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Renal insufficiency in overt hypothyroidism

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ABSTRACT

Hypothyroidism is a common endocrine disorder worldwide. In hypothyroidism, there is altered regulation of renal hemodynamics and basal metabolic rate. This hospital-based case-control study was done to evaluate the changes in uric acid level in hypothyroid subjects. This study includes 25 hypothyroid cases with age and sex-matched controls. Serum total thyroid profile was estimated by Chemiluminiscence Immunoassay (CLIA) and uric acid by the Uricase method in fully automated Vitros 5600. The mean uric acid level is increased in hypothyroid. Triiodothyronine(T_3) & Thyroxine(T_4) level of hypothyroid patients showed a significant negative correlation with uric acid with 'r' values of 0.45 and 0.51, respectively. A positive correlation was observed between Thyroid-stimulating hormone (TSH) and uric acid (p=0.22) in hypothyroid subjects. The raise in uric acid is hypothyroid subjects is due to hemodynamic changes like reduction in renal plasma flow and disordered thyroid state affects purine metabolism, leading to hyperuricemia and gout. Hence, these parameters should be monitored regularly in hypothyroid patients.

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INTRODUCTION

Hypothyroidism, a disorder of the thyroid gland due to reduced synthesis and secretion of thyroid hormones. 50% of hypothyroidism is of autoimmune aetiology and the remaining 50% it is due to other causes. Hypothyroidism is characterized by a range of clinical spectrum from an overt myxedematous state, end-organ effects and multisystem failure to an asymptomatic or subclinical condition with normal levels of Triiodothyronine (T3) and Thyroxine (T4) with mildly elevated levels of serum thyrotropin (Cooper, 2001; Krassas *et al.*, 2010). The prevalence of hypothyroidism is about 4-5% in the developed countries (Hollowell *et al.*, 2002; Hoogendoorn, 2006). A study conducted in 2013 (Unnikrishnan *et al.*, 2013) reported a prevalence of hypothyroidism in Chennai to be 9.77%.

Hypothyroidism in experimental animals has been shown to result in a reduction in glomerular filtration rate (Davis *et al.*, 1983). Hypothyroidism is associated with many biochemical abnormalities, including high serum creatinine and uric acid levels due to hemodynamic changes in severe hypothyroidism, contributing to low glomerular filtration rate (GFR). Further hypothyroidism, associated autoimmune diseases may also modify the underlying renal problem. Further hypothyroidism, associated autoimmune diseases may also modify the underlying renal problem (Zimmerman *et al.*, 1988; Karanikas *et al.*, 2004). Hypothyroid patients had a greater chance of developing hyperuricemia and gout (Giordano *et al.*, 2001).

Table 1: Comparison of biochemical variables among euthyroid and hypothyroid Subjects

Study Parameters	Hypoyroid Cases (N=25)	Euthyroid Control(N=25)	P-Value
T3 (pg/ml)	1.90 + 4.3	3.48 + 0.20	0.07
T4 (ng/dl)	0.67±0.32	0.85±0.18	0.001
TSH(mIU/ml)	36.65 + 7.63	3.18 + 1.49	<0.001
Uric acid (mg/dl)	7.36 + 0.95	5.5 + 0.91	<0.001

Values are expressed as mean +SEM * p<0.05- Significant; **p<0.001 – Highly significant; ***p<0.0001– Extremely significant

Table 2: Correlation of uric acid with total thyroid profile in the hypothyroid subject

Pearson's correlation coefficient (r-value)	T3	T4	TSH
Uric acid	-0.45*	-0.51**	0.25

Values are expressed as mean +SEM * p<0.05- Significant; **p<0.001– Highly significant; ***p<0.0001 – Extremely significant

The study was designed to evaluation uric acid levels in hypothyroid patients and that might be helpful for monitoring and management of hyperuricemic hypothyroid patients.

MATERIALS AND METHODS

Study design

It's a case-control study done after obtaining written informed consent.

Inclusion criteria

1. Known case of hypothyroidism attending years presented to Saveetha Medical College and hospital, Thandalam.
2. Age and sex-matched cases and controls in the age group 18 to 60 years.

Exclusion criteria

1. Known case of diabetes mellitus, renal and liver disorders or other inflammatory conditions
2. Patients are taking drugs like allopurinol, probenecid and
3. Known case of gout
4. Pregnancy
5. Smoking and alcoholism

Case definition

The subjects were marked as Hypothyroid from the definition of TSH levels > 6.0 mIU / ml.

Sample processing and Instrumentation

After overnight fasting, a 3ml venous blood sample was collected. Uric acid and thyroid function tests were performed. Vitros 5600 kits were used for the estimation of serum total thyroid profile and uric acid. Serum total thyroid profile was estimated by the CLIA method and uric acid by the Uricase method in a fully automated Vitros 5600 analyzer.

Statistical Analysis

Data was entered under the Microsoft Excel sheet and data was analyzed using the software Graph pad. An unpaired t-test was used for demographic data. For correlation analysis, Pearson's correlation coefficient is used. A P-value of <0.005 was considered to be statistically significant.

RESULTS AND DISCUSSION

The study is carried out with 25 hypothyroid subjects (cases) and 25 euthyroid subjects (controls) selected based on inclusion and exclusion criteria. Case group had 60% females and 40% males. Controls had 45% of females and 55% males. Both groups were age and sex-matched. The mean age group of hypothyroid subject44.48 + 8.57 years and that of euthyroid subjects was 43.84 + 9.88 years. Table 1 shows a comparison of mean values among cases and controls. Hypothyroid subjects had significantly higher levels of serum TSH and serum uric acid as compared to euthyroid subjects (p<0.001). Table 2 shows the correlation between thyroid function tests and the uric acid level. T_3 had a significant (p<0.05) negative correlation with uric acid with an r-value of 0.45 and T_4 had a highly significant (p<0.001) negative correlation with uric acid. Whereas TSH had a positive correlation(r=0.25) with uric acid.

Out of 50 subjects, 25 were hypothyroid and 25 were euthyroid. Higher female preponderance is seen in our study, which is in accordance with Unnikrishnan *et al.* (2013) study. In our study, serum uric acid level was found significantly higher in cases (7.36 + 0.95) compared to controls (5.5 + 0.91) similar to Arora *et al.* (2009) study. In hypothyroidism, the hyperuricemia is secondary to decreased renal plasma flow and impaired glomerular filtration (Karanikas *et al.*, 2004; Giordano *et al.*, 2001). Reduced renal blood and plasma flow and decreased GFR is the reason for renal impairment caused by reduced cardiac output and increased systemic and renal vasoconstriction.

CONCLUSION

Mean serum uric acid levels was found significantly higher in hypothyroid patients compared to controls, which shows that hypothyroidism is associated with deteriorating renal function. Moreover, patients on medications cleared by the kidneys have adverse clinical consequences due to hypothyroid-induced renal dysfunction. The understanding of this association Hypothyroidism must be considered in patients with acute renal failure and elevated muscle enzymes. Therefore patients presenting with hypothyroidism are recommended to be investigated for uric acid.

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