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ASSESSMENT OF RENAL FUNCTION TESTS IN SUBCLINICAL HYPOTHYROIDISM

Biochemistry

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ABSTRACT

Background: Subclinical Hypothyroidism is a progressive disorder that presents with diverse degrees of thyroid failure and metabolic consequences. It potentially affect metabolism which may influence renal development, kidney structure, renal plasma flow, glomerular filtration rate, and nephron transport system. This leads to changes in various biochemical constituents in patients. Hemodynamic changes occur in hypothyroidism that leads to reduction in renal plasma flow and glomerular filtration rate, which also causes increase in the levels of serum urea and serum creatinine.

Objectives: To estimate serum creatinine and urea levels in healthy controls and subclinical hypothyroid patients; and to compare the results of the above two groups and correlate these values with TSH values in subclinical hypothyroidism cases.

Materials and methods: A cross-sectional study was done and included 200 individuals (100 Subclinical hypothyroid cases and 100 normal controls). Serum TT3, TT4, TSH levels were estimated by Chemiluminescent microparticle Immunoassay(CMIA) method to assess the subclinical hypothyroid cases. Serum Urea and Creatinine were estimated by colorimetric method on Semi automated chemistry analyser. Statistical analysis was done using students't' test. Pearson's correlation coefficient test was done to establish the relationships between the parameters.

Results: The serum creatinine level was significantly elevated in subclinical hypothyroidism cases in comparison to controls. Serum urea concentrations were not significantly different in the studied groups.

Conclusion: Subclinical Hypothyroid state is associated with hemodynamic changes like reduction in renal plasma flow and glomerular filtration rate, which causes increase in the levels of serum urea and creatinine.. Hence these parameters should be regularly monitored in Subclinical hypothyroid patients.

KEYWORDS

Thyroid stimulating hormone; TT3, TT4, urea; creatinine; subclinical hypothyroidism.

Introduction

Thyroid gland is one of the largest endocrine glands in the body, which secretes thyroxine (T4) and triiodothyronine (T3). The production of T4 and T3 in the thyroid gland is regulated by the hypothalamus and pituitary gland. 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. Hypothyroidism is a clinical syndrome caused by the deficiency of thyroid hormones that cause a generalized slowing of metabolic processes1, 2. It affects 5-20% of population worldwide and is one of the most common endocrine disorders in India. Women are more commonly affected compared to men3.

By definition, subclinical hypothyroidism refers to biochemical evidence of thyroid hormone deficiency in patients who have few or no apparent clinical features of hypothyroidism4. It is characterized by slightly elevated TSH and low to normal serum T4 levels. TSH elevation in subclinical hypothyroidism is modest with the values typically between 5 – 15 µIU/ L5. It affects virtually every tissue in the body. This includes slowing of physical and mental activity6. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Hypothyroidism is accompanied by a decrease in glomerular filtration, elevation of serum creatinine and alteration of the ability for water excretion6,7.

Hence to understand the effect of subclinical hypothyroidism on renal function, we estimated and compared serum urea and serum creatinine levels with TSH, T3, T4 in subclinical hypothyroid cases and healthy controls.

Materials and Methods

Source of data: This case control study comprised of 100 newly diagnosed subclinical hypothyroidism cases and 100 age and sex matched healthy controls, attending Endocrinology outpatient department of Government General Hospital, Kurnool. Duration of the study was from January 2016-December 2016. Institutional ethical committee clearance was obtained for the study. Informed consent was taken from all the participants

Inclusion criteria: Patients with newly diagnosed subclinical hypothyroidism in the age group of 20 to 59 years of both genders were included. The diagnosis was based on low to normal serum T3 and T4 levels associated with increased TSH levels of 5-15µIU/ ml. The normal reference ranges of thyroid profile according to the kits are TSH 0.4- 4.2 µIU/ml, TT3 70 – 204 ng/dl, TT4 5.1 - 11 µg/dl.

Exclusion criteria: Patients with diabetes, hypertension, chronic kidney disease, muscular dystrophies, gout, pregnancy, patients on high protein diet and patients on drugs for treatment of thyroid disorders or any other medications that might affect renal function are excluded from the study.

Method of sample collection: Detailed history was taken from all the subjects. 3 ml of venous blood was obtained in plain tube. TT3, TT4, TSH were estimated by using CMIA in Beckman Coulter Random Access 2 series. Serum urea and serum creatinine were measured using semi auto-analyser ERBACHEM-5x and kits supplied by ERBA. Parameters were estimated by following methods:

a) Estimation of serum creatinine by modified Jaffe's method8,9.
b) Estimation of serum urea by GLDH-Urease method8,10

Statistical analysis: The variables were presented in terms of mean and standard deviation. The data were analyzed using student's unpaired't' test. 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.

Results:

The age of participants ranged between 20 and 59 years-old with mean age of 41 years, as shown in Table1. The values of thyroid hormones and biochemical markers of renal function are presented in table 2. TSH levels were higher in the sub-clinical hypothyroid group as compared to the euthyroid group ($p<0.001$).

As mentioned in Table 2, mean serum urea levels in cases were compared with controls and no significant difference was observed between the groups. Mean serum creatinine concentrations were significantly increased in cases as compared to controls and significant

difference (p<0.001) was found between the groups. Table 3, Figure 1 shows significant positive correlation between TSH and serum creatinine levels with p<0.001, but correlation between TSH and serum urea levels (Figure 2) were not significant.

Table 1: Age and gender distribution in cases and healthy controls

	Cases	Controls
Age (yrs)	41.55±11.403	41.27±13.105
Gender (M/F)	7/50	8/50

Table 2: Comparison of levels of T3, T4, TSH, Urea and Creatinine between cases and controls

	Cases	Controls	p-value
T3 (ng//dl)	105.996±30.105	119.665±46.209	0.29
T4(µg/dl)	7.990±3.994	9.650±2.996	0.20
TSH(µIU/ml)	15.226±34.065	3.253±0.641	<0.001
Urea(mg/dl)	20.828±4.896	20.021±9.727	0.807
Creatinine(mg/dl)	1.574±0.165	0.638±0.099	<0.001

*p<0.001 statistically significant

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

Cases	P value	Pearson correlation (r value)
TSH vs urea	P=0.903	+ 0.0002
TSH vs creatinine	P<0.001*	+ 0.1754
*p<0.001 statistically significant		

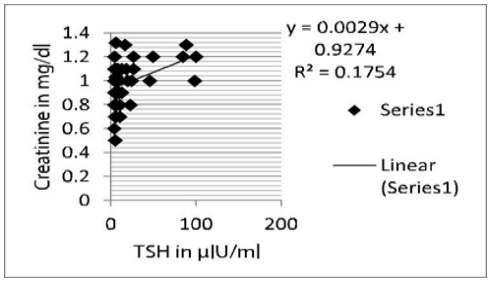

Figure 1: Positive correlation of serum creatinine with TSH

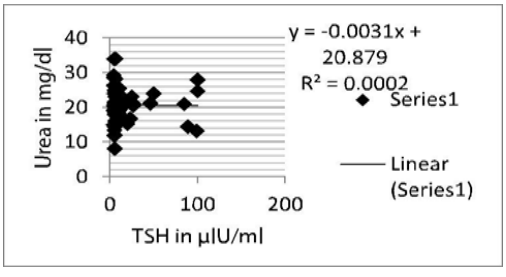

Figure 2: Positive correlation of serum urea with TSH

Discussion

The present case-control study evaluated the biochemical markers of renal function such as urea and creatinine in subclinical hypothyroid subjects and compared the results with those of euthyroid subjects. The present study shows that there is significant increase in creatinine levels in subclinical hypothyroid patients as compared to controls. Similar changes in serum creatinine with hypothyroidism have been reported in support of the present study5,7,11,12.

Elevated Serum creatinine levels in the present study is in accordance with study done by Ajaykumar13, showed an increase in serum creatinine with a mean of 1.11 in primary subclinical hypothyroidism cases and these metabolic parameters were found to be reversible after thyroxine replacement therapy11. The increase in serum creatinine may be either due to increased production or decreased renal clearance. Decreased glomerular filtration rate (GFR) is believed to be due to the generalized hypodynamic circulation in hypothyroid patients13.

In another study done by Md. Aminul Haque Khan on 80 hypothyroid patients, serum creatinine level was found significantly higher in hypothyroid patients14. Iglesias study on thyroid dysfunction and kidney disease shows elevation of serum creatinine levels due to decreased GFR and due to decreased renal plasma flow. Sarika Arora et al study showed that there is significant increase in creatinine levels (0.85±0.29) in overt hypothyroid subjects as compared to euthyroid subjects(0.71±0.27). These changes may result in physiological effects including alterations in renal hemodynamics, decrease in GFR and hence reduced clearance of creatinine.15 Sara Abdalseed Hamed study confirms that the hypothyroid state is associated with a consistent elevation in the serum creatinine level and reduced creatinine clearance, presumably due to a decrease in the GFR, and hyperthyroid state associated with increase in creatinine clearance compared with euthyroid control group.16 Study conducted by Sinisa et al, observed increase in serum creatinine in hypothyroid subjects 115±12 µmol/L which decreased after treatment to 95±14µmol/L. Decreased GFR, decreased creatinine clearance and decreased creatinine tubular secretion together with the increased release of creatinine from muscle cells explain the higher values of serum creatinine in hypothyroidism.17

In the present study mean serum urea level in subclinical hypothyroid subjects was not significantly higher than in control subjects. This finding is consistent with the studies done by other investigators.7, 16, 18. In the present study we got significant positive correlation of TSH with serum creatinine (p< 0.001) with r value +0.175, whereas there was no significant correlation between TSH and serum urea levels though we got positive correlation of TSH with serum urea. This is in contrast to a study by Devika Tayal MD et al, in which they got significant positive correlation of TSH with serum creatinine in overt hypothyroidism group but not in subclinical hypothyroidism group.7

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.6,11

Conclusion: This study confirms that the subclinical hypothyroid state is associated with a consistent elevation in the serum creatinine levels due to a decrease in the GFR. Therefore we would suggest assessment of thyroid function in patients presenting with deranged renal function. And also hypothyroidism should be taken into account, in patients presenting with the biochemical abnormalities of chronic kidney diseases.

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