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Association of Visceral Fat with Pulmonary Function in Hypothyroidism Patients

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Abstract **Original Research Article**

Introduction: Hypothyroidism is divided in primary, caused by failure of thyroid function and secondary (central) due to the failure of adequate thyroid-stimulating hormone (TSH) secretion from the pituitary gland or thyrotrophin-releasing hormone (TRH) from the hypothalamus. Secondary hypothyroidism can be differentiated in pituitary and hypothalamic by the use of TRH test. In some cases, failure of hormone action in peripheral tissues can be recognized. Primary hypothyroidism may be clinical, where free T4 (FT4) is decreased and TSH is increased or subclinical where FT4 is normal and TSH is increased. In secondary hypothyroidism FT4 is decreased and TSH is normal or decreased. Primary hypothyroidism is most commonly caused by chronic autoimmune thyroiditis, less common causes being radioiodine treatment and thyroidectomy. ***Material and Methods:*** This is a case control study conducted in the Department of General Medicine, NC Medical College & Hospital, Israna, Panipat over a period of 1 year. A total of 120 patients with age between 18 to 60 years were included in the study. The study included 2 groups, group 1 consisted of 60 newly detected hypothyroids and group 2 with 60 controls who were age, sex matched and from similar environment as that of cases. Group 1 hypothyroid patients include both clinical (TSH >5 milli units/L with clinical features of hypothyroidism or low Free thyroxine (FT4)) and subclinical hypothyroidism (TSH>5 with no clinical features of hypothyroidism or normal FT4). ***Results:*** In this study, there is no significant difference in age and BMI in cases and controls. TSH was significantly higher while FT3 and FT4 were significantly lower in cases compared to controls. FVC between cases and controls did not show statistical significance, although the mean FVC was found to be lower in cases (1.73) as compared to controls (2.23). Furthermore, observed that there was no significant correlation between TSH or FT4 with FVC, FEV1, and FEV1/FVC as seen in (Table 3 and 4). ***Conclusion:*** FT3 level and FT4 level was each significantly associated with fat volume and BMI. Thyroid hormone levels can affect cardiovascular risk through regulation of pericardial fat deposition, in addition to other known mechanisms. In hypothyroidism, there is significant reduction in the dynamic lung functions as compared with controls.

Keywords: Pulmonary function tests, Hypothyroidism free triiodothyronine, Free thyroxine, Thyroid stimulating hormone.

INTRODUCTION

Hypothyroidism is a relatively common disease in world wide. It is Characterized by a clinical finding include an effect, cold intolerance, weight gain, swelling of extremities, hair loss, bradycardia, hoarseness of speech, menorrhagia, neurological symptoms, hearing disorders, dry skin and fatigue. The prevalence of hypothyroidism in the developed world is about 4-5% [1].

In India, hypothyroidism was usually categorized under the cluster of iodine deficient disorders (IDDs), which were represented in terms of total goiter rates and urinary iodine concentrations, typically assessed in school aged children in 1983 India adopted the universal salt iodization program, there has been a decreased in goiter prevalence in several countries, which were previously endemic. The prevalence of hypothyroidism was high, affecting approximately one in 10 adults in the study population [2]. Female gender and older age were found to have significant association with hypothyroidism. Metabolic abnormalities associated with hypothyroidism include anemia. The prevalence of anemia and hematological abnormalities in patients with hypothyroidism has been shown to be 20-60%. Thyroid dysfunction is usually associated with body weight and subclinical hypothyroidism is more frequently associated with weight gain [3].

Studies focused mainly on investigating whether an increase of body weight might be related to an underlying thyroid disturbance. An elevated serum concentration of TSH, suggesting subclinical hypothyroidism, was frequently reported in human obesity. Several investigations, mostly represented by cross-sectional population studies, demonstrated a positive correlation between serum levels of thyroid stimulating hormone (TSH) and body mass index (BMI) [4]. Thyroid hormones are potent modulators of adaptive thermo genesis. Overt hypothyroidism leads to increased body weight by increasing mucin deposits and by salt and water retention. Extreme obesity also leads to increased TSH due to hypothalamic-pituitary thyroid axis abnormality. Leptin produced by adipocytes directly stimulates Thyrotrophin-releasing hormone (TRH) neurons in the paraventricular nucleus, thus increasing TSH [5].

Increased body weight has been associated with deterioration of pulmonary functions. Weight and BMI as measures of overall adiposity are used as predictors of pulmonary function in many epidemiologic studies. While these measures are widely accepted as determinants of pulmonary function, high visceral fat may influence pulmonary function through a mechanism that is distinct from that of overall adiposity. [6] Visceral fat is implicated in the pathogenesis of the metabolic syndrome (MS). Visceral and subcutaneous fat (SF) expresses thyroid hormone receptors as well as TSH receptors that may also directly influence various functions of adipose cells [7]. However; it is not known whether the type of fat could be implicated in the associations of thyroid function parameters with deterioration of pulmonary function and anaemia.

MATERIAL AND METHODS

This is a case control study conducted in the Department of General Medicine, NC Medical College & Hospital, Israna, Panipat over a period of 1 year. A total of 120 patients with age between 18 to 60 years were included in the study. The study included 2 groups, group 1 consisted of 60 newly detected hypothyroids and group 2 with 60 controls who were age, sex matched and from similar environment as that of cases. Group 1 hypothyroid patients include both clinical (TSH >5 milli units/L with clinical features of hypothyroidism or low Free thyroxine (FT4)) and subclinical hypothyroidism (TSH>5 with no clinical features of hypothyroidism or normal FT4).

Patients already on thyroxine therapy, BMI>23 kg/m^2, history of smoking, anemia, respiratory, cardiac patients and pregnant women were excluded from the study. All patients underwent a detailed clinical examination and routine investigations such as thyroid function test (TSH, FT3 FT4), chest x ray and spirometry were also done. Spirometry was done by vitalograph, software that is installed in a computer in the department of General Medicine.

All patients were asked to rest for 10 to 15 mins in a private quiet room, and they were briefed about the technique. Pulmonary function tests (PFT) is carried out in a quiet room in sitting position with a nose clip. An average of 3 readings was taken. Spiro metric parameters recorded for analysis are: Forced vital capacity (FVC), Forced expiratory volume in 1st second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEFR), Forced expiratory flow 25%-75% (FEF25%-75%).

Inclusion criteria

- Age 18-60 years
- Newly detected hypothyroidism both clinical (TSH >5milliunits/L with clinical features of hypothyroidism or low FT4) and Subclinical hypothyroidism (TSH>5 with no clinical features of hypothyroidism or normal FT4).

Exclusion criteria

- Patients already on thyroxin treatment
- BMI >23kg/m2
- H/o smoking, respiratory illness
- Pregnancy
- Anemia
- Cardiac illness

STATISTICAL METHODS

Data was tabulated in Microsoft Office Excel and statistical analysis was done by using SPSS for windows (version 20.0). The thyroid function test parameters were analysed by paired t test and Pearson's correlation analysis was used to analyze the relationships between TSH, FT4 with respiratory parameters, p-value less than 0.05 was considered statistically significant. r value ranges from -1 to +1 using linear correlation analysis.

RESULTS

Table 1, demonstrates no significant difference in age and BMI in cases and controls. TSH was significantly higher while FT3 and FT4 were significantly lower in cases compared to controls.

Table-1: Baseline characteristics of cases and controls

Variable	Cases Mean±SD	Controls Mean±SD	Pvalue
Age	43.85±9.74	42.43±9.28	0.632
BMI	23.35±2.32	22.64±2.64	0.42
FT3	0.91±0.29	2.83±0.43	<0.0001
FT4	0.63±0.18	1.29±0.37	<0.0001
TSH	9.34±1.65	3.39±0.79	<0.0001
Total body fat	10.32±3.53	6.37±1.32	<0.0001
Visceral fat	18.33±3.37	19.32±2.51	0.532

Table-2: Pulmonary function tests parameters

Variable	Cases Mean±SD	Controls Mean±SD	Pvalue
FVC(L)	1.73±0.63	2.23±0.56	0.231
FEV1	1.21±0.13	1.98±0.10	0.000
EFV1/FVC	69.49±9.73	79.37±9.36	0.000

In table 2, FVC between cases and controls did not show statistical significance, although the mean FVC was found to be lower in cases (1.73) as compared to controls (2.23).

Table-3: Correlation of FT4 with lung function parameters

		FEV1	FVC	FEV1/FVC
FT4	r	-0.19	-0.29	-0.01
	p	0.23	0.09	0.93

r = Correlation coefficient, p<0.05 considered statistically significant

Table-4: Correlation of TSH with lung function parameters

			FEV1	FVC	FEV1/FVC
TSH	Cases	r	0.13	0.29	-0.17
		p	0.49	0.19	0.42
	Control	r	0.12	0.12	-0.09
		p	0.53	0.51	0.73

r = Correlation coefficient, p<0.05 considered statistically significant

Furthermore, observed that there was no significant correlation between TSH or FT4 with FVC, FEV1, and FEV1/FVC as seen in (Table 3 and 4).

DISCUSSION

In this study in subjects, lower levels of FT3 and FT4 were significantly associated with increased visceral fat deposition, independent of age. Moreover, FT3 and FT4 level was inversely correlated with BMI.

Thyroid hormones regulate the basal metabolic rate of all cells, thereby modulating all metabolic process in the body. Changes in thyroid status can alter metabolic processes and lead to metabolic syndrome, comprising abdominal obesity, dyslipidemia, hypertension, and glucose intolerance. Thus, efforts have been made to demonstrate the association between thyroid status and metabolic syndrome. Metabolic syndrome is cluster of several cardiovascular risk factors; thus, it is an important problem because it poses a serious risk of cardiovascular diseases [8].

The association of thyroid disease with atherosclerotic cardiovascular disease may in part be explained by thyroid hormones regulation of lipid metabolism and its influence on systemic vascular resistance, diastolic and systolic function, and blood pressure. [9] However, the impact of various degrees of thyroid dysfunction on these factors continues to be debated.

The association of cardiovascular diseases with overt hypothyroidism is undoubted, but there is controversy as to whether a similar association exists with subclinical hypothyroidism. However, many recent studies have shown that subclinical hypothyroidism was also associated with an increased risk of coronary heart disease, and low FT4 levels in subjects were a risk factor for carotid atherosclerosis [10]. Previous study reported that increased visceral fat volume was an independent risk factor for coronary artery disease (CAD), possibly because it aggravated vessel wall inflammation [11]. On the basis of these findings, can postulate that a low level of FT3 or FT4 play a role in pericardial fat deposition and aggravates vessel wall inflammation and atherosclerosis. In this study result is also consistent with previous reports addressing the concept that low FT3 levels were associated with the presence and severity of CAD in the subjects [12].

Interestingly, in this study, FT3 and FT4 levels were inversely correlated with BMI or waist circumference, which are common parameters for obesity. Overt hypothyroidism is associated with weight gain and adiposity, with weight gain commonly occurring after treatment of Graves' disease. Indeed, a great deal of research has been conducted to elucidate

the association between thyroid function and BMI. However, data conflict with regard to whether mild hypothyroidism, subclinical hypothyroidism, or both are associated with obesity [13]. Although the studies showing positive relationships mostly involved morbidly obese subjects [14]. In this study a significant relationship between thyroid function and visceral fat accumulation in no obese, thyroid persons, in spite of a relatively small sample.

In this study, significant association between thyroid hormone levels and abdominal visceral fat, which is also considered a metabolic organ. The design of present study was cross-sectional, and hence, cannot explain exactly why thyroid hormone levels were associated with visceral fat volume area. However, FT4 level was inversely correlated with abdominal visceral fat area. Therefore, abdominal visceral fat area could have an association with thyroid hormone similar to that of pericardial fat volume. One of the main reasons for more significant results with pericardial fat is that able to measure pericardial fat volume more exactly than abdominal visceral fat volume.

In this study no association between serum TSH level and body fat distribution. This result suggests that FT3 or FT4, rather than TSH, plays a more sensitive role in controlling metabolic parameters. This is in accordance with the reports that FT4, but not TSH, was related to plasma Low-density lipoprotein cholesterol (LDL-C), High-density lipoprotein (HDL) and Homeostatic model assessment insulin resistance (HOMA-IR) [15].

The limitations of the study are small sample size and cross-sectional design. Cannot determine whether this association is a cause-and-effect relation-ship. Further longitudinal studies are needed to solve this problem. In addition, measured thyroid hormone levels only once. All the participants in this study were visiting our hospital for routine health screening and had no acute health problems. Therefore, even though transient thyroid hormonal change cannot be completely ruled out, there were likely very few cases of persistent thyroid dysfunction.

CONCLUSION

FT3 level and FT4 level was each significantly associated with fat volume and BMI. Thyroid hormone levels can affect cardiovascular risk through regulation of pericardial fat deposition, in addition to other known mechanisms. In hypothyroidism, there is significant reduction in the dynamic lung functions as compared with controls.

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