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Title: Pulmonary function tests in patients with hypothyroidism: A Prospective study

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Abstract:

Background: Body adiposity, especially ectopic fat accumulation, has a range of metabolic and cardiovascular effects. This study aimed to investigate whether thyroid function is associated with various regional fat quantities in euthyroid subjects. **Material and Method:** This is a cross sectional study conducted on 90 patients divided into 2 groups (a) newly detected hypothyroids (b) normal control group. Cases were matched with controls in having similar environment exposure and age group. All patients had routine symptom and clinical assessment. Laboratory investigations such as complete blood picture, pulmonary function test, chest x ray and thyroid function test were done. Data was entered and analyzed. **Results:** In this study author observed a significant decrease in FEV1 and FEV1/FVC ratio in hypothyroids. FVC between cases and controls did not show statistical significance, although the mean FVC was found to be lower in cases (1.44) as compared to controls (1.79). The various respiratory patterns seen in cases were as follows: obstructive pattern (32%), followed by mixed pattern and restrictive pattern (28%, 22% respectively). Furthermore, we observed that there was no significant correlation between TSH or fT4 with FVC, FEV1, and FEV1/FVC. **Conclusion:** This study shows that hypothyroidism causes significant decrease in FEV1 and FEV1/FVC ratio, thereby suggesting obstructive patterns of lung involvement. Therefore, PFT can be used routinely as a screening test for all hypothyroid patients to detect early respiratory dysfunction and thereby optimize treatment especially in obese patients and patients with pre-existing lung disease as hypothyroidism adds to their respiratory dysfunction.

Keywords:

Hypothyroid, Obstructive pattern, pulmonary function test, Restrictive pattern, Hypothyroidism, TSH, Visceral fat, Obesity, Anemia.

Introduction

Thyroid hormone regulates basal metabolic rate, energy expenditure, and body weight. Overt hypothyroidism is associated with weight gain and increased adiposity, which could be one of the reasons for the increased cardiovascular risk observed in hypothyroid patients along with hyperlipidemia, hypercoagulability, and systolic and diastolic hypertension, which are features of hypothyroidism (1, 2). Not only overt thyroid dysfunction but also subtle variation of thyroid function within the normal range has been reported to be associated with the presence and severity of coronary artery disease (CAD) [(3, 4, and 5)].

Obesity is an important cause of insulin resistance (IR) and is also associated with cardiovascular morbidity and mortality. However, the level of cardio- vascular risk may vary between different cases of obesity, with body fat distribution constituting an important

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risk factor. Ectopic fat accumulated as non- subcutaneous adipose tissue has a significant association with IR, which, depending on the location of ectopic fat depots, leads to a range of metabolic and cardiovascular effects [6]. Among various regional fat depots, accumulated pericardial fat was previously reported to be associated with coronary artery calcium and coronary heart disease, possibly because it aggravates vessel wall inflammation [7, 8, 9]. These findings indicate that a milder variation in thyroid hormone levels, within the normal range, may play a role in pericardial fat deposition and aggravate coronary atherosclerosis. However, there are no reports investigating the effects of thyroid function on body fat distribution, and little is known as to whether thyroid function is associated with body adiposity in euthyroid subjects.

Methods

This study was a case control study conducted in the Department of Physiology at Tertiary care teaching Hospital. The study was approved by institutional ethical committee and written informed consent was taken from all patients who were included in the study. A total of 90 patients with age between 18 to 60 years were included in the study. The study included 2 groups, group 1 consisted of 45 newly detected hypothyroids and group 2 with 45 controls who were age, sex matched and from similar environment as that of cases. Group 1 hypothyroid patients include both clinical (TSH>5 milliunits/L with clinical features of hypothyroidism or low fT4) and subclinical hypothyroidism (TSH>5 with no clinical features of hypothyroidism or normal fT4).

Patients already on thyroxine therapy, BMI>23 kg/m2, 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 vital graph, a software that is installed in a computer in the department of Physiology.

All patients were asked to rest for 10 to 15 mins in a private quiet room, and they were briefed about the technique. 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
- Patients giving informed consent
- 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

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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 analyzed 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.

Result

Demonstrates no significant difference in age, BMI in cases and controls. TSH was significantly higher while fT4 was significantly lower in cases compared to controls (Table 1). In this study author observed a significant decrease in FEV1 and FEV1/FVC ratio in hypothyroids as shown in (Table 2). FVC between cases and controls did not show statistical significance, although the mean FVC was found to be lower in cases (1.44) as compared to controls (1.79).

The various respiratory patterns seen in cases were as follows: obstructive pattern (32%), followed by mixed pattern and restrictive pattern (28%, 22% respectively).

Furthermore, we observed that there was no significant correlation between TSH or fT4 with FVC, FEV1, and FEV1/FVC as seen in (Table 3 and 4).

Table 1: Baseline characteristics of cases and controls.

	Cases		Controls		
Variable	**Mean**	**Std Deviation**	**Mean**	**Std Deviation**	**P Value**
Age	30.23	7.534	30.54	6.457	0.08
BMI	15.98	1.59	15.46	1.00	0.31
Hemoglobin	9.46	1.21	9.37	0.59	0.35
TSH	30.38	14.38	2.34	0.43	0.00
fT4	0.58	0.14	1.01	0.18	<0.0001

Table 2: Pulmonary function tests parameters.

	Cases		Controls		
Variable	**Mean**	**Std Deviation**	**Mean**	**Std Deviation**	**P Value**
FVC (L)	1.44	0.513	1.79	0.400	0.113
FEV1	1.12	0.29	1.46	0.28	0.00
EFV1/FVC	60.34	13.64	70.56	9.37	0.00

Table 3: Correlation of FT4 with lung function parameters.

		FEV1	**FVC**	**FEV1/FVC**
Ft4	r	-0.10	-0.10	-0.01
	p	0.10	0.04	0.41

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	0.05	0.10	-0.07
		p	0.16	0.08	0.18
	Controls	r	0.04	0.05	-0.03
		p	0.24	0.23	0.33

r = Correlation coefficient, p<0.05 considered statistically significant

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Discussion

Joseph G, Hollowell. Et al, calculated mean concentrations of TgAb, TPOAb, T4 and TSH levels in 16,533 subjects with normal thyroid function were included. [11] Subjects are selected from the disease-free population. Subjects with history of hyperthyroidism, hypothyroidism, pregnant females and taking androgen pills were excluded in this study. The influence of demographics on TSH, T4, and antibodies were examined. TSH and the prevalence of ant thyroid antibodies are greater in females, increase with age, and are greater in whites and Mexican Americans than in blacks. [12] TgAb alone in the absence of TPOAb is not significantly associated with thyroid disease. The lower prevalence of thyroid antibodies and lower TSH concentrations in blacks need more research to relate these findings to clinical status. [13] A large proportion of the U.S. population unknowingly have laboratory evidence of thyroid disease, which supports the usefulness of screening for early detection. [14] Elizabeth H.H, randomly selected 9371 inhabitants of the eastern part of the Netherlands, received a postal questionnaire on lifestyle and medical history, of which serum TSH, FT4 and TPOAbs are measured from 6434 responders. 5167 individuals were selected by excluding those at risk for thyroid disease. [15]

Overt thyrotoxicosis (0.4%), subclinical thyrotoxicosis (0.8%), overt hypothyroidism (0.4%) and subclinical hypothyroidism in 4.0% was found in total population. The present study stated that serum FT4 concentrations increased due to the development of thyroid autonomy after long standing borderline sufficient iodine intake and mean TSH decreased with age. In total population, 8.6% of males and 18.5% of females had positive TPOAbs. The presence of TPOAbs was associated with abnormally high and low TSH concentrations. Umesh Kapil, conducted a cross sectional study for, assessment of IDD by following WHOUNICEF-ICCIDD guidelines. [16]

A total of 30 clusters were selected and in each, one primary school was selected using random sampling. A total of 6911 school children's in the age group of 8-10 years were included. The total goiter prevalence rate was 8.6% and the median urinary iodine excretion was 17 mcg /dl. Salt with nil iodine content was consumed only by 1.4% of the beneficiaries. 41% of families consumed salt with an iodine content of less than 15 ppm. This study represents that there is a need of strengthening the existing monitoring system for the quality of iodised salt. [17]

Ambika Gopalakrishnan et al, the cross sectional study was carried out in 8 cities to study the prevalence of hypothyroidism. About five thousand three hundred seventy six (5376) subjects adult non pregnant women or adult men participants (≥18 years), of which 5360 (mean age: 46±14.68 years; 53.70% females) were evaluated. The overall prevalence of hypothyroidism was 10.95% (n=587) of which 7.48% (n=401) patients self reported the condition, whereas 3.47% (n=86) were previously undetected. [18] Inland cities showed a higher prevalence of hypothyroidism as compared to coastal cities. A significantly higher (P<0.05) proportion of females vs. males (15.86% vs 5.02%) and older vs. younger (13.11% vs 7.53%), adults were diagnosed with hypothyroidism. Additionally, 8.02% (n=430) patients were diagnosed to have subclinical hypothyroidism. Antiab TPO were detected in 21.85% (n=171) patients. [19]

This study shows that the prevalence of hypothyroidism was high, affecting approximately one in 10 adults in the study population. Female gender and older age were found to have significant association with hypothyroidism. Subclinical hypothyroidism and anti-TPO antibody positivity were the other common observations. [20] Nils Knudsen, Peter Laurberg et al conducted a cross-sectional population study to investigate the association between thyroid function and BMI or

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obesity in a normal population. Results showed a positive association between BMI and category of serum TSH and a negative association between BMI and category of serum free T4. No association was found between BMI and serum free T3 levels. The difference in BMI between the groups with the highest and lowest serum TSH levels was 1.9 kg/m2, corresponding to a difference in body weight of 5.5 kg among women. [21] Similarly, the category of serum TSH correlated positively with weight gain during 5 yr (P=0.04), but no statistically significant association was found with weight gain during 6 months (P = 0.17). There was an association between obesity (BMI > 30 kg/m2) and serum TSH levels (P = 0.001). [22]

The study stated that thyroid function could be one of several factors acting in concert to determine body weight in a population. Even slightly elevated serum TSH levels are associated with an increase in the occurrence of obesity. [23] Nathalie. V, Laurence. M, et al, investigated the effects of T3 on gene expression in human adipocytes, primary cultures of human sc adipose tissue explants after treating with T3. 32P-labeled cDNA probes prepared from isolated adipocyte total RNA were hybridized to cDNA arrays representing 1,176 genes. [24] Among the statistically significant variations in mRNA levels with more than 1.3-fold difference, 13 and 6 genes were positively and negatively regulated, respectively (n= 3). The genes encoded proteins that were involved in signal transduction, lipid metabolism, apoptosis, and inflammatory response. Using RT competitive PCR, showed a down-regulation of phosphodiesterase 3B, α 2A-adrenergic receptor, and G protein αi2 subunit mRNAs, and an up-regulation of α2 – adrenergic receptor mRNA. [25] These regulations explain the T3-mediated increase in catecholamine-induced lipolysis. The down-regulation of sterol regulatory element binding protein-1c, a transcription factor controlling lipogenic gene expression, may constitute a link between thyrotoxicosis and insulin resistance. Thus, these data suggest that T3 modulates expression of genes with a wide range of function in human adipose tissue. [26]

Conclusion

Hypothyroidism there is significant reduction in the dynamic lung functions as compared with controls. Therefore, respiratory system can be affected in hypothyroidism and a simple spirometry can be considered for the evaluation of pulmonary function in these patients.

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