in hypothyroidism reduces the renal function.

There was positive correlation of creatinine clearance with T₃, which was statistically significant in overt hypothyroids ($r=0.396$, $p=0.041$). This is in accordance to the study of Tayal D et al⁷ which says that lack of T₃ causes vasoconstriction ultimately leading to reduced glomerular filtration rate. Although the findings of this study may be utilized for the proper management of hypothyroid cases, further studies on more number of hypothyroid cases along with follow up studies are needed to explore the actual differences in the effects of thyroid hormones in subclinical and overt hypothyroids.

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Parameter	Range	Overt hypothyroids
Serum creatinine mg/dl	Above normal	14.8%
Creatinine clearance ml/min/1.73 m ²	Below normal range	77.8%

Table 1: Percentage of individuals studied with altered levels of serum creatinine and creatinine clearance among overt hypothyroids

	Parameters	r value	P value
T ₃ ng/dl	Serum creatinine	-0.406	0.000
	Creatinine clearance	0.361	0.002
T ₄ μg/dl	Serum creatinine	-0.484	0.000
	Creatinine clearance	0.429	0.000
TSH μIU/ml	Serum creatinine	0.510	0.000
	Creatinine clearance	-0.451	0.000

Table 2: Correlation of T₃, T₄ and TSH with other parameters in hypothyroids

Parameters		Serum creatinine		Creatinine clearance	
		r value	p value	r value	p value
T ₃ ng/dl	Controls	0.314			
	Overt hypothyroids	0.126		-0.053	0.800
		-0.552*		0.396*	0.041
		0.003			
T ₄ μg/dl	Controls	0.162		-0.076	0.717
	Overt hypothyroids	0.438		0.377	0.053
		-0.596*			
		0.001			
TSH μIU/ml	Controls	-0.189		0.061	0.773
	Overt hypothyroids	0.364		-0.264	0.183
		0.351			
		0.073			

Table 3: Correlation of serum creatinine, and creatinine clearance in the study groups

* P value < 0.05

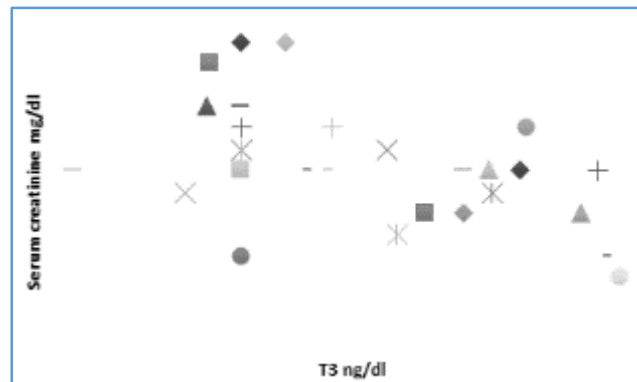


Fig. 1: Correlation of serum creatinine with T₃ in overt hypothyroids

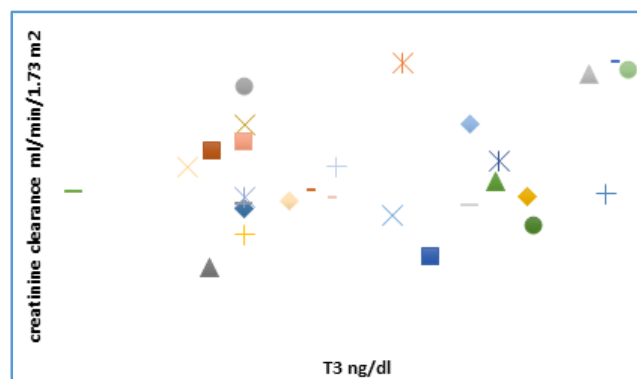


Fig. 2: Correlation of creatinine clearance with T₃ in overt hypothyroids

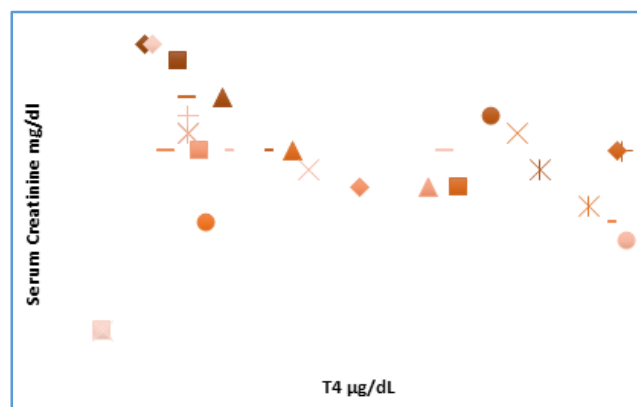


Fig. 3: Correlation of serum creatinine with T₄ in overt hypothyroids