RESEARCH ARTICLE

Pulmonary function tests in subclinical hypothyroidism-a comparative cross-sectional study

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) reflects the earliest stage of thyroid dysfunction with subjects having normal free thyroid hormones T3, T4 with elevated Thyroid-stimulating hormone (TSH) values. Hypothyroidism may depress the central ventilator control and affects respiratory muscle strength which is linearly related to the thyroid hormone levels. In hypothyroidism, the impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism. Aim and Objectives: The present study was designed to derive Forced Vital capacity (FVC), Forced expiratory volume in 1 second (FEV1), FEV1/FVC, Peak expiratory flow rate and FEF 25–75 % in subclinical hypothyroid subjects and to compare the values with that of healthy controls. Materials and Methods: A cross-sectional comparative study was conducted in subjects aged between 25 and 60 years in which 85 subclinical hypothyroid cases were selected after proper exclusion and informed consent. 85 age and sex matched healthy controls were also studied. Statistical package for social sciences version 18 was used for statistical analysis. Results: All spirometric variables were found to be lower in subclinical hypothyroid subjects than in healthy controls and the abnormalities were of mixed pattern-both obstructive and restrictive. All values obtained were statistically significant (P < 0.05). Conclusion: Patients with SCH should be regularly screened with pulmonary function tests as respiratory derangement starts even at this stage. This will help for early diagnosis and treatment, and to prevent future complications.

KEY WORDS: FVC, FEV1, FEV1/FVC, FEF, PEFR, SCH, Subclinical Hypothyroidism, PFT

INTRODUCTION

Hypothyroidism is common among the various metabolic and endocrine disorders, in the world. It is due to insufficient secretion of thyroid hormone from thyroid gland due to some structural and/or functional impairment of thyroid hormone production. All organ systems are affected by hypothyroidism and the clinical findings include weakness, fatigue, cold intolerance, hair loss, and lack of concentration and memory.

The earliest stage of thyroid dysfunction with subjects having normal free thyroid hormones T3, T4 with elevated thyroid-stimulating hormone (TSH) values is Subclinical hypothyroidism (SCH). It indicates minor thyroidal decompensation with a compensatory increase in TSH secretion. Even though SCH is considered as an asymptomatic condition nearly 30% of patients have symptoms of thyroid hormone deficiency. Studies have shown that the prevalence of SCH was higher in elderly populations. SCH poses an enormous burden in India as the prevalence rates of SCH in India exceed those in the developed nations. The prevalence of SCH in United States is 4–8.5% while different prevalence rates from Indian studies have been reported as 11.3% with...
All body systems and organs including respiratory system are affected by hypothyroidism. It can cause respiratory function disorders and ventilatory disturbances. Hypothyroidism may depress the central ventilator control and affects the strength of respiratory muscles which is linearly related to the thyroid hormone levels. In hypothyroidism, both inspiratory and expiratory muscles weakness is present. Both affects pulmonary functions accordingly, the impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism.

The disease involvement can range from mild dyspnea to severe and life threatening respiratory failure. Restrictive pattern of impairment in lungs have shown in studies. Inspiratory and expiratory muscle weakness, alveolar hypoventilation due to depression of hypoxic and hypercapnic ventilatory drives and decrease in maximal breathing capacity are evident in patients with hypothyroidism. Few studies suggested that decreased inspiratory muscle strength, hypventilation, hypercapnia are the cause for reduced respiratory function and it is related to the degree and duration of the thyroid disorders. Many hypothyroid patients complaints of fatigue and exercise intolerance and it is due to decreased muscle strength and limited pulmonary and cardiac reserve.

Patients with SCH have been evaluated particularly for inspiratory and expiratory muscles as it may lead to the development of myopathy. Diaphragm is the major inspiratory muscles that is involved. This weakness can be very severe and associated with hypventilation and hypercapnia. Hence, in patients with sub clinical hypothyroidism assessment of pulmonary function with spirometry is important.

Pulmonary function tests are noninvasive tests that show how well the lungs are working. The tests measure lung volume, capacity, rates of flow, and gas exchange. The most useful pulmonary function test is spirometry which measures the volume of air exhaled at specific points of time during a forceful and complete exhalation after a maximum inhalation. The maximal volume of air exhaled with maximally forced effort from a maximal inspiration is the Forced vital capacity (FVC). The maximal volume of air exhaled in the first second of a forced expiration from a position of full inspiration is Forced Expiratory volume in 1 second (FEV1), and their ratios (FEV1/FVC) are the most important variables reported. Other parameters are, Mean expiratory flow rate during middle 50% of FVC (FEF 25–75%), and Peak expiratory flow rate (PEFR).

Some studies show that impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism.

To the best of our knowledge, no such studies have been conducted in this population. Hence, this study was aimed to assess the pulmonary function tests (FVC, FEV1, FEV1/FVC, FEF 25-75%, and PEFR) in subclinical hypothyroid subjects to find out impaired lung function if any.

**MATERIALS AND METHODS**

The present study was a comparative cross-sectional study done at Department of Physiology, Government Medical College, Kozhikode, after getting Institutional Ethics Committee clearance. The duration of study was 1 year. 85 patients with SCH in the age group 25–60 years were taken as cases and 85 age and sex matched subjects with normal thyroid profile were taken as controls. Prior informed consent and detailed history has been taken in the proforma. Relevant clinical examination was done. Pulmonary function tests (FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEFR) were assessed by spirometry.

**Inclusion Criteria**

SCH was considered in patients who may have elevated TSH levels and normal free T3, T4 levels.

**Group A (cases)**

Subclinical hypothyroid patients (normal free T3, T4 with elevated TSH levels) in the age group 25–60 years who attended Departments of General Medicine and Endocrinology Out Patient Departments during the study period were included in this group.

**Group B (controls)**

Subjects with normal thyroid profile in the same age group were taken as controls which include bystanders, medical and paramedical staffs and volunteers.

**Exclusion Criteria (Both Groups)**

- Subjects with history of smoking
- Patients with acute and chronic respiratory diseases
- Subjects with obesity, goiter, pregnancy
- Subjects with other inflammatory diseases
- Subjects on treatment for thyroid illness
- Subjects on infertility treatment.

**Blood Investigations**

Using standard methods and precautions Free T3, Free T4 and TSH were done.

**Spirometry**

The equipment used for spirometry in this study was Spiro excel spirometry system. The procedure was explained clearly to the subject and ensured that subject is sitting erect.
with feet firmly on the floor. FVC, FEV1, FEF 25–75%, PEFR and FEV1/FVC ratio were found out.

**Statistical Analysis**

The present study was a comparative cross-sectional study. Using Statistical Package for Social Sciences version 18 the data were analyzed. The mean and standard deviation of spirometric parameters were calculated and the results were expressed as Mean ± Standard deviation (Descriptive statistics) using the student’s “t” test the significance of the difference of mean of each parameter between the two groups were analyzed. A \( P \leq 0.05 \) was taken as the level of significance for all statistical tests. The results were summarized as figures and tables.

**RESULTS**

The present study was done in cross-sectional observational design involving 170 subjects. 85 patients with SCH of both sexes in the age group of 25–60 years and 85 controls with normal thyroid profile were included in the study group. Using spirometry, their pulmonary function tests (FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEFR) were assessed. Using SPSS version 18 statistical analysis was done. The results were summarized in Table 1.

All tested Spirometric parameters were found to be less in subjects with SCH comparing normal. All values were found to be statistically significant \( (P < 0.05) \).

**DISCUSSION**

Hypothyroidism can affect all organ systems and SCH can progress to overt hypothyroidism. At the subclinical state the impairment of respiratory functions may be initiated. The present study utilized simple and non-invasive spirometry method to evaluate respiratory parameters in the subjects of SCH. Spirometry is the most frequently performed lung function test. The two groups in this study were euthyroid and subclinical hypothyroid subjects. 91% of the cases in our study were females and only 9% were males. The spirometric parameters, forced vital capacity (FVC), forced expiratory volume in first second (FEV1), FEV1 as a percentage of FVC (FEV1%), forced mid expiratory flow rate (FEF 25–75%), and PEFR were studied in both between euthyroid and subclinical hypothyroid of 85 subjects. Examining the dynamic parameters of lung function, we found a significantly lower value of FVC between the euthyroid and subclinical hypothyroid group. All results obtained represented in Table 1.

The values of FVC obtained in the present study (2.51 ± 0.47 and 2.3 ± 0.45, respectively) were comparable with the study conducted by Siafkas et al. in 1990, done on subjects with comparable groups, where the mean FVC was 2.63 ± 0.51 in euthyroid and 2.37 ± 0.57 in subclinical hypothyroid subjects.\(^{[14]}\) In the present study, among euthyroid subjects, mean FEV1 was 2.12 ± 0.41 liters and 1.8 ± 0.49 liters in subclinical hypothyroid individuals with a significant \( P \) value (0.001). In the study by Siafkas et al., mean FEV1 was 2.34 ± 0.8 in euthyroid and was 2.12 ± 0.47 in subclinical hypothyroid subjects which again was comparable with the data we arrived at.\(^{[14]}\) In the present study, the mean FEV1/FVC ratio in euthyroid and subclinical hypothyroid subjects were 83.6 ± 4.38 and 78.2 ± 3.9, respectively. The \( P < 0.05 \). These values were comparable with the study done by Cakmak et al. in 1991, where the values were 85.87 ± 7.05 in euthyroid and 76.53 ± 6.17 in SCH.\(^{[10]}\) Again, the mean FEV1/FVC ratio was 88.5 ± 5.2 and 78.4 ± 5.5 in euthyroid and subclinical hypothyroid respectively in the study done by Siafkas et al. Mean forced mid expiratory flow (FEF 25-75%) in the euthyroid and subclinical hypothyroid subjects were 2.99 ± 0.86 liters/second and 2.21 ± 0.76 liters/second. This mean value in subclinical hypothyroid was comparable with a study done by Siafkas et al. where the value was 2.06 ± 0.28. However, the mean value in euthyroid was found to be 3.16. The values in study done by Cakmak et al. Is 3.00 ± 1.20 in euthyroid and 2.05 ± 0.60 in subclinical hypothyroid subjects. The mean value of PEFR in the euthyroid and subclinical hypothyroid in this study were 4.84 ± 1.16 liters/sec. and 3.83 ± 1.07 liters/sec. respectively. The \( p \) value was significant, (0.0001) This value was comparable with the mean PEFR done by Siafkas et al. where mean PEFR was 4.93 ± 1.88 in euthyroid and 3.25 ± 1.16 in subclinical hypothyroid subjects. In another study done by Cakmak et al. the mean PEFR was 3.92 ± 1.72 in euthyroid and 2.04 ± 1.67 in subclinical hypothyroid.

In the present study, subclinical hypothyroid patients showed a significant reduction in pulmonary function tests (FVC, FEV1, PEFR, FEF 25–75% and their predictive values) indicating that pulmonary functions may get affected in SCH. The decreased PEFR values in current study can suggest early deterioration of ventilatory functions. In the present study, decreased values of FVC suggest a restrictive pattern and decreased values of FEV1 and FEF 25–75% suggest an obstructive pattern. Thus, deterioration of pulmonary function tests in the study points to a mixed pattern of

<table>
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<th>Table 1: Mean of spirometric parameters</th>
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<td><strong>Variables</strong></td>
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SD: Standard deviation, FVC: Forced Vital capacity, FEV1: Forced expiratory volume in 1 second, PEFR: Peak expiratory flow rate
respiratory disorder. Present results are consistent with results of Cakmak et al.,[8] who also observed a significant reduction in FVC, FVC%, FEV1, FEV1%, PEFR, PEFR%, FEF25-75, FEF25-75% in patients with SCH.

Our results in hypothyroid subjects are consistent with the results of Martinez et al.[15] Moreover, Ladenson et al.[16] who also confirmed that the hypothyroidism is associated with decreased vital capacity, FEV1, FVC and total lung capacity. The authors suggested that the inspiratory muscle weakness, alveolar hypoventilation might be a possible explanation. Martinez et al.[15] have confirmed that hypothyroid patients develop diaphragmal dysfunction, which can vary from mild forms associated with reduced tolerance to physical effort, to very severe forms of diaphragmatic weakness. The authors of the study showed, with, Levothyroxine therapy these changes are reversible.

Ladenson et al.[16] found better pulmonary functions in treated patients of hypothyroidism as compared to untreated newly diagnosed patients. The possible advantages of treating SCH are described by Kek et al.[2] as preventing its progression to overt hypothyroidism; decrease cardiovascular risk and therapy may reverse symptoms of mild hypothyroidism.

The study done by Swami et al.[17] found decreased pulmonary functions in hypothyroid patients who were already on thyroid hormone therapy and on doing pranayama for 6 months these patients showed significant improvement in FEV1, Maximum Voluntary Ventilation and Inspiratory Capacity and suggested that this beneficial effect of yoga could be due to respiratory muscle strength improvement and increased oxygen concentration at tissue level by increased air entry. Birring et al.[18] Noted that in subclinical hypothyroid patients there is a significant reduction in lung function. The authors evaluated lung function parameters in subclinical hypothyroid patients and in the healthy group of controls and found significantly lower values of FVC, FVC%, FEV1 and FEF 25–75 in patients with SCH.

The significant reduction in PFT values, found in subclinical hypothyroid patients in the present study, may be due to weakness of respiratory muscles and defective ventilatory drive. SCH is very common, thus all systems including the respiratory system should be clinically evaluated thoroughly. It is also recommended that the populations at higher risk for developing the overt disease (females, older persons and individuals positive for anti-thyroid peroxidase antibodies) should be regularly screened for thyroid function tests and pulmonary function tests as the early diagnosis and treatment can prevent future complications.

**CONCLUSION**

In the present study, the spirometric parameters of subclinical hypothyroid subjects were compared to that of euthyroid individuals. The study group included 170 subjects, of which 85 were Euthyroid and 85 were subclinical hypothyroid individuals in the age group of 25 and 60 years belonging to both sexes. The spirometric parameters were studied and compared between both the groups. Significantly lower spirometric parameters were found in subclinical hypothyroid patients. Interpretation of the pulmonary function tests shows mixed pattern of involvement. It may be attributed to the weakness of inspiratory and expiratory muscles in SCH.

Depending on the duration, cause and the degree of deficiency of thyroid hormone, the clinical presentation of thyroid hormone deficiency alters from person to person. In patients with SCH the decrease in both inspiratory and expiratory muscle strength, alveolar hypoventilation due to depression of hypoxic and hypercapnic ventilatory drives and decrease in maximal breathing and diffusing capacity are evident.

The result of the present study shows that respiratory derangement starts even at subclinical state of hypothyroidism. Hence, subclinical hypothyroid patients should be regularly screened with pulmonary function tests for early diagnosis and treatment, and to prevent future complications.

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