CORRELATION BETWEEN THYROID HORMONES AND THYROID STIMULATING HORMONE WITH LIPID PROFILE PARAMETERS IN EUTHYROID PATIENTS.

Biochemistry

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ABSTRACT

Background: Thyroid function regulates wide ranges metabolic parameters, the most striking action being an increase in energy expenditure. Thyroid function significantly affects lipoprotein metabolism, thus influencing overall CVD risk factors. Hyperthyroidism occurs due to hyper secretion of thyroid hormones. Hypothyroidism is a clinical condition where there is hypo secretion of thyroid hormones. This is usually due to thyroid failure but can also be due to disease of the pituitary or hypothalamus.

Materials and Methods: A cross-sectional study was conducted in the Department of Biochemistry, Index Medical College Hospital and Research Centre from July 2018 to January 2020. Total 114 patients were enrolled of group age between 21 to 80 yrs. Lipid profile and thyroid profile were estimated and their values were compared.

Result: TSH significantly negative correlated with fT3 ($r = -0.277$, $p < 0.05$) fT4 ($r = -0.290$, $p < 0.05$) and statistically positive correlation with TC ($r = 0.277$, $p < 0.05$) and LDL-C ($r = 0.278$, $p < 0.05$). fT3 was positively correlated with LDL-C ($r = 0.373$, $p < 0.01$)

Conclusion: Thyroid dysfunction especially hypothyroidism was more prevalent among women.. Thyroid dysfunction is associated with the altered lipid metabolisms responsible for cardiovascular diseases. Therapeutic measures to control thyroid disorders could be beneficial for the better regulation of dyslipidemia and its complications.

KEYWORDS

Thyroid Dysfunction, Free T3, Free T4, Total Cholesterol (TC), LDL-Cholesterol

1. INTRODUCTION:

Thyroid function regulates a wide array of metabolic parameters. Thyroid function significantly affects lipoprotein metabolism as well as some cardiovascular disease (CVD) risk factors, thus influencing overall CDV risk [1], [2]. Thyroid hormones have profound metabolic effects, the most striking action being an increase in energy expenditure [3].

In hyperthyroidism, the metabolic effects include the increased utilization and oxidation of all major fuel substrates that is, protein, glucose and lipids [4]. Hypothyroidism is a clinical condition in which there is hypo secretion of thyroid hormones. This is usually due to thyroid failure but can also be due to disease of the pituitary or hypothalamus. Such subjects will have lower metabolic rate and clinical manifestations such as overweight, fatigue, hypotension and depression. The metabolic effects of hypothyroidism are not well characterized. The condition is characterized by increased fasting plasma cholesterol and triglycerides [5], [6]. The effect of hypothyroidism on HDL cholesterol level has been contradictory. HDL cholesterol levels have been reported to be increased [6], decreased [7] and normal [8] in hypothyroidism. It is well-known that hypothyroidism is associated with hypercholesterolemia and increases the risk of atherosclerosis [9], [10].

Although thyroid hormones have an impact on lipid metabolism, connection between subclinical hypothyroidism, dyslipidemia and increased risk for atherosclerosis is still a matter of debate [11], [12]. It is known that LDL-C plays an important role in development of atherosclerosis but there is more evidence which highlight the importance of its qualitative composition. There are two distinct LDL subclass phenotypes: phenotype A, with a larger buoyant LDL subfraction, and phenotype B, with smaller and denser LDL sub fraction. This small, dense low-density lipoprotein cholesterol (sdLDL-C) particles have been recognized as more atherogenic due to their better penetration into the arterial wall, their lower binding affinity for the LDL receptor, their prolonged plasma half-life and lower resistance to oxidative stress compared to large buoyant LDL-C [13- 16].

Hyperthyroidism occurs when there is hyper secretion of thyroid hormones. It is also termed as thyrotoxicosis. It is caused due to Grave's disease which results from the over production of TSH that activates TSH receptor. This causes diffused enlargement of the thyroid and excessive, uncontrolled production of T3 and T4. Excess thyroid hormone can cause symptoms such as weight loss, tiredness,

increased heart rate, heat intolerance, sweating, irritability, anxiety, muscle weakness and thyroid enlargement.[17] The incidence of hyperthyroidism is lower (2.2%) compared with hypothyroidism in the general population. [18]

2. MATERIALS AND METHODS

A cross-sectional study was conducted in the Department of Biochemistry, index medical college hospital and research centre from July 2019 to January 2020. A total of 114 patients with suspicion of thyroid disorders were enrolled in the group age was between 21 to 80 yrs old. 5 ml fasting blood sample was collected and lipid profile estimated by spectrophotometric principle and with semi - Auto analyzer. Estimation of thyroid profile was quantitatively estimated by ELISA method.

Inclusion criteria:

Newly diagnosed Hyper- and Hypothyroidism (TSH: 4.9-10, normal fT4: 9-19pmol/L), Euthyroid subjects: (TSH: 0.35-4.9 μ IU/L, fT4: 9-19 pmol/L)

Exclusion criteria:

Previously diagnosed thyroid disease, Diabetes mellitus, Pregnancy Polycystic ovary syndrome, Renal and hepatic dysfunction, previous cardiovascular disease, Cancer, Subjects receiving drugs known to affect the thyroid or lipid metabolism

Ethical consideration-

All the study process was started only after obtaining ethical approval from the institutional ethical committee. All the information about the participants was also kept confidential.

3. RESULTS

Table 3.1 : Clinical characteristics of the study population

	Mean
Age	49.07 $\pm$ 11.35 years
TC	195.63 $\pm$ 44.77 mg/dl
TG	188.89 $\pm$ 98.17 mg/dl
HDL-C	37.75 $\pm$ 8.48 mg/dl
LDL-C	123.26 $\pm$ 34.69 mg/dl
Free T3	2.70 $\pm$ 1.06 pg/ml
Free T4	1.49 $\pm$ 0.96 ng/dl
TSH	5.67 $\pm$ 6.18 μ IU/ml

Table 3.1 shows the clinical characteristics of the study population. The average age of the 114 patients was 49.07 $\pm$ 11.348 years. Lipid

profile and thyroid hormone test were carried out. The mean total cholesterol (TC) level, mean triglycerides (TG) level, HDL-cholesterol (HDL-C) level and LDL-cholesterol (LDL-C) level were determined to be 195.63 ± 44.77 mg/dl, 188.89 ± 98.17 mg/dl, 37.75 ± 8.48 mg/dl and 123.26 ± 34.69 mg/dl respectively. Similarly, mean free T3 level was 2.7000 ± 1.06 pg/ml, mean free T4 level was 1.49 ± 0.96 ng/dl and mean TSH level was 5.67 ± 6.18 μ IU/ml

Table 3.2: Distribution according to Gender

Gender		TC	TG	HDL-C	LDL-C	T3	T4	TSH
		(mg/dl)	(mg/dl)	(mg/dl)	(mg/dl)	(pg/ml)	(ng/dl)	μ IU/ml
Male	Mean	205.65	232.35	36.4	122.6	2.94	1.5	4.58
	S. E.	8.04	28.6	1.88	8.09	0.27	0.16	0.78
Female	Mean	190.22	165.41	38.49	123.62	2.57	1.49	6.26
	S. E.	7.97	11.32	1.41	5.65	0.16	0.18	1.19
p-value (t-test)		0.217	0.22	0.01	0.38	0.92	0.22	0.96

The mean values of lipids and thyroid hormones were compared among male and female, it was found that the mean triglyceride level was significantly at $p < 0.05$ higher in male (232.35 ± 28.60 mg/dl) than in females (165.41 ± 11.32 mg/dl). Similarly, mean total cholesterol was also higher in males (205.65 ± 8.04 mg/dl) than in females (190.22 ± 7.97 mg/dl) but the difference was not significant at $p < 0.05$. Mean HDL-cholesterol and mean LDL-cholesterol levels were lower in males than in females. Male subjects had higher T3 and T4 levels than female subjects while mean TSH was higher in females than in males.

Table 3.3: Distribution according to Age Group.

Age Group		TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	T3 (pg/ml)	T4 (ng/dl)	TSH (μ IU/ml)
21-40	Mean	186.67	202.13	36.80	122.47	2.42	1.13	5.93
	S. E.	15.28	33.85	2.34	7.95	0.19	0.10	0.92
41-60	Mean	198.97	161.72	39.34	127.13	2.71	1.68	6.08
	S. E.	6.52	11.14	1.51	6.41	0.19	0.21	1.31
61-80	Mean	198.40	256.00	34.10	112.10	3.08	1.43	3.97
	S. E.	14.69	34.10	2.06	11.39	0.41	0.13	1.54
p-value (anova)		0.672	0.67	0.02	0.21	0.50	0.32	0.19

Mean TC (198.97 ± 6.52 mg/dl), HDL-C (39.34 ± 1.51 mg/dl), LDL-C (127.13 ± 6.41 mg/dl) and TSH (6.08 ± 1.31 μ IU/ml) levels were the highest in the age group 41-60 whereas the age group 61-80 had the highest mean TG (256.00 ± 34.10 mg/dl), T3 (3.08 ± 0.41 pg/ml) and T4 (1.43 ± 0.13 ng/dl) levels. While comparing the mean lipid levels and mean thyroid hormone levels in different age groups, it was observed that only HDL-C had significantly different mean values among the groups at $p < 0.05$

Table 3.4: Distribution according to Thyroid Disorder

Thyroid Disorder		TC (mg/dl)	TG (mg/dl)	HDL-C (mg/dl)	LDL-C (mg/dl)	T3 (pg/ml)	T4 (ng/dl)	TSH (μ IU/ml)
Hyper (n=2)	Mean	175.00	184.00	32.00	106.00	4.60	1.85	0.15
	S. E.	68.00	10.00	5.00	65.00	0.40	0.15	0.05
Normal (n=38)	Mean	186.16	180.87	36.16	118.92	2.69	1.59	2.91
	S. E.	7.07	15.32	1.08	4.80	0.16	0.18	0.23
Hypo (n=17)	Mean	219.24	207.41	42.00	135.00	2.49	1.22	12.51
	S. E.	8.37	27.21	2.62	9.17	0.28	0.13	1.84
p-value (anova)		0.029	0.03	0.66	0.04	0.22	0.03	0.37

The study population was divided into 3 categories: hypothyroidism, normal and hyperthyroidism according to the level of TSH. Subjects having hypothyroidism had the highest lipid levels while those having hyperthyroidism had the lowest. Between the groups, there was a statistically significant difference in the mean values of total cholesterol and HDL-cholesterol at $p < 0.05$. The thyroid hormones T3 and T4 were the highest in hyperthyroidism and the lowest in hypothyroidism but only the mean difference in the T3 levels was significant at $p < 0.05$.

Table 3.5: Correlations between different parameters

		TSH	ft3	ft4	TC	TG	HDL-C	LDL-C
TSH	Pearson Correlation	1	-.277*	-.290*	.277*	.009	.231	.278*
	Sig. (2-tailed)		.037	.029	.037	.948	.083	.036
ft3	Pearson Correlation	-.277*	1	.029	-.202	-.068	-.060	-.373**
	Sig. (2-tailed)	.037		.831	.131	.613	.657	.004
ft4	Pearson Correlation	-.290*	.029	1	-.102	-.058	-.030	-.130
	Sig. (2-tailed)	.029	.831		.451	.667	.823	.335
TC	Pearson Correlation	.277*	-.202	-.102	1	.241	.118	.721**
	Sig. (2-tailed)	.037	.131	.451		.070	.383	.000
TG	Pearson Correlation	.009	-.068	-.058	.241	1	-.272*	-.179
	Sig. (2-tailed)	.948	.613	.667	.070		.040	.183
HDL-C	Pearson Correlation	.231	-.060	-.030	.118	-.272*	1	.216
	Sig. (2-tailed)	.083	.657	.823	.383	.040		.107
LDL-C	Pearson Correlation	.278*	-.373**	-.130	.721**	-.179	.216	1
	Sig. (2-tailed)	.036	.004	.335	.000	.183	.107	
N		114	114	114	114	114	114	114

There was a statistically significant negative correlation of TSH with ft3 ($r = -0.277$, $p < 0.05$) ft4 ($r = -0.290$, $p < 0.05$) and statistically positive correlation with TC ($r = 0.277$, $p < 0.05$) and LDL-C ($r = 0.278$, $p < 0.05$). Increase in the level of TSH is correlated with decreases in the levels of ft3 and ft4 and increases in the levels of TC and LDL-C. Similarly, there was a statistically significant strong correlation of ft3 with LDL-C ($r = -0.373$, $p < 0.01$) meaning that increases in the level of ft3 is correlated with decreases in the level of LDL-C

4. DISCUSSION

Thyroid dysfunction may lead to the serious alteration in the composition and transport of the lipoproteins.[19]

In our study, the relationship between the thyroid hormone and the lipid profile parameters (total cholesterol, Triglycerides, HDL-C, LDL-C) were evaluated. Out of the total 114 subjects, 66% were normal, 30% were hypothyroid and 3.4% were hyperthyroid patients.

The number of female subjects was more than that of male subject which indicates the prevalence of thyroid dysfunction to be more in female population than male which were similar to the findings reported by various studies. [20],[21]

In our study, we observed a higher mean TC, TG and LDL-C cholesterol level in hypothyroid subjects as compared to the normal subjects. The result was comparable to the studies performed by Dr. Ashok Kumar et.al [22] and Jung et.al.[23]

The data analysis from our study should that these was statistically significant negative correlation of TSH with ft_3 and ft_4 and significant positive correlation with TC and LDL-C. Increase in the level of TSH was correlated with the decreased level of ft_3 and ft_4 and increased level of TC and LDL-C. Similarly, there was a significant strong positive correlation of ft_3 with LDL-C. Our study shows quite similar results reported by Duntas et.al and Anubhuti et.al. [24]

Free T₃ has property to up regulate LDL receptors by controlling the LDL receptor gene activation.[25] Also it has ability to protect LDL from oxidation.[26] In hypothyroidism, the increase in LDL relates to the decreased clearances of LDL particles which are caused by the changes in the expression of LDL receptor in liver cell surface.[27] Whereas in hyperthyroidism, these is increased metabolism of cholesterol and increased turnover of LDL leading to decrease in TC and LDL-C. On the other hand, the HDL-C may be decreased or may not be affected. [1]

Although the present study was a single centered study and had relatively fewer number of subject within a limited time frame, the results favored with various similar studies conducted in different time period and group of population. The present study has some limitation as well as it was a clinical study in a single centre with limited sample size and few parameters. Still extensive studies in larger population with added parameters like BMI, Ethnicity, and Iodine status level in body could also be included for better study. Overall this study would act as a pilot study and provide a baseline data required for further research in this area.

5. CONCLUSION:

In the present study, the thyroid dysfunction especially hypothyroidism was more prevalent among women. The thyroid dysfunction is associated with the altered lipid metabolisms which are responsible for various cardiovascular diseases. So, therapeutic measures to control thyroid disorders could be beneficial for the better regulation of dyslipidemia and its complications.

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