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Association of thyroid stimulating hormone with lipid profile in hypothyroid females of Mansa District of Punjab (India)

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ABSTRACT

Hypothyroidism is defined as the underproduction of the thyroid hormones triiodothyronine (T_3) and thyroxine (T_4) and an increase in the thyroid stimulating hormone levels. It can lead to the lipid abnormalities which increase the risk of endothelial dysfunction, hypertension and cardiovascular diseases. The data for the present case-control study was collected on 175 females (100 thyroid patients and 75 controls), in the age range of 25 to 55 years from various hospitals and other areas of Mansa district of Punjab. The objectives of the study were to find out the association of the thyroid stimulating hormone with lipid profile and then compare it between cases and controls. The lipid profile (total cholesterol, high density lipoproteins, low density lipoproteins, triglycerides and very low density lipoproteins) and thyroid stimulating hormone analysis was done to evaluate dyslipidemia in hypothyroid patients. It was observed that the mean values for various components of lipid profile and thyroid stimulating hormone were significantly greater in cases as compared to the controls. Further, thyroid stimulating hormone showed a highly significant association with total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein. It can be concluded that the hypothyroid females were suffering with dyslipidemia, which may be a risk factor for any heart ailment.

Keywords: Dyslipidemia, hypothyroidism, thyroid hormones, females.

INTRODUCTION

Thyroid is one of the largest endocrine gland, which is found in the neck, inferior to the cartilage ('Adam's Apple'). It produces the thyroid hormones such as triiodothyronine (T_3) and thyroxine (T_4). The thyroid hormones help in regulating the rate of metabolism. They affect the growth and rate of function of many other systems in the body. The triiodothyronine and thyroxine hormones are synthesized with the help of both iodine and tyrosine. The hormonal output of the thyroid is regulated by thyroid-stimulating hormone (TSH), which is produced by the anterior pituitary gland. The anterior pituitary gland itself is regulated by thyrotropin-releasing hormone (TRH) which is produced by the hypothalamus.

The thyroid disorder is a disorder of irregular production of thyroid hormones. The overproduction of hormones is known as hyperthyroidism and the underproduction of hormones is termed as hypothyroidism. Hypothyroid disorder is defined as a deficiency of thyroid hormones. It occurs due to reduced secretion of T_3 and T_4 hormones from the thyroid gland that leads to hyper secretion of thyroid stimulating hormone (TSH). It is caused as a result of the congenital thyroid abnormalities, autoimmune disorders (Hashimoto's thyroiditis) or removal of the thyroid gland for treating severe hyperthyroidism following surgery (Nazario, 2002). The typical symptoms of hypothyroid disorder are weight gain, tiredness, baldness, cold intolerance and bradycardia. Subclinical hypothyroidism is defined as an increase in the level of thyroid stimulating hormone while the levels of triiodothyronine and thyroxine hormones are normal. When the thyroid gland is unable to secrete the thyroid hormones due to iodine deficiency, it may cause an increase in size of the gland and then the condition is known as non-toxic goiter. Despite its size, goiter does not produce any toxic quantities of thyroid hormones in the body.

Thyroid disorder is the most common endocrine disorder which is associated with dyslipidemia. It affects the synthesis, mobilization and metabolism of lipids (Erem *et al*., 1999). In hypothyroidism, the levels of total cholesterol, low density lipoprotein and triglycerides are significantly increased while the levels of high density lipoprotein are decreased as compared to controls (Shashi and Sharma, 2012; Shilpashree *et al.,* 2014). Studies have shown that high density lipoprotein cholesterol is also increased in hypothyroidism (Jung *et al.,* 2003; Regmi *et al.,* 2010).

The global prevalence of thyroid disorder is more than 2 billion, with approximately 42 million in India (Vasudevan *et al.,* 2011). An estimated 108 million people are suffering from endocrine and metabolic disorders in India and the thyroid disorders are the most common among them (Kochupillai, 2000). In India, the prevalence of hypothyroidism was 25% (Riaz *et al.,* 2009). Age, sex and especially iodine intake have an impact on the prevalence of thyroid disorders. The prevalence of hypothyroidism is greater in older age and a greater percentage of women are affected as compared to men (Laurberg *et al.,* 1998). The subclinical hypothyroidism has a higher prevalence than overt hypothyroidism (Danese *et al.,* 2000; Tunbridge *et al.,* 1977). Therefore, early treatment of subclinical hypothyroidism can prevent the occurrence of overt hypothyroidism.

The present case-control study was designed to find out the association of thyroid stimulating hormone with lipid profile and compare the parameters between the cases (hypothyroid) and controls for biochemical analysis.

MATERIAL AND METHODS

For the present study, data on 175 female subjects (100 hypothyroid patients and 75 controls) in the age range of 25-55 years were collected from various hospitals of Mansa district of Punjab. Only newly diagnosed hypothyroid patients were taken and their detailed history related to impaired thyroid functioning was recorded. The consent of the subjects was taken before their enrolment into the study. The present study was approved by the Institutional Ethical Committee of Punjabi University, Patiala.

With the help of expert laboratory technician, 5 ml venous blood (fasting) of each subject was collected in simple vials. The collected blood sample was centrifuged and the separated serum was stored at -20°C. For each sample, the level of serum thyroid stimulating hormone (TSH) was analyzed by enzyme immuno assay method using Elisa reader. Serum total cholesterol was assayed by the CHOD-PAP method (Allain *et al*., 1974), high density lipoprotein cholesterol was assayed by Phosphotungestate method (Allain *et al*., 1974) in the supernatant after precipitation with phosphotungastic acid $MgCl_2$ and triglyceride was estimated using GPO-POD method with TBHA AS CHROMOGEN (Jacobe *et al.,* 1960). All these parameters were analyzed using the Biochemical auto analyzer instrument. The low density lipoprotein (LDL) was calculated by using the formula given by Friedewald (1972).

Statistical analysis:

The results have been presented as Mean ± SD and SEM. For comparison between the cases and controls, t-test was applied and the differences with p values equal to or less than 0.05 were considered significant. Pearson Correlation was performed using SPSS software 16.0 version. Scatter plots of regression lines were drawn by using MS Office 2007 version.

RESULTS

In hypothyroid patients, the level of thyroid stimulating hormone was significantly more as compared to controls. The differences were statistically significant ($p<0.001$). The values of total cholesterol, high density lipoprotein, low density lipoprotein, triglyceride and very low density lipoprotein cholesterol were also significantly higher in hypothyroid patients than their control counterparts and the differences were statistically significant ($p<0.01$; $p<0.001$) for all these parameters (**Table 1, Fig. 1)**.

Table 1: Mean, S.D. and S.E.M. of thyroid stimulating hormone (TSH) and lipid profile parameters of hypothyroid and control females.

Biochemical parameters	Hypothyroid cases (n=100)		Controls (n=75)		t-values
	Mean ± SD	SEM	Mean ± SD	SEM	
Thyroid stimulating hormone (TSH) (µIU/ml)	16.60± 12.78	1.28	3.32 ± 0.85	0.098	10.34**
Total cholesterol (TC) (mg/dl)	204.00 ± 33.85	3.38	168.4 ± 16.21	1.87	9.22**
High density lipoprotein (HDL) (mg/dl)	43.08 ± 4.67	0.47	41.39± 3.18	0.37	2.82*
Low density lipoprotein (LDL) (mg/dl)	118.40 ± 27.24	2.72	92.14 ± 13.22	1.53	8.41**
Triglyceride (TG) (mg/dl)	212.62 ± 65.31	6.53	174.39 ± 12.99	1.50	5.21**
Very low density lipoprotein (VLDL) (mg/dl)	42.52 ± 13.06	1.31	34.88 ± 2.60	0.30	5.68**

***Statistically significant p<0.01**

**** Statistically significant p<0.001**

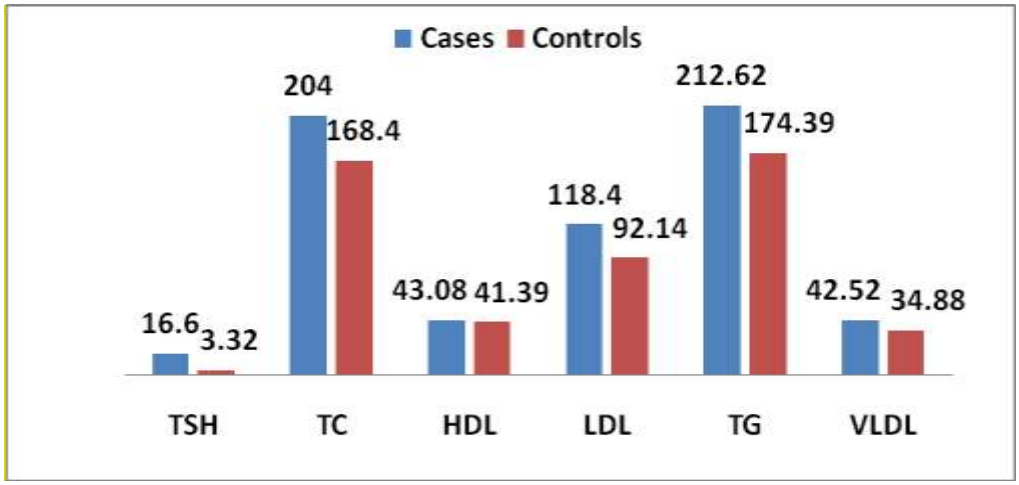

Fig 1. Mean values of TSH, TC, HDL, LDL, TG and VLDL in cases and control females.

TSH- Thyroid stimulating hormone; TC-Total cholesterol; HDL-High density lipoprotein; LDL-Low density lipoprotein; TG-Triglyceride; VLDL-Very low density lipoprotein.

In both hypothyroid and control females, the thyroid stimulating hormone showed significant positive correlation with the total cholesterol ($r = 0.73$, $y = 1.933x + 171.9$, $R^2 = 0.532$, $p<0.01$; $r = 0.31$, $p<0.01$), low density lipoprotein ($r = 0.64$, $y = 1.372x + 95.61$, $R^2 = 0.414$, $p<0.01$; $r = 0.29$, $p<0.01$), triglyceride ($r=0.26$, $y = 2.495x + 171.2$, $R^2 = 0.238$, $p<0.03$; $r = 0.26$, $p<0.03$ and very low density lipoprotein ($r=0.26$, $y = 0.499x + 34.23$, $R^2 = 0.238$, $p<0.03$). The association between thyroid stimulating hormone and high density lipoprotein ($r=0.17$, $y = 0.062x + 42.05$, $R^2 = 0.028$, $p=0.09$; $r = 0.20$, $p=0.08$) was not significant in both groups of female (**Table 2**). In the hypothyroid females, the thyroid stimulating hormone had strong association with lipid profile parameters as compared to control ones.

Table: 2 Correlation of thyroid stimulating hormone (TSH) with lipid profile parameters in hypothyroid females.

Biochemical Parameters	Groups	Total cholesterol (TC)	High density lipoprotein (HDL)	Low density lipoprotein (LDL)	Triglyceride (TG)	Very low density lipoprotein (VLDL)
		(r)	(r)	(r)	(r)	(r)
Thyroid stimulating hormone (TSH)	Hypothyroid females	0.73** p<0.01	0.17 p=0.09	0.64** p<0.01	0.49** p<0.01	0.49** p<0.01
	Control females	0.31 p<0.01	0.20 p<0.08	0.29 p<0.01	0.26 p<0.03	0.26 p<0.03

***Statistically significant p<0.05**
**** Statistically significant p<0.01**

Correlation/Scatter plots

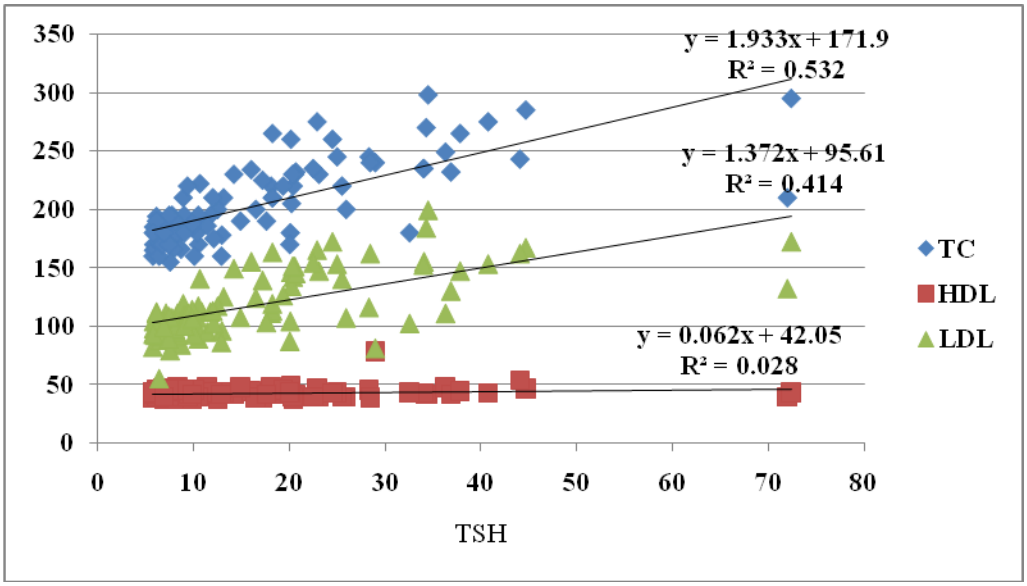

Fig 2. Scatter plot showing inter-relationship of thyroid stimulating hormone (TSH) with total cholesterol (TC), high density lipoprotein (HDL) and low density lipoprotein (LDL) in hypothyroid females. X axis indicates TSH (µIU/ml) and Y axis indicates TC, HDL and LDL (mg/dl).

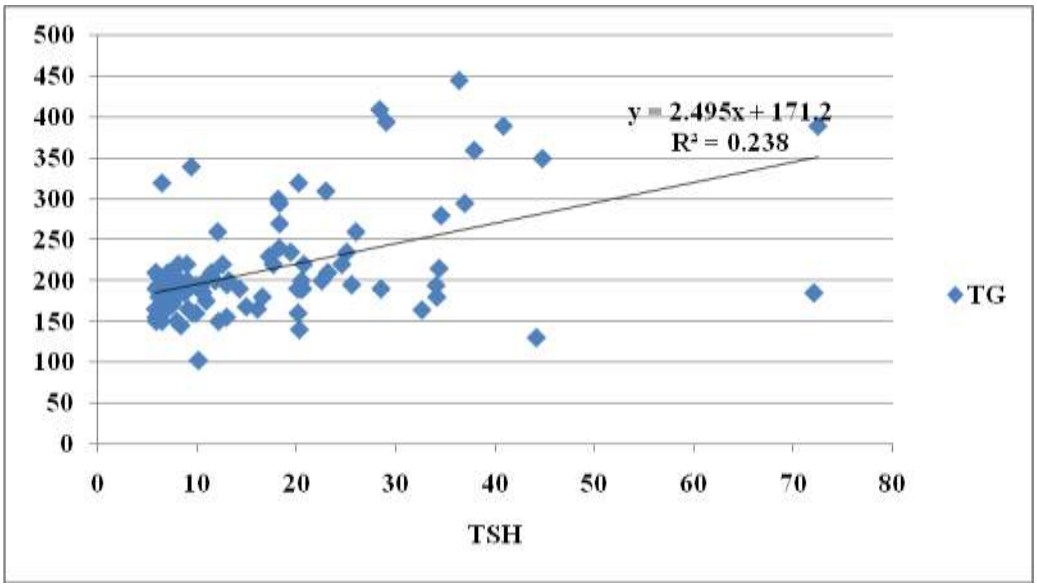

Fig 3. Scatter plot showing inter-relationship of thyroid stimulating hormone (TSH) with triglycerides (TG) in hypothyroid females. X axis indicates TSH (µIU/ml) and Y axis indicates TG (mg/dl).

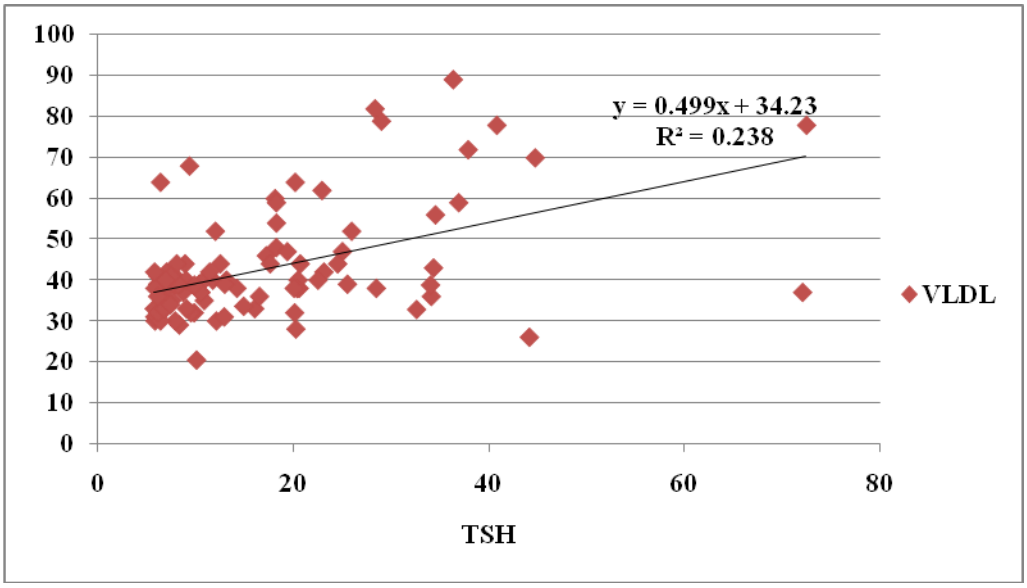

Fig 4. Scatter plot showing inter-relationship of thyroid stimulating hormone (TSH) with very low density lipoprotein (VLDL) in hypothyroid females. X axis indicates TSH (µIU/ml) and Y axis indicates VLDL (mg/dl)

DISCUSSION

In the present study, the mean total cholesterol, low density lipoprotein cholesterol and triglyceride were lower in hypothyroid case and control groups as compared to the population of Bangladesh (Mondal *et al.*, 2011), except for the high density lipoprotein cholesterol. In comparison to population of Karnataka (Shilpashree *et al.*, 2014), the mean total cholesterol, high density lipoprotein, triglyceride and very low density lipoprotein were higher in the hypothyroid case group of the present study, whereas the value for thyroid stimulating hormone, total cholesterol, very low density lipoprotein and triglyceride were higher in the control group of the present study.

In both hypothyroid and control females, the thyroid stimulating hormone had significant positive association with total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein in the present study. In the population of Andhra Pradesh, thyroid stimulating hormone showed a significant correlation with total cholesterol and low density lipoprotein (Shekhar *et al.*, 2011) in hypothyroid patients. Aggarwal and Sharma (2012) reported that the thyroid stimulating hormone had a significant positive association with total cholesterol, low density lipoprotein and triglyceride in the population of Himachal Pradesh. Some other studies have shown that thyroid stimulating hormone had association with total cholesterol (Mahajan

and Singh, 2011), low density lipoprotein and triglyceride in hypothyroid patients (Iqbal *et al.*, 2006; Teixeira *et al.*, 2008) whereas in euthyroid females, the thyroid stimulating hormone within the normal range had positive correlation with total cholesterol and triglyceride (Wanjia and jiajun, 2012).

Table: 3 Comparison of lipid profile and TSH (present study) with different populations.

Parameters (Hypothyroidism)	Present study		Mondal *et al.* 2011		Shilpashree *et al.* 2014	
	Hypothyroid case Group	Control Group	Hypothyroid case Group	Control Group	Hypothyroid case Group	Control Group
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
TSH	16.60 ± 12.78	3.32 ± 0.85	-	-	37.19 ± 47.35	2.39 ± 1.07
Total cholesterol	204.00 ± 33.85	168.4 ± 16.2	209.89 ± 60.38	191.49 ± 45.95	202.57 ± 61.11	166.70 ± 31.50
HDL	43.08 ± 4.67	41.39 ± 3.18	38.05 ± 10.94	36.82 ± 8.75	39.05 ± 10.55	45.30 ± 14.27
Triglyceride	212.62 ± 65.31	174.39 ± 12.99	231.47 ± 130.01	186.04 ± 92.46	186.10 ± 10.19	122.53 ± 40.01
LDL	118.40 ± 27.24	92.19 ± 13.22	121.72 ± 37.90	118.95 ± 38.25	125.4 ± 48.11	95.03 ± 28.27
VLDL	42.52 ± 13.06	34.88 ± 2.60	-	-	38.77 ± 21.82	27.31 ± 12.22

Conclusions

From the present study, it can be concluded that the levels of thyroid stimulating hormone and lipid profile are higher in hypothyroid patients as compared to controls. Further, thyroid stimulating hormone has a significant positive association with total cholesterol, low density lipoprotein, triglyceride and very low density lipoprotein parameters in both hypothyroid and control females. But, the associations between thyroid stimulating hormone and lipid profile parameters are stronger in hypothyroid females than controls. Therefore, the thyroid disorder could be one of the several factors for development of dyslipidemia in hypothyroid females.

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