

Assessment of Renal Impairment and Dyslipidemia in Subclinical Hypothyroidism

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Abstract: Subclinical hypothyroidism also referred to as mild thyroid failure and is diagnosed when peripheral thyroid hormone levels are within the normal range, but thyroid stimulating hormone (TSH) is mildly elevated. It is common, occurring in 3-8% of the population increasing with age and being more common in women. Mild thyroid failure represents an early stage of thyroid disease that will commonly progress to overt hypothyroidism. Progression has, in fact, been reported to occur in approximately 3-18% of affected patients per year. To maintain the growth and metabolism of renal system, they play an indispensable role. Decrease or fall in the activity of renal system is accompanied by compensatory alteration in the level, synthesis and metabolism of thyroid hormones. It is well established fact that renal system is affected by hypothyroid states of the body. Hence; we evaluated the effect of hypothyroidism on the renal functions of the body. Hypothyroidism is associated with many biochemical abnormalities including increased serum creatinine and uric acid levels. The serum creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism. Therefore, patients presenting with these biochemical abnormalities are recommended to be investigated to explore hypothyroidism. In general, overt and subclinical hypothyroidism is associated with hypercholesterolemia mainly due to elevation of low density lipoprotein (LDL) cholesterol levels, whereas high density lipoprotein (HDL) cholesterol concentration is usually normal. Therefore; hypothyroidism constitutes a significant cause of secondary dyslipidemia. Thyroid dysfunction causes significant changes in kidney function. Goal of treatment is to replace sufficient amount of thyroid hormone so as to reduce the TSH to within the normal range to prevent the renal complications of hyperuricemia and hypercreatinemia.

Keywords: Thyroid stimulating hormone (TSH), subclinical hypothyroidism, dyslipidemia, LDL, HDL.

INTRODUCTION

Elevated serum TSH levels with normal free thyroxine (T4) and triiodothyronine (T3) concentrations is termed subclinical hypothyroidism, or mild thyroid failure. The thyroid gland produces two principle hormones, thyroxine (T4) and triiodothyronine (T3). These thyroid hormone act through α and β receptors and play a critical role in cell differentiation during development and to maintain thermogenic and metabolic homeostasis in the adult [1]. Thyroid hormones secreted by the thyroid gland are regulated by the anterior pituitary hormone -thyroid stimulating hormone (TSH), which is under the control of the hypothalamic thyrotropin-releasing hormone (TRH). Thyroxine (T4) is produced primarily by the thyroid gland and is converted to the more biologically active form triiodothyronine (T3). The kidney is implicated in the production of T3 through local

deiodination of T4 by the isoform D1 of the enzyme T4-5' -deiodinase [2]. These thyroid hormones (T4 and T3) regulate the rate of metabolism, affect growth, and modulate energy utilization by increasing the basal metabolic rate and increasing oxygen consumption, and facilitating heat production.

To maintain the growth and metabolism of renal system, they play an indispensable role. Decrease or fall in the activity of renal system is accompanied by compensatory alteration in the level, synthesis and metabolism of thyroid hormones. It is well established fact that renal system is affected by hypothyroid states of the body. Hence we evaluated the effect of hypothyroidism on the renal functions of the body. Hypothyroidism is associated with many biochemical abnormalities including increased serum creatinine and uric acid levels [3]. In our review analysis, serum

creatinine level has been found to be significantly higher in hypothyroid patients. So, hypothyroidism should be taken into account in patients presenting with chronic kidney diseases. On the other hand, chronic kidney diseases also affect thyroid function in many ways leading to decreased T3 and T4. Therefore, it is important for the clinician to differentiate between chronic kidney diseases (CKDs) and hypothyroidism with respect to their causal and consequential entities[4]. Hypothyroidism is associated with many biochemical abnormalities including increased serum creatinine and uric acid levels. The serum creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism[5]. Serum creatinine level may also be increased due to hypothyroid myopathy. In hypothyroidism, associated autoimmune diseases may also play role in modifying the underlying renal problem[6]. It is of paramount clinical importance. So, proper knowledge of these abnormalities and their consequential effects are very important and useful for clinical management of the patients. Hypothyroidism is associated with hyperuricemia. In comparison to the prevalence reported in the general population, a significant increase of both hyperuricemia and gout was found in the hypothyroid patients. In hypothyroidism the hyperuricemia is secondary to a decreased renal plasma flow and impaired glomerular filtration[7]. Thyroid hormone is known to play a role in regulating the synthesis, metabolism, and mobilization of lipids. In patients with overt hypothyroidism there is an increase in serum total cholesterol, low-density lipoprotein (LDL) cholesterol, apolipoprotein B, lipoprotein (a) levels, and possibly triglyceride levels. An elevated serum thyroid-stimulating hormone (TSH) level is the hallmark of hypothyroidism[8]. Goal of treatment is to replace sufficient amount of thyroid hormone so as to reduce the TSH to within the normal range.

MATERIALS AND METHODS

A total of 30 diagnosed subclinical hypothyroidism patients and the control groups consisted of 30 nonhospitalized adults with no history of systemic disease (matched for age and sex). Subject was fasting 12-14 hr. at the time of blood withdrawal. Their age range between 25-60 years were included in

this study. The thyroid investigations were estimated by Chemiluminescent Immune Assay (CLIA).

Normal values of tft

- Free Triiodothyronine(FT3), -1.2-4.18 pg/ml
- Free Thyroxine (FT4) -8.9-17.2 pg/ml
- Thyroid stimulating hormone(TSH) – 0.3-4.5 μIU/ml

The Following investigations were done using standard kits.

- Serum Urea
- Serum Creatinine,
- Serum uric acid,
- Total cholesterol(TC),
- Triglyceride(TGL),
- High density lipoprotein (HDL).

Low density lipoprotein (LDL), very low density lipoprotein (VLDL) is derived from the total cholesterol, TGL and HDL by Friedwald’s formula. Inclusion criteria: 1) Adult patients age between 20-60 years of either sex. 2) Patients who did not receive supplementations with thyroid hormone. 3) Patients who did not received supplementations with lipid lowering medication. Exclusion criteria: 1) Patients with history of underlying disease. 2) Chronic renal failure (CRF). 3) Liver disease. 4) Pregnancy, 5) Hypertension (HTN), 6) Age under 20 years with hypothyroidism, 6) Patients with history of diabetes mellitus.

RESULTS AND ANALYSIS

Table 1 shows the lipid profile fractions such as Total cholesterol (TC), TGL and LDL were higher and statistically significant in cases compared to controls. In both cases and controls group the HDL were within normal range.

Table 2 shows the thyroid function tests in both groups. In both groups, the fT3 and fT4 were within normal range and TSH in the cases were statistically higher and was significant.

Table 3 shows the renal function tests. The blood urea, serum creatinine and uric acid were higher in the cases and were statistically significant.

Table-1: Comparison of lipid profile in cases and controls

	Group	Mean	SD	t value	p value
TC	Case	201.633	26.140	7.554	0.001
	Control	158.2	17.434		
TGL	Case	181.306	26.552	11.514	0.001
	Control	104.766	21.168		
HDL	Case	43.266	7.772	-4.553	0.01
	Control	52.333	6.233		
VLDL	Case	36.260	5.311	11.510	0.001
	Control	20.953	4.233		
LDL	Case	122.283	26.616	6.217	0.001
	Control	84.913	17.530		

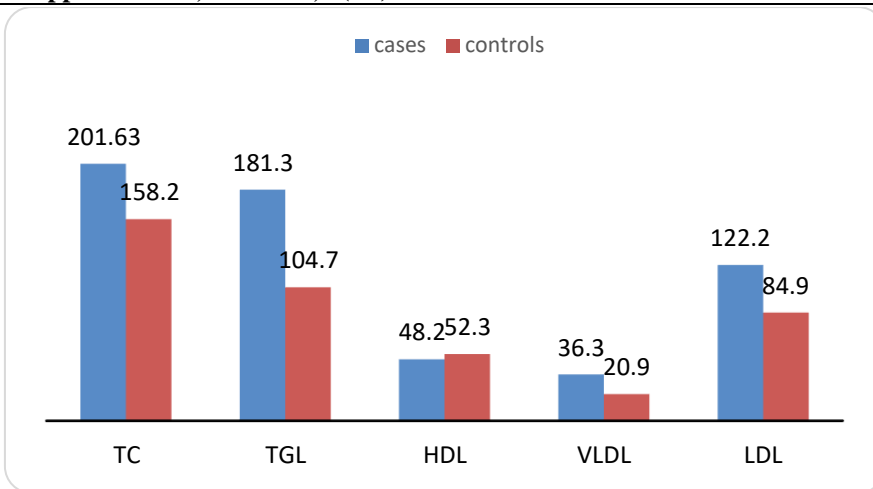


Fig-1: Comparison of lipid profile in cases and controls

Table-2: comparison of thyroid function tests in cases and controls

PARAMETERS	Group	Mean	SD	t value	p value
FT3	Case	2.400	0.688	-1.128	0.268
	Control	2.560	0.575		
FT4	Case	11.630	2.256	-0.056	0.956
	Control	11.656	1.939		
TSH	Case	7.476	2.050	12.221	0.001
	Control	2.463	0.862		

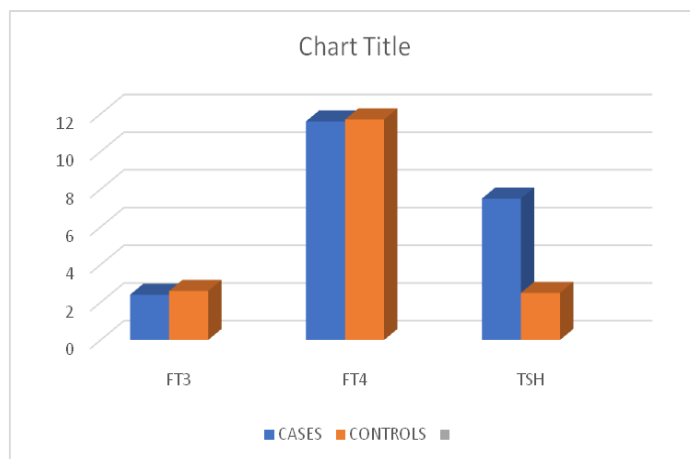


Fig-2: Comparison of thyroid function tests in cases and controls

Table-3: Comparison of serum urea, creatinine and serum uric acid in cases and controls

	Group	Mean	SD	t value	p value
UREA	Case	41.973	4.916	12.941	0.001
	Control	24.866	5.315		
CRE	Case	1.880	0.328	21.165	0.001
	Control	0.763	0.147		
U.ACID	Case	7.190	1.092	11.433	0.001
	Control	4.510	0.617		

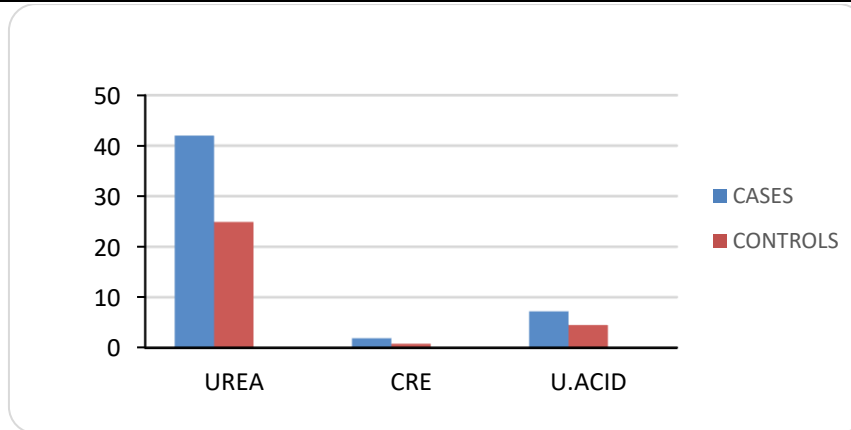


Fig-3: Comparison of serum urea, creatinine and uric acid in cases and controls

DISCUSSION

This study was carried out with an objective to evaluate whether hypothyroidism is associated with dyslipidemia and impaired renal function. A significant correlation between thyroid function and purine nucleotide metabolism has been established in hypothyroidism.

The study, even if based on a limited number of cases, showed a high prevalence of hyperuricemia in hypothyroid patients. Moreover, our study showed that hyperuricemia in hypothyroidism is associated with increased serum creatinine. Hypothyroidism may contribute to the development of atherosclerosis by other mechanisms as outlined below: a) Decreased thyroid function not only increases the number of LDL particles but also promotes LDL oxidation[9]. Our study shows that primary hypothyroidism may alter renal functions. There is significant increase in the serum levels of all parameters tested in this study- urea, creatinine and uric acid in hypothyroid patients as compared to euthyroid controls. Our study also showed a significant difference in serum creatinine levels in cases. The serum Creatinine concentration increases in hypothyroid patients due to reduction of glomerular filtration rate because of hemodynamic changes in severe hypothyroidism Serum Creatinine level may also be increased due to hypothyroid myopathy. The renal impairment could be due to reduced cardiac output and increased systemic and renal vasoconstriction leading to reduced renal blood and plasma flow and decreased GFR[10]. A highly significant difference in values of uric acid, p value <0.001 was seen.

CONCLUSION

Mean serum urea, creatinine & uric acid levels were found significantly higher in hypothyroid patients compared to controls which shows that hypothyroidism is associated with deteriorating renal function. The understanding of this association can prevent unnecessary investigations, treatment cost and worry in patients presenting with either increased urea, creatinine or gout with undetermined thyroid status[11].

In our analysis, serum creatinine level has been found to be significantly higher in hypothyroid patients. So, hypothyroidism should be taken into account in patients presenting with chronic kidney diseases. On the other hand, chronic kidney diseases also affect thyroid function in many ways leading to decreased T3 and T4. Therefore, it is important for the clinician to differentiate between chronic kidney diseases (CKDs) and hypothyroidism. Moreover, hypothyroid-induced renal dysfunction may lead to adverse clinical consequences, especially among patients on medications cleared by the kidneys. The thyroid function should, therefore, be regularly monitored for evaluation of patients presenting with deranged renal function and vice versa. A multisystem approach should be taken to evaluate and treat patients with hypothyroidism. Biochemical screening for thyroid dysfunction is of paramount importance in all dyslipidemic patients, as well as in all patients with unexpected improvement or worsening of their lipid profile.

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