

## Correlation of Altered Lipid Profile, Uric Acid and Fasting Plasma Glucose Levels in Females with Hypothyroidism

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### Abstract

**Introduction:** Hypothyroidism is a common endocrinal disorder in which thyroid gland does not produce enough thyroid hormones. The disease mainly occurs in female and its prevalence rises with age. Hypothyroidism may be the underlying cause of dyslipidemia and alteration of plasma glucose levels as thyroid hormones plays a key role in lipid and carbohydrate metabolism. It also helps in the growth and development of kidney; hence hypothyroidism may alter the uric acid level in serum due to altered secretion of uric acid at renal tubules.

**Aims and Objectives:** To evaluate if there is any significant correlation between lipid parameters, uric acid, fasting plasma glucose with thyroid parameters in female.

**Methodology:** We included 35 cases and 35 controls (Aged between 20-45 years) and estimated their serum TSH, FT4 by ELISA method and total cholesterol, triglycerides, LDL-c, HDL-c, VLDL-c, uric acid and fasting plasma glucose levels by chemical methods using random access auto-analyzer.

**Results:** Results showing positive and negative correlation of TSH and FT4 with TC, TG, LDL-C and VLDL-C in cases compared to controls, whereas, HDL-C, UA and FPG didn't show any positive/negative correlation with hypothyroid parameters in either cases or controls.

**Conclusion:** Hypothyroid status is associated with dyslipidemia. So, earlier biological screening for lipid profile can be done in those patients.

**Keywords:** Hypothyroidism; Dyslipidemia; Hyperuricemia; Insulin resistance

### Introduction

The thyroid gland produces two hormones, tri-iodothyronine (T3) and thyroxine (T4). T3 is made from T4 and is the more active hormone. Thyroid hormones influence a wide array of metabolic pathways including protein, carbohydrate and lipid metabolism. Thyroid hormones affect metabolism, brain development, breathing, heart and nervous system functions, body temperature, muscle strength, skin dryness, menstrual cycles, weight, and cholesterol level. Hypothyroidism is a disorder that occurs when the thyroid gland does not make enough thyroid hormone to meet the body's needs. Thyroid hormone production is regulated by thyroid-stimulating hormone (TSH), which is made by the pituitary gland in the brain. When thyroid hormone levels in the blood are low, the pituitary releases more TSH. When thyroid hormone levels are high, the pituitary responds by dropping TSH production. Hypothyroidism is common endocrinal disorder in general population, especially in women and its prevalence increase with age. It affects 0.5-2.4% of the general population [1].

The hormone T3 plays a critical role in lipid metabolism by regulating genes involved in lipogenesis and lipolysis [2]. Thyroid hormones also maintain the initial level of phospholipids in cell membranes and fatty acids composition of the lipids [3]. In hyperthyroidism generally serum level of total, LDL and HDL cholesterol decreases [4]. Hypercholesterolemia is found in hypothyroidism due to the increment of low density lipoprotein cholesterol levels. High density lipoprotein cholesterol levels usually remain normal or elevated [5]. It is also known that overt hypothyroidism is associated with increased fasting plasma triglyceride levels [6] along with increased lipoprotein a levels [7], which may be explained by the occurrence of a more severe and diffuse CAD in hypothyroidism [8]

Thyroid hormones are responsible for growth and development of kidney. Hypothyroid is also associated with hyperuricemia [5]. In general population a high prevalence of gout and hyperuricemia

is found mainly due to impaired renal plasma flow and altered glomerular filtration rate [9]. However hyperuricemia is secondary in case of hypothyroid patients [10]. Some study revealed that in women, hypothyroid status was not associated with hyperuricemia or gout whereas hypothyroid is not associated with hyperuricemia in male also [11]. There is contradiction among the authors about the serum uric acid status in hypothyroid patients.

Though there are limited studies indicating the link between plasma glucose levels and hypothyroidism and the existing studies are mostly contradictory to each other, fasting plasma glucose taken in our study as a considerable parameter as there is a certain correlation exists between insulin resistance status and dyslipidaemia, moreover hypothyroidism has a probable association with dyslipidaemia. Therefore, we tried to find in this study if there is also lying any significant association between hypothyroid status and fasting plasma glucose level.

So, here we are undertaking this study to find whether there is any significant association between hypothyroid status with altered lipid profile, increased uric acid level and fasting plasma glucose especially in women.

### Aims and objectives

To estimate Serum Lipid profile, Uric acid and Fasting plasma

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glucose in case of hypothyroid female patients as well as in normal healthy controls and to find whether there is existing any significant association of these parameters with hypothyroid status.

## Materials and Methods

The study was carried out in the 'Department of Biochemistry', of College of medicine and JNM hospital, Kalyani, Nadia.

### Study design

35 cases and 35 controls were included in the study. All the participants were female, ethnicity Indian. The subjects were divided into two groups:

Group 1 consists of 35 cases of hypothyroid female with age group between 20 to 45 years (As after 45 years of age most of the female attends their post-menopausal phase of life where they shows features similar to hypothyroidism mainly due to decreased estrogen level in their blood. So, after 45 years of age post-menopausal females are hard to be chosen as the cases of hypothyroidism, therefor highest age limit taken for hypothyroid female cases in this study are 45 years.), whereas group 2 consists of 35 non hospitalized female healthy controls of same age group with no history of previous hypothyroidism. All the subjects remained fasting 12-14 hr. at the time of blood withdrawal. A total of 5 ml venous blood from antecubital vein was collected from the subjects. 2 ml of blood was collected in a fluoride vial for estimation of fasting plasma glucose and 3 ml in a clotted vial for estimation of other parameters. Then the blood samples were sent to the service laboratory and it was centrifuged at 1500 rpm for 5 minutes. Then serum was separated from non Hemolysed blood sample and estimation of total cholesterol, triglycerides, LDL cholesterol, HDL cholesterol, VLDL cholesterol, fasting plasma glucose uric acid were done in a random access auto analyzer using the commercially available kits and FT4 and TSH was measured by ELISA reader.

An informed consent was obtained from the subjects after explaining the entire study guidelines to them. Approval from the ethical committee, COMJNMandH was taken.

Ethical Clearance was taken. (Ref No.F-24/PR/COMJNMH/IEC/17/1079)

### Inclusion criteria

- Willing adult females aged between 20 to 60 years.
- Patients who did not receive any lipid lowering medications.

### Exclusion criteria

- Patients with history of severe diseases such as chronic renal failure, liver diseases, hypertension and diabetes mellitus.
- Pregnant females.

## Methodology

All the biochemical parameters i.e. fasting plasma glucose, Lipid profile, Uric acid were assessed by conventional Laboratory Methods. FT4 and TSH were measured by ELISA technique. However, VLDL-C calculated by dividing the value of Triglycerides by 5 and LDL-C was measured by applying Friedwald's formula.

### Data Analysis

All the data statistically analyzed by SPSS software (Version 17).

## Results and Discussion

The present study investigated the lipid profile status, uric acid levels and fasting plasma glucose levels in hypothyroid female.

In our study we found that high prevalence of hypercholesterolemia in hypothyroid females with significant positive correlation with r value of 0.587 (p<0.01) for TSH in compare to control having r value of 0.048 (p=0.793), whereas correlation coefficient (r) for cholesterol with FT4 for cases and controls are -0.549 (p<0.01) and -0.208 (p=0.201) respectively. Not only that, we found high levels of serum triglycerides with r value of 0.572 (p<0.01), LDL-c with r value of 0.564 (p<0.01) and VLDL-c with r value of 0.593 (p<0.01) for TSH in cases and r values for the above said parameters for FT4 in cases are -0.482 (p<0.01), -0.458 (p<0.01) and -0.455 (p<0.01) respectively. On the other hand, no significant correlation between HDL-c (r=-0.112, p=0.535 for TSH and r=0.03, p=0.850 for FT4) and hypothyroidism was found. There is also no significant correlation found between hypothyroid status and serum uric acid level (r=0.211, p=0.253 for TSH and r=-0.134, p=0.33 for FT4 in cases) and fasting plasma glucose level (r=0.290, p=0.085 and r=-0.287, p=0.12 for TSH and FT4 respectively).

Previous studies reported that hypothyroid patients generally have elevated levels of total cholesterol, triglycerides, LDL-c and VLDL-c which is consistent with our findings [12]. Robertson and Kirkpatrick found increased levels of serum cholesterol in hypothyroid patients. Nikkila showed that a moderate increase in serum triglycerides in hypothyroid patients [13]. Jaiprabhu [5] also reported about hyperlipidemia in hypothyroid patients [10]. All of these studies support our results. In hypothyroid patients hypercholesterolemia occurs mainly due to the down regulation of LDL receptor present in liver cells. LDL receptors are responsible for cholesterol uptake from blood to the liver and these receptors are up regulated by thyroid hormones. For this reason LDL-c level in serum also increases in hypothyroid patients. Besides it, thyroid hormones also regulate the enzyme 3- cholesterol 7 $\alpha$  hydroxylase which is the rate limiting enzyme in the synthesis of bile acid from cholesterol [14]. Thyroid receptor  $\beta$  acts as a transcription factor of this gene. In hypothyroid patents this enzyme is down regulated, resulting in a minor conversion to bile acid from cholesterol thereby cholesterol clearance [15]. Thyroid hormone also increases the activity of hepatic lipase [16]. In hypothyroidism as

Case	FPG	UA	TC	TG	HDL-c	LDL-c	VLDL-c
TSH	r=0.290 p=0.085	r=0.211 p=0.253	r=0.587 p<0.01	r=0.572 p<0.01	r=-0.112 p=0.535	r=0.564 p<0.01	r=0.593 p<0.01
FT4	r=-0.287 p=0.12	r=-0.134 p=0.33	r=-0.549 p<0.01	r=-0.482 p<0.01	r=0.03 p=0.850	r=-0.458 p<0.01	r=-0.455 p<0.01

[N = 35]

N = Number of cases.

**Table 1:** This table showing the correlation coefficient (r) and their significance (p) between the hypothyroid parameters i.e. TSH & FT4 with FPG, UA, TC, TG, HDL-C, LDL-C & VLDL-C.

[p<0.01 is showing highly significance level & r value lies between +1 to -1, more towards +1 is more positively correlated & more towards -1 is more negatively correlated. r value of 0 shows no positive/negative correlation]

Control	FPG	UA	TC	TG	HDL-c	LDL-c	VLDL-c
TSH	r=0.172 p=0.284	r=0.242 p=0.119	r=0.048 p=0.793	r=0.188 p=0.276	r=-0.269 p=0.114	r=0.068 p=0.742	r=0.145 p=0.220
FT4	r=-0.122 p=0.423	r=-0.052 p=0.739	r=-0.208 p=0.201	r=-0.236 p=0.145	r=0.278 p=0.082	r=-0.096 p=0.547	r=-0.238 p=0.156

[N = 35]

N = Number of controls.

**Table 2:** This table showing the correlation coefficient (r) & their significance (p) between the hypothyroid parameters i.e. TSH & FT4 with FPG, UA, TC, TG, HDL-C, LDL-C & VLDL-C.

[p<0.01 is showing highly significance level & r value lies between +1 to -1, more towards +1 is more positively correlated & more towards -1 is more negatively correlated. r value of 0 shows no positive/negative correlation].

the activity of hepatic lipase decreases catabolism of HDL2 particles also decreases as well as triglycerides level increases.

The correlation between TSH, FT4 and serum uric acid levels was at best very weak. In this study we found that hypothyroid status in female is not associated with hyperuricemia. Some previous studies support our findings. Lai-Chu See investigated the risks of hyperuricemia and gout with thyroid dysfunction in 87,813 people and reported that hypothyroid status was not associated with hyperuricemia in men or women though the risk of gout was increased by about 40% in hypothyroid patients [17]. Other studies also showed that the correlation between TSH and serum uric acid levels was weak [18,19]. Indeed, there are contradictions among the researchers about the uric acid levels in hypothyroid patients.

We found no significant correlation between fasting plasma glucose and hypothyroidism. There are limited studies about the correlation between hypothyroidism and blood glucose levels. Some previous studies found that recurrent hypoglycemic episodes are the presenting signs for the development of hypothyroidism in patients with type 1 diabetes and replacement with thyroid hormones reduced the fluctuations in blood glucose levels [20].

## Conclusion

In female, hypothyroidism is associated with altered lipid profile though fasting plasma glucose and serum uric acid level did not show any significant association with hypothyroidism. Significant elevation of TC, TG, LDL-c and VLDL-c found in this study and there is a high risk of developing coronary artery diseases. High prevalence of atherosclerosis is also found in those patients but they have generally a low frequency of angina pectoris and myocardial infarction. So, biological screening of lipid profile should preferably be done in hypothyroid females (Tables 1 and 2).

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