Original Research Paper

Volume : 5 | Issue : 8 | August 2016 • ISSN No 2277 - 8179 | IF : 3.508 | IC Value : 69.48

Altered Metabolic Profile in Newly Diagnosed Primary Hypothyroidism

Medical Science

KEYWORDS : Hypothyroidism, lipid profile, creatinine, uric acid, haemoglobin

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ABSTRACT

Hypothyroidism is a clinical syndrome characterized by the clinical and biochemical manifestation of thyroid hormone deficiency in the target tissue, leading to generalized slowing of all metabolic processes. By affecting the metabolism of lipids, thyroid hormones accelerate the process of atherogenesis and it increases the cardiovascular risk. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions and electrolyte and water homeostasis. Thyroid hormone is involved in haemoglobin synthesis and by affecting the hematopoietic process, hypothyroidism results in anaemia through slowing the oxygen process.

Aims and objectives: *To estimate serum lipid profile, serum creatinine, uric acid, Haemoglobin levels in hypothyroid patients and to compare it with euthyroid normal controls.*

Materials and methods: *We measured serum lipid profile [Total cholesterol (TC), Triglyceride (TG), HDL-Cholesterol (HDL-C), LDL-Cholesterol (LDL-C), VLDL-Cholesterol (VLDL-C)] serum creatinine, uric acid and haemoglobin (Hb) levels in 100 newly diagnosed primary hypothyroid patients and compared it with 100 euthyroid normal controls. Fasting venous sample was used for analyzing the parameters. Statistical analysis was done using student't' test. Pearson's correlation coefficient test was done to establish the relationships between the parameters.*

Results: *The serum creatinine, uric acid, TC, TG, LDL-Cholesterol, VLDL-Cholesterol were significantly elevated ($p<0.001$) and HDL-Cholesterol and Hb levels were significantly decreased ($p<0.001$) in primary hypothyroid cases when compared to euthyroid controls*

Conclusion: *Hypothyroidism is associated with metabolic derangements and multisystem approach is required to treat patients with hypothyroidism.*

Introduction:

The thyroid gland synthesizes and releases $T_3$and T_4. The biologically active hormones T_3 and T_4 play a significant role in the growth, development and function of all major tissues[1, 2]. Thyroid hormone synthesis and secretion is regulated by the negative feedback system that involves the hypothalamus, pituitary and the thyroid gland [3].

Hypothyroidism is a clinical syndrome characterized by the clinical and biochemical manifestation of thyroid hormone deficiency in the target tissue, leading to generalized slowing of all metabolic processes[3, 4]. Raised TSH and lower T_3 and T_4 levels were diagnostic of overt hypothyroidism. Primary hypothyroidism is due to abnormality in thyroid gland itself and secondary hypothyroidism may be due to deficiency of TSH. Thyroid hormone deficiency affects virtually every tissue in the body. The clinical finding is slowing of physical and mental activity. The incidence of overt hypothyroidism has been estimated to be 4.1cases per 1000 women per year and 0.6 cases per 1000 men per year[5]. Women are more commonly affected compared to men[6]. The prevalence has been reported to be approximately 1-2% in women and 0.1% in men in large population studies[7].

Thyroid hormones are known to play a role in the synthesis, metabolism and mobilization of lipids. By affecting the metabolism of lipids, thyroid hormones accelerate the process of atherogenesis and it increases the cardiovascular risk. Thyroid dysfunction causes remarkable changes in glomerular and tubular functions, electrolyte and water homeostasis. Hypothyroidism is accompanied by a decrease in glomerular filtration, elevation of serum creatinine and alteration of the ability for water excretion [8,9]. The prevalence of anaemia in patients with hypothyroidism has been shown to be 20-60% [10]. Thyroid hormone is involved in haemoglobin synthesis in adults and maturation of haemoglobin in foetus[11, 12] and by affecting the hematopoietic process, hypothyroidism results in anaemia through slowing the oxygen process[13, 14].

Long standing hypothyroidism can cause reversible changes in the metabolic parameters such as increase in serum uric acid, serum creatinine levels, abnormal lipid profile and low levels of Hb%. The present study was carried out to determine the changes produced by thyroid hormone deficiency on metabolic parameters in newly diagnosed primary hypothyroid patients.

Materials and methods:

With the approval of the Institutional ethics committee and the informed consent of the participants, 100 newly diagnosed hypothyroid patients of 30-65 years of age were chosen and were compared with euthyroid normal controls. All the study participants were free of any confirmed renal, hepatic or cardiovascular disease and diabetes mellitus. All female patients were asked about their menstrual period duration, frequency, and amount of bleeding. Patients with a menstrual period lasting for more than 5 days or more than usual amount of bleeding were excluded from study.

Sample collection: After an overnight fast of 10-12 hours, 4 ml of venous blood was collected in EDTA and plain vacutainer [BD Biosciences] from antecubital vein from each patient. Serum creatinine was estimated by Jaffe's method[15], uric acid by modified Trinder method[16], serum lipid profile was estimated by the enzymatic CHOD-POD method[17]for TC, GPO-Peroxidase method[18] for Triglycerides, CHOD, CHER-POD method[19] for HDL-Cholesterol, by using Erba Mannheim reagent kits obtained from Transasia Bio-Medicals and all the parameters were estimated by using fully automated analyser – Erba Mannheim (EM 100). LDL-Cholesterol concentrations were calculated by Friedewald's formula[20].EDTA Anti coagulated blood samples were pro-

cessed in Haematology Analyser (cell counter) Erba –Sysmax (XP-100) for determination of Haemoglobin (Hb). Estimation of thyroid profile was done by Lilac kit by using a Chemiluminescence method. The following three parametes were estimated under thyroid profile.Tri-iodo-L-thyronine (T_3), Tetra-iodo-L-thyronine (T_4), Thy- roid stimulating hormone (TSH).Diagnosis of Hypothyroidism was established based on clinical signs and symptoms and the T_3, T_4 and TSH estimations.

Statistical Analysis:
Data obtained was entered into Microsoft Excel sheet and statistical analysis was performed. Results were analysed and presented as numbers and mean± standard deviation (SD). Kruskal Wallis test, Mann Whitney –U test and the Fisher test and student's unpaired't' test were applied for the descriptive analysis and the correlation was done by the Pearson's correlation coefficient. A *p*-valueof <0.001 was considered as statistically significant.

Results:
The mean ages of hypothyroid and euthyroid patients were 50.56 and 51.15 respectively as shown in **Table-1**. More of females were there in hypothyroid group when compared to euthyroid group.

Table-2 shows the serum TSH and thyroid hormone levels in hypothyroid and euthyroid groups. As compared to the controls, the meanTSH level was significantly higher with lower T3 and T4 valuesin the hypothyroid group.

Table-3 illustrates significant dyslipidemia in the hypothyroid pool with increased TC, TG, LDL-Cholesterol and VLDL-Cholesterol levels and decreased HDL-Cholesterol levels. Serum creatinine and uric acid concentrations were significantly increased and Haemoglobin concentration was decreased in the cases as compared to controls and significant difference (p<0.001) was found between the two groups.

Discussion:
Lack of thyroid hormones in hypothyroidism causes an elevation of the LDL-cholesterol synthesis due to an increase in the cholesterol synthesis and absorption, a decrease in the hepatic lipase and the lipoprotein lipase activities, defects in the receptor- mediated catabolism of LDL-cholesterol[21,22], an increase in the oxidation of plasma cholesterol, mainly TC and LDL-cholesterol and a decrease in the HDL receptors on the hepatocytes.

In the hypothyroid pool which was diagnosed, based on the raised TSH and the lower T3 and T4 levels, the triglycerides were found to be significantly elevated, along with TC, LDL-Cholesterol, VLDL-Cholesterol and there was a significant decrease in serum HDL-Cholesterol level **(Table-3).** Evidence is available, to say that not only TC and LDL-cholesterol, but triglycerides were also independent risk factors for coronary heart disease (CHD), cerebrovascular disease, and peripheral artery disease[23,24]. Of notable importance was a marked increase in the TG and LDL cholesterol levels. The findings in relation to the lipid status point to the high susceptibility of the hypothyroid subjects to the development of cardiovascular diseases, cerebrovascular disease and peripheral arterial disease.

Our study shows significant increase in creatinine levels in hypothyroid patients as compared to controls **(Table-3).**Similar changes in serum creatinine with hypothyroidism have been reported in support of our study[25-28]. The increase in serum creatinine may be either due to increased production or decreased renal clearance. Decreased renal blood flow and glomerular filtration rate(GFR) is believed to be due to the generalized hypo dynamic state of the circulatory system in hypothyroid patients. Thyroid hormones have a role in the maturation of the Renin Angiotensin Aldosterone system (RAAS) system[1]. Our study confirms the association of hypothyroidism with elevated uric acid and creatinine which may be due to a decrease in GFR levels and alteration in the RAAS. In another study done by Md. Aminul Haque Khan on 80 hypothyroid patients, serum creatinine and uric acid level was found significantly higher in hypothyroid patients[29-31]. 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[32].

Thyroid diseases are frequently associated with erythrocyte abnormalities[33]. Anaemia of hypothyroidism has been ascribed to a physiological compensation for the diminished need of tissues for oxygen. The low plasma erythropoietin levels found in hypothyroid anaemia is in accordance with this hypothesis[34]. Patients with hypothyroidism have a decreased erythrocyte mass due to reduction of plasma volume and may be undetectable by routine measurement such as haemoglobin concentration[35].

Conclusion:
Our study concluded that there is a significant increase in the serum TC, TG, LDL-Cholesterol, VLDL- Cholesterol, Serum creatinine and uric acid levels and decrease in HDL-Cholesterol and Hb levels. Thyroid dysfunction alters the lipid status and increases the risk of Myocardial Infarction or Stroke. 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. Hencehypothyroidism should also be considered in patients presenting with the biochemical abnormalities of chronic kidney diseases. The findings in the current study help us to understand the complex interaction between the thyroid gland and major organ systems. It also denotes the importance of early intervention of hypothyroidism which will help in the prevention of long term complications like CAD, CVD and decrease in mortality rate. We suggest those people with thyroid disorder should have routine screening of haematological, biochemical and hormonal profile assay and simultaneously proper management of this metabolic disease should be provided base on American endocrinologist guidelines.Hence a multisystem approach is required to treat patients suffering from hypothyroidism.

TABLE 1: DEMOGRAPHIC PROFILE

TESTS	SUBJECTS		MEAN AGE
	M	F	
EUTHYROID	50	50	50.56±9.30
HYPOTHYROID	74	26	51.15±9.56

TABEL 2: THYROID STATUS OF STUDY GROUPS

TESTS	EUTHYROID	HYPOTHYROID	P -value
T3 (ng/ml)	0.99±0.19	0.28±0.09	⊚0.001*
T4 (µg/dl)	8.87±2.02	2.43±0.68	⊚0.001*
TSH (µ IU/ml)	3.27±1.41	54.81±7.09	⊚0.001*

TABLE 3: METABOLIC PARAMETERS OF STUDY GROUPS

TESTS	EUTHYROID	HYPOTHYROID	p-value
TC (mg/dl)	188.90±13.88	245.82±18.06	⊚0.001*

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TG (mg/dl)	132.27±37.98	214.76±21.16	⊚0.001*
HDL (mg/dl)	44.10±2.44	39.08±1.94	⊚0.001*
LDL (mg/dl)	118.35±14.09	163.79±19.48	⊚0.001*
VLDL (mg/dl)	26.45±7.60	42.95±4.23	⊚0.001*
CREATI-NINE (mg/dl)	0.92±0.15	1.40±0.06	⊚0.001*
URIC ACID (mg/dl)	4.86±0.94	7.13±0.33	⊚0.001*
Hb% (gm/dl)	12.72±1.58	8.57±0.61	⊚0.001*

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