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Correlation of Thyroid Stimulating Hormone (TSH) with altered lipid profile and serum uric acid levels in Hypothyroid Indian Females

Shama Tyagi[1], Manpreet kaur[1],Anita yadav[2] and Ranjan Gupta[1*]
[1]Department of Biochemistry, Kurukshetra University, Kurukshetra
[2]Department of Biotechnology, Kurukshetra University, Kurukshetra
*Corresponding author - Department of Biochemistry, Kurukshetra University, Kurukshetra, (136119), Haryana, India. E-Email - r.gupta@kuk.ac.in

ABSTRACT

Hypothyroidism is a common endocrine problem all over the world. The role of lipid profile and serum uric acid in predicting the risk of hypothyroidism in females is not established. The condition primarily affects women, and as age rises, its frequency increases. There are contradictory statements about the relationship between TSH and uric acid in previous research Therefore, the main objective of this study is to find out whether altered lipid or uric acid levels are associated with TSH in hypothyroid females. The current study comprised 100 hypothyroid female patients (aged 20 to 65 years) and 100 healthy control subjects who were age-matched with the patients. TSH and FT4test were performed on all subjects by using chemiluminescent immunoassay (CLIA). An auto-analyzer was used to examine serum uric acid levels and lipid profile test parameters. In addition, BMI of each participant in the study was measured. ***Results:*** *Our findings indicate that TSH had positive correlations with TC, TG, LDL-C, serum uric acid (UA) and BMI in hypothyroid females when compared to healthy control group with significant p-values (0.031, 0.00, 0.006, 0.014 and 0.00). On the contrary, FT4 had a negative correlation with TC, TG, LDL-C and BMI, with significant p-values (0.036, 0.047, 0.008 and 0.043). HDL-C has a significant negative correlation with TSH and a positive correlation with FT4 with a significant p-value (0.00 and 0.018) This research investigation founda strong connectionof TSH with lipid profiles and serum uric acid levels in hypothyroid women. Therefore, hypothyroid women should be advised to get their serum uric acid level and lipid profiles checked from time to time to control or prevent complications of heart and kidney diseases.*

Keywords: *Hypothyroidism, Hyperlipidemia, BMI, Hyperuricemia*

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INTRODUCTION

Overt and subclinical hypothyroidism is common metabolic disorder affecting adults. The pituitary gland reacts to elevated thyroid hormone levels by decreasing the synthesis of TSH. Hypothyroidism is a common endocrine condition that is more frequent in women and gets worse with age [1]. Hypercholesterolemia patients have been seen more common in subclinical and overt hypothyroidism (approximately 11.2% and 4.3%, respectively) compared in the general population [2, 3]. Individuals with both overt and subclinical hypothyroidism with blood TSH levels of more than 10mlU/L were more likely to die from cardiovascular disease [4]. Several studies suggest that TSH and thyroid hormone are two significant risk factors for diseases related to lipid metabolism [5-7].

Various metabolic pathways of protein, carbohydrates, fat metabolisms and several activities like brain development, heartbeat, thermo-genesis, muscle strength, dry skin, menstruation problem, weighting, and alteration in cholesterol levels are all affected by thyroid hormones. Correlation Hyperlipidemia is also a common metabolic abnormality that results from thyroid hormones' effects on all aspects of lipid metabolism, changing triglycerides, phospholipids, cholesterol, and other lipoproteins in different ways [8]. T3 hormone regulates genes involved in lipogenesis and lipolysis, which are important in lipid metabolism [9]. Hypercholesterolemia in hypothyroidism has been associated with raised blood levels of lower-density lipoprotein cholesterol. In most cases, elevated or normal high-density lipoprotein cholesterol levels are seen [10]. A more severe and diffuse form of cardiovascular disease may be present in hypothyroidism, which might account for the increased triglyceride levels associated with overt hypothyroidism [11, 12].

Hypothyroidism is also associated with hyperuricemia [10]. The high frequency of both conditions (hyperuricemia and gout) in the population as a whole is attributable to decreased flow of plasma

through the kidneys and glomerular filtration rate. [12]. Hyperuricemia, on the other hand, is secondary in hypothyroid. [13]. No association has been reported between hypothyroidism and gout or hyperuricemia in womenby some researcher hypothyroidism in men was not associated with hyperuricemia either [14]. Several investigations by different researcher shows contradictory or ambiguous pattern with regards to the effect of TSH, uric acid levels in the general population.
In view of the above, the objective of the investigation was to check the level of uric acid in newly diagnosed hypothyroid women. The study also aims to explore potential significant correlation between newly diagnosed hypothyroid women with altered lipid profile.

MATERIAL AND METHODS

Subjects

Present investigation was planned as a case-control study. The case group included 100 hypothyroid patients (subclinical + overt) aged between 20 to 65 years and the age matched 100 healthy controls. All subjects were chosen from various locations of Haryana and Delhi in India. The Kurukshetra University Institutional Human Ethical Committee (IHEC) gave the approval for research proposal (see letter no. DZ/17/IHEC/445).

Sample collection

All research participants provided signed, pre-informed consent to collect 5ml venous blood sample. Relevant demographic information was collected including, age, gender, history of thyroid and other disorders, history of smoking, and usage of medications. Enzymatic techniques (Erba kit) were used to analyze biochemical markers. The chemiluminescent immunoassay (CLIA) method was used to assess the thyroid hormone levels FT4 and TSH in all the subjects. The FT4 concentrations were within the range of 4.5-12.0 ug/dl. Serum TSH levels typically range from 0.3 to 3.6 mIU/L. Subclinical hypothyroidism is indicated by TSH levels <10 mIU/L >3.6 mIU/L, whereas overt hypothyroidism is indicated by values >10 mIU/L. The normal reference range of all the clinical parameters as were according to the ICMR guideline

Inclusion criteria/ Exclusion criteria

Newly diagnosed hypothyroid females patient between the ages of 20 to 65 was included in the study. Participant with any kind of surgery, diabetic patients, infectious disease or pregnant women were all excluded from the research to prevent any confounding variables that might impede the interpretation of hypothyroidism.

Statistical Analysis

A case-control research is being conducted here. The Student's t-test was utilized to see whether the means of the two groups differed significantly; p-values greater than 0.05 are considered significant. Version 23 of IBM SPSS Statistics was used to compute Pearson's correlation coefficient.

RESULTS

Our study examined the fasting lipid profile, serum uric acid, and body mass index (BMI) of female hypothyroid patients. When we compared the mean of control and case group, our study found that the levels of TSH, TG, TC, LDL and VLDL were all significantly higher in hypothyroid cases (p-value 0.0001).Additionally, the female patients' high-density lipoprotein cholesterol (HDL-C) was considerably lower than the control group's (p-value = 0.0001). Additionally, It was also found that the level of HDL-C was significantly lower in the hypothyroid female case group when compared with the control group (p-value= 0.0001). (Table 1).
The study found a strong correlation between TSH and high level of serum cholesterol in hypothyroid females with a significant +r value 0.217 (p-0.031) when compared r value of healthy control group 0.031 (p -0.759). The correlation coefficients r between FT4 values for cholesterol in hypothyroid females and controls were -0.209 (p -0.036) and -0.194 (p - 0.053), respectively. Furthermore, the study observed (+r value) and significant (p-value) with increased level of LDL-C (r- 0.271, p-0.006), HDL-C (r value -0.593) p- value (0.01), triglycerides (r value - 0.336) p- value (0.000), serum uric acid (r value-0.244) p - value(0.014), and BMI (r value - 0.32) p-value (0.00) correlated with TSH in hypothyroid cases. The r and p values for biochemical parameters in cases are as follows for FT4;-0.26 (p -0.008) for LDL-C, 0.235 (p - 0.018) for HDL-C, -0.199 (p - 0.047) for TG, -0.186 (p - 0.063) for UA, and -0.202 (p - 0.043) for BMI, respectively.(Table 2)

Table1: Comparative analysis of biochemical parameters between hypothyroid females and healthy control females.

Observations	Hypothyroid female (100)	Healthy control (100)	p-value
FT3 (nmol/L)	1.19±0.42	1.58±0.58	**0.0001***
FT4 (ug/dl)	4.63±2.24	8.08±1.80	**0.0001***
TSH (mIU/L)	15.56±13.39	1.93±1.18	**0.0001***
TC (mg/dl)	234.78±30.99	131.36±17.22	**0.0001***
TG (mg/dl)	218.12±22.24	115.86±16.26	**0.0001***
HDL-C (mg/dl)	27.73±6.84	47.08±7.20	**0.0001***
LDL-C (mg/dl)	141.72±21.35	81.32±7.89	**0.0001***
VLDL-C (mg/dl)	41.36±4.59	26.57±3.57	**0.0001***
BMI kg/m^2	26.79±2.86	22.25±2.99	**0.0001***
UA(mg/dl)	6.058±1.162	4.84±1.198	**0.0001***

p-value < 0.05 are measured as a significant count.

Table2: Correlation of TSH and FT4 with biochemical parameters in healthy control group and hypothyroid females.

Observation Biochemical parameters in cases	TSH (cases) r (p) value	FT4 (cases) r (p) value	Biochemical parameters in healthy control	TSH (control) r (p) value	FT4 (control) r (p) value
TC	0.217**(0.031*)**	0.209**(0.036*)**	TC	0.031(0.759)	0.194(0.053)
TG	0.336**(0.00*)**	-0.199**(0.047*)**	TG	0.012(0.905)	0.131(0.193)
HDL-C	-0.33**(0.00*)**	0.235**(0.018*)**	HDL-C	-0.068(0.501)	0.089(0.378)
LDL-C	0.271**(0.006*)**	-0.26**(0.008*)**	LDL-C	0.14(0.164)	0.92(0.362)
VLDL	0.035(0.729)	0.09(0.37)	VLDL-C	0.059(0.860)	0.193(0.052)
BMI	0.382**(0.00*)**	-0.202**(0.043*)**	BMI	-0.0112(0.913)	0.0115(0.909)
UA	0.244**(0.014*)**	0.186(0.063)	UA	0.118(0.242)	-0.03(0.767)

p-value< 0.05showing significant correlation. r-value are between the range +1 to -1. +r shows positive correlation –r shows negative correlation

DISCUSSION

An abnormal lipid profile has been identified as a coronary heart disease risk factor. Examining the correlation between thyroid hormone and lipid profile is crucial in preventing coronary heart disease in thyroid patients. [15-17]. The primary cause of hypercholesterolemia in hypothyroid individuals is the downregulation of the LDL receptor, which is found in liver cells. Thyroid hormones up-regulate LDL receptors, which help in absorption of cholesterol from the blood into the liver. For this reason, hypothyroid individuals also have higher blood LDL-C levels. In addition, thyroid hormones control cholesterol 7 hydroxylase activity, which restricts the rate at which cholesterol is converted into bile acid [18]. This 7α hydroxylase is transcriptionally regulated by thyroid receptor β, and downregulated in hypothyroid patients, leading to decreased conversion of cholesterol to bile acid and consequent clearance of cholesterol [19].

Our results are in accordance with the earlier studies reveling high triglyceride, low density lipoprotein, very low density lipoprotein and total cholesterol level in hypothyroid patients [20, 21]. Previous studies have suggested a strong link between obesity and higher level of TSH [22].Hypothyroidism is commonly related with weight gain, reduced thermogenesis, and metabolic rate. Our study also observed that the average BMI was significantly greater in hypothyroid female patients compared to the healthy control group. Similar to our findings, a meta-analysis study observed that obesity was significantly related to an elevated risk of hypothyroidism [23]. Therefore, our study indicates that a statistically significant higher BMI and higher hyperlipidemia in female hypothyroidism has been connected to obesity, which increases the risk of heart disease.

The possible cause of the correlation between uric acid levels and hypothyroidism in hypothyroid individuals might be attributed to reduced glomerular filtration rate and renal perfusion. [24, 25]. In the present study, hypothyroid female patients exhibited higher uric acid levels compared to the healthy control group and the findings of our study are corroborated with the previous research [26-28]. However ,Jia and See *et a*l. experiment revealed low blood uric acid levels in hypothyroid individuals, which is in contradiction to our results. [29, 30]. Few studies, meanwhile, have shown no connection between hypothyroidism and uric acid (UA). It is uncertain how hypothyroidism and uric acid

metabolism are related. Our findings, however, confirm that there is a substantial correlation between hyperuricemia and hypothyroid females.

CONCLUSION

A substantial correlation has been seen between hypothyroidism and a changed lipid profile, with a substantial increase in TG, TC, LDL-C, and VLDL-C among North Indians females who are at a high risk of coronary heart disease. Serum uric acid and TSH were shown to be statistically significantly correlated. Therefore, in order to control thyroid hormone levels and avoid heart and renal disorders in females, biological screening for uric acid and lipid profile should be performed on hypothyroid females.

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Manpreet kaur - Data investigation
Anita Yadav - Methodology
Ranjan Gupta - Conception, approach, materials, data analysis, and editing
The final draught has been read by all authors and approved.

DECLARATIONS

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