

# Does thyroid replacement therapy affect pulmonary function tests in patients with subclinical hypothyroidism?

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## ABSTRACT

**Objective:** Subclinical hypothyroidism is an elevation in serum thyroid-stimulating hormone (TSH) while having normal serum free thyroxine (FT4) and triiodothyronine (FT3) levels. The purpose of this prospective observational study was to evaluate the pulmonary function of patients diagnosed with subclinical hypothyroidism, both before and after treatment with thyroid hormone.

**Methods:** This study took place at the Medical Faculty, Celal Bayar University, Manisa, Turkey between February 2003 and June 2004. Thirty-eight patients (37 females, one male) with subclinical hypothyroidism between 20 and 65 years of age were included in the study. Most were mildly obese. Arterial blood gases and pulmonary function tests were performed before treatment with thyroid hormone, and afterwards, the TSH value reached the normal range (indicating euthyroidism).

**Results:** Oxygen saturation, but not partial oxygen pressure or partial carbon dioxide pressure, was statistically, but not clinically significantly higher after treatment with thyroid hormone ( $p=0.01$ ). Pulmonary function tests were not significantly different before and after treatment with thyroid hormone.

**Conclusion:** In our subclinical hypothyroidism patients, pulmonary function tests were normal and did not significantly change with thyroid hormone replacement. The advantages of thyroid hormone replacement therapy, at least regarding respiratory function, seem to be clearly present in patients with overt, clinical hypothyroidism but not in patients with subclinical hypothyroidism.

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Subclinical hypothyroidism is characterized by either no symptoms or minimal symptoms of hypothyroidism with a normal serum free thyroxine (FT4) and triiodothyronine (FT3) levels along with an elevated serum thyrotropin (TSH) concentration.<sup>1-5</sup> Researchers have found a decrease in pulmonary function tests (forced expiratory volume in one second [FEV1] and forced vital capacity [FVC]), a decrease in diffusing capacity for carbon monoxide,

and an increased incidence of pleural effusions in patients with overt hypothyroidism before undergoing appropriate treatment.<sup>6-10</sup> However, changes in the respiratory system have yet to be described in patients with subclinical hypothyroidism. For this reason, we evaluated the pulmonary function of patients diagnosed with subclinical hypothyroidism, both before and after treatment with thyroid hormone.

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**Methods.** Our institutional review board granted permission to enroll patients for this prospective observational study. Patients with subclinical hypothyroidism (elevated TSH with normal FT4 and FT3 levels), between the ages of 20 and 65, evaluated in the Endocrinology Clinic of our Tertiary University Medical Center, Turkey between February 2003 and June 2004 were considered eligible for inclusion into the study. Subclinical hypothyroidism was determined to be present if, on 2 separate laboratory evaluations within a week, the TSH level was increased (normal range: 0.27-4.2  $\mu$ IU/mL), while both the FT3 and FT4 levels were within normal limits (1.8-4.6 pg/mL, and 0.9-1.7 ng/dL). After an appropriate informed consent, patients were asked and examined about general health status, signs and symptoms of thyroid disease. Patients with a positive bronchial provocation (BPT)(examined in patients with an FEV1 of >80%) or positive reversibility testing (RT)(examined in patients with an FEV1 of <80%), or with known lung disease or those with smoking history of >10 years were excluded from the study.

Serum samples were obtained after an overnight fast, both in the pre-therapy phase and in the post-thyroid hormone replacement phase. Hormone levels (TSH, FT3, and FT4) were measured by chemiluminescence assay on an Immulite One® analyzer (IMMULITE, Diagnostic Products Co., Los Angeles, CA, USA). An immunoassay was also used (using the same analyzer equipment) to quantify serum autoantibodies against thyroglobulin (anti-T) and autoantibodies against thyroid peroxidase (anti-M). Arterial blood gases (ABG) were obtained for determination of partial oxygen pressure (PO<sub>2</sub>), partial carbon dioxide pressure (PCO<sub>2</sub>), oxygen saturation (SaO<sub>2</sub>), pH and bicarbonate levels. Chest x-ray and thyroid ultrasonography were also performed in all

patients. Pulmonary function tests were performed with a Jaeger Master Screen Pneumo® device (Jaeger Co., Hoechberg, Germany). Thirty-eight patients with negative BPT or RT results were given a thyroid hormone as L-thyroxine (dosage ranged from 50-100  $\mu$ g/day), and patients were followed for effectiveness of treatment by measuring a TSH level every month. After the TSH value reached a normal range (indicating euthyroidism), pulmonary function tests were repeated.

The study data were evaluated in SPSS for Windows® version 10.0 (SPSS Inc., Seattle, USA) using descriptive and paired t-test methods. All means were reported as mean±standard deviation (SD). The  $p < 0.05$  was considered statistically significant.

**Results.** Thirty-eight patients (37 females, one male) with subclinical hypothyroidism were included in the study. The mean age was 42.84±9.49 years (range 23-65 years). On detailed history examination, our patients had the following symptoms: fatigue (31%), menstrual irregularity (10.5%), hoarseness, obstructive sense of throat, palpitation, weight gain (7.8%), nervousness (5.2%), alopecia, diaphoresis, menorrhagia, dyspnea, and hand swelling (2.6%). Clinical and laboratory findings before and after thyroid hormone replacement therapy are shown in **Table 1**. The weight ( $p=0.83$ ) and BMI ( $p=0.19$ ) of patients before and after treatment was not significantly different ( $p=0.3$  and  $p=0.4$ ) (**Table 1**). Thyroid function laboratory parameters (TSH, FT3, FT4) changed significantly with treatment (**Table 1**). Euthyroid states within patients were attained 35 to 138 days after the thyroid hormone replacement therapy was begun. Oxygen saturation, but not PaO<sub>2</sub> or PaCO<sub>2</sub>, was significantly higher after treatment with thyroid hormone (**Table 2**). Pulmonary function

**Table 1** - Clinical and laboratory findings before and after thyroid hormone replacement therapy

Parameters	Before treatment	After treatment	p value
Weight (kg)	75.96 ± 13.22	75.78 ± 12.95	0.83
BMI (kg/m <sup>2</sup> )	29.58 ± 4.96	29.20 ± 4.82	0.19
FT3 (NV:1.8-4.6 pg/mL)	2.86 ± 0.46	3.13 ± 0.58	0.02
FT4 (NV:0.9-1.7 ng/mL)	1.03 ± 0.20	1.36 ± 0.26	0.00
TSH(NV:0.27-4.2 $\mu$ IU/mL)	13.34 ± 5.79	2.25 ± 1.38	0.00
Anti T (NV:0-115 IU/mL)	190.52 ± 312.84	176.69 ± 190.38	0.64
Anti M (NV:0-34 IU/mL)	147.78 ± 186.62	171.15 ± 284.50	0.58

BMI - body mass index, NV - normal value, FT4 - free thyroxine, FT3 - triiodothyronine, TSH - thyrotropin, Anti-T - autoantibodies against thyroglobulin, Anti-M - autoantibodies against thyroid peroxidase

**Table 2** - Arterial blood gases results before and after thyroid hormone replacement therapy.

Parameters	Before treatment	After treatment	P value
Partial oxygen pressure (mm Hg)	97.58 ± 22.29	96.04 ± 17.42	0.64
Partial carbon dioxide pressure (mm Hg)	35.16 ± 9.65	35.31 ± 9.79	0.84
Oxygen saturation (%)	97.21 ± 1.73	97.82 ± 1	0.01

SaO<sub>2</sub> - Oxygen saturation, PaO<sub>2</sub> - partial oxygen pressure, PaCO<sub>2</sub> - partial carbon dioxide pressure

**Table 3** - Pulmonary function results before and after treatment with thyroid hormone replacement therapy.

Parameters	Before treatment	After treatment	P value
Forced vital capacity (%)	103.04 ± 9.49	105.22 ± 13.15	0.08
Forced expiratory volume in one second (%)	101.76 ± 10.44	102.86 ± 10.78	0.36
FEV <sub>1</sub> /FVC (%)	104.39 ± 7.67	103.60 ± 6.69	0.53

FEV<sub>1</sub>/FVC - the ratio of forced expiratory volume in one second to forced vital capacity,  
% - percent of the predicted value in relation to the expected value

tests were not significantly different in our patients with subclinical hypothyroidism before and after treatment with thyroid hormone (Table 3).

**Discussion.** The term “subclinical hypothyroidism” was first used in the early 1970’s when the ability to measure serum thyrotropin (thyroid-stimulating hormone) was achieved. The term is currently used for patients with minimal or no symptoms of hypothyroidism who has a normal serum free T<sub>4</sub> and T<sub>3</sub> and elevated serum TSH concentrations.<sup>1-5</sup> Almost all our patients were female, as the predilection for subclinical hypothyroidism to occur in females is well-recognized.<sup>11</sup> Thyroid function tests responded to thyroid hormone therapy in expected fashion in our study population. While all arterial blood gases results in our patients were within normal range both before and after thyroxine treatment, the SaO<sub>2</sub> parameter was the only one to have changed significantly, by statistical methods. We feel that this small change, from 97.2-97.8%, to not be clinically significant; however, similar to Cooper et al study on subclinical hypothyroid patients, we found no change in weight or BMI with thyroid hormone treatment.<sup>12</sup> Previous studies of respiratory function in hypothyroid patients have all been performed in patient’s populations with overt clinical findings,

including myxedema. The decline in respiratory function in these patients may be carried out more to obesity than hormonal effects on the lungs.<sup>6</sup> Frequently reported findings include decreased vital capacity, FEV<sub>1</sub>, FVC, and total lung capacity, which some authors have explained as occurring through alveolar hypoventilation and inspiratory muscle power weakness.<sup>13-16</sup> Our subclinical hypothyroid patients had no abnormal pre-treatment values in FEV<sub>1</sub>, FVC, or FEV<sub>1</sub>/FVC; and these normal levels did not change significantly after they became euthyroid. No other studies exist against which these findings can be compared.

In our mildly obese subclinical hypothyroidism patients, pulmonary function tests were normal and did not significantly change with thyroid hormone replacement. The advantages of thyroid hormone replacement therapy, at least regarding respiratory function, seem to be clearly present in patients with overt, clinical hypothyroidism but not in patients with subclinical hypothyroidism.

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