

## Original article

# Study of Pulmonary Function tests in patients of primary hypothyroidism

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### Abstract:

Whilst respiratory manifestations are seldom the major complaints in hypothyroidism, respiratory system like other body systems and organs is affected by hypothyroidism. Assessment of pulmonary function with spirometry in patients with thyroid disorders are particularly important to demonstrate whether any impairment in lung function parameters exists in hypothyroidism.

A cross-sectional single centered study in a tertiary care centre comprising 55 hypothyroid and 55 age & sex matched controls. All patients underwent general examinations, anthropometric, spirometric and thyroid function tests using standard procedures. Spirometric parameters recorded for analysis included Forced vital capacity (FVC), Forced expiratory volume in 1<sup>st</sup> second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEFR), Forced expiratory flow 25%-75% (FEF<sub>25%-75%</sub>).

**Keywords:** Hypothyroidism, Pulmonary Function tests, Alveolar hypoventilation

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### Introduction:

Hypothyroidism is a relatively common disease worldwide. It is defined as a clinical state resulting from insufficient secretion of thyroid hormone from thyroid gland due to some structural and/or functional impairment of thyroid hormone production<sup>1,2</sup>. Hypothyroidism affects all organ systems and the clinical findings include fatigue, dryness of skin, cold intolerance, weight gain without loss of appetite, constipation, swelling of extremities, dyspnea, and hoarseness of voice, menorrhagia, hair loss, bradycardia and multiple neurological symptoms<sup>2</sup>. Respiratory system like other body systems and organs is affected by hypothyroidism though respiratory manifestations are seldom the major complaints in hypothyroidism<sup>3</sup>. The spectrum of diseases involvement can range from mild dyspnea

to more severe and life threatening respiratory failure<sup>4,5</sup>. Lung volumes are usually normal but few studies have shown findings suggestive of restrictive pattern of impairment. This has been attributed to decrease in both expiratory and inspiratory muscle strength, alveolar hypoventilation due to depression of hypoxic and hypercapnic ventilatory drives and decrease in maximal breathing capacity and diffusion capacity in patients with hypothyroidism<sup>6,7,8</sup>. Difficulty in weaning hypothyroid patients from assisted ventilation is another associated complication<sup>9</sup>. Many patients with hypothyroidism complain of fatigue and exercise tolerance and these subjective sensations could arise from limited pulmonary reserve, limited cardiac reserve, decreased muscle strength or increased ease of muscle fatigue<sup>10</sup>. Dyspnea as a subjective sensation which is prevalent

in hypothyroidism, seems secondary to limited cardiac reserve<sup>11</sup>. So, assessment of pulmonary function with spirometry in patients with thyroid disorders are particularly important. Thereby, in the present study, pulmonary function tests were done on hypothyroid patients to show whether there was any impairment in lung function parameters.

#### **Material and methods:**

A cross-sectional study was done in the Department of Physiology, Medical College Kolkata with 55 hypothyroid patients in the age group 18- 65 years. They were recruited from the OPD of the Endocrinology Department of Medical College Kolkata. Fifty five age & sex matched controls were taken from among the staff of Medical College Kolkata. The hypothyroid patients included both clinical (TSH >10 with low fT4) and subclinical hypothyroidism (TSH >4.5 with normal fT4). Patients of BMI > 30Kg/m<sup>2</sup>, patients with h/o smoking & respiratory illness, patients on levothyroxine treatment were excluded from the study. The study was done after proper ethical clearance from the Institutional Ethics Committee. A written informed consent was taken from the patients. Proper occupational, medical & family history were taken. Besides general Examination, anthropometry, and spirometry were done. Thyroid function tests were done in one particular laboratory where TSH, fT4 were measured by Chemiluminescence. Pulmonary function tests were done by Spirotech®, a software installed in a desktop computer in the Department of Physiology, Medical College, Kolkata. After rest for 10-15 min & briefing the technique of FVC (maximum inhalation followed by maximum exhalation) was carried out in a private and quiet

room, in a sitting position with the nose clip held in position on the nose. An average of 3 readings was taken. Spirometric parameters recorded for analysis were: Forced vital capacity (FVC), Forced expiratory volume in 1<sup>st</sup> second (FEV1), FEV1/FVC, Peak expiratory flow rate (PEFR), Forced expiratory flow 25%-75% (FEF<sub>25%-75%</sub>).

#### **Statistical Methods:**

Data were tabulated in Microsoft Office Excel 2010, and statistical analysis was done by using SPSS for windows (version 20.0). The thyroid function tests and respiratory parameters were analyzed by paired t test and Pearson's correlation analysis (including correlation coefficient r and two-tailed P value) was performed to assess the relationship between TSH & respiratory parameters and fT<sub>4</sub> & 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 the weight between the two groups though weight was more in the cases while the height was significantly more in controls and BMI was significantly higher in the hypothyroids. TSH values were significantly higher in hypothyroids compared to euthyroids while FT<sub>4</sub> values were significantly lower in hypothyroids. In our study, we observed a highly significant decreased FVC and FEV1 in hypothyroids as shown in Table 2. Furthermore, we observed a significant negative correlation between TSH with FVC, FEV1 but significant positive correlation with FEF 25-75% and FEV1/FVC. Also fT<sub>4</sub> was found to have a significant positive correlation with FVC, FEV1 and FEV1/FVC.

**Table 1: Baseline Characteristics of the Study Population**

Variable	Case		Control		p
	Mean	Std. Dev.	Mean	Std. Dev.	
Weight (in Kg)	58.93	11.28	57.46	8.809	0.519
Height(in m)	1.54	0.07	1.6	0.08	0.001
BMI(Kg/m <sup>2</sup> )	24.96	5.198	22.42	2.363	0.003
Pulse(/min )	76.84	10.48	75.25	3.586	0.315
SBP(mm of Hg)	116	15.94	113.9	7.48	0.399
DBP(mm of Hg)	74.76	8.84	74.64	8.11	0.951
TSH(miU/L)	33.95	42.92	2.23	1.01	<0.0001
fT <sub>4</sub> (ng/dl)	0.77	0.26	1.03	0.35	<0.0001

*P<0.05 considered as statistically significant*

**Table 2: Pulmonary Function Tests**

Variable	Case		Control		p
	Mean	Std. Dev.	Mean	Std. Dev.	
FVC(L)	1.71	0.45	3.11	0.35	<0.001
FEV <sub>1</sub> (L)	1.55	0.40	2.45	0.31	<0.001
PEFR(L/sec)	3.56	1.10	3.80	0.82	0.32
FEF <sub>25-75%</sub>	94.20	5.35	80.80	6.50	<0.001
FEV1/FVC	0.90	0.05	0.75	0.04	<0.001

*P<0.05 considered as statistically significant*

**Table 3: Correlation of TSH & Ft4 with Lung Function Parameters**

		FVC	FEV1	PEFR	FEF 25-75%	FEV1/FVC
<b>TSH</b>	<b>r</b>	-0.426	-0.423	-0.138	0.182	0.232
	<b>p</b>	0.001	0.001	0.441	0.049	0.046
<b>Ft4</b>	<b>r</b>	0.356	0.353	0.086	0.217	0.219
	<b>p</b>	<.0001	<.0001	.212	0.100	<0.001

*r – Correlation coefficient, p <0.05 considered as statistically significant*

**Discussion:**

Hypothyroidism can cause disorders of respiratory function and disturbances of ventilation. It is characterized by hypoventilation and the ventilatory response to hypoxia and hypercapnia are reduced in hypothyroidism<sup>6,12</sup>. Many patients complain of

dyspnea, fatigue and exercise intolerance and all these might be due to limited pulmonary reserve<sup>10</sup>. Hypothyroidism may lead to the development of myopathy and has been evaluated particularly for the inspiratory and expiratory muscles<sup>7</sup>, diaphragm being one of the most important muscle. Supplementation

has shown to restore respiratory muscle function<sup>7</sup>. With this background in view, this study was undertaken to compare the Pulmonary Function Tests between diagnosed hypothyroid patients and age and sex matched euthyroids. Table 1 shows that there was no significant difference in the weight between the two groups though weight was more in the cases while the height was significantly more in controls and BMI was significantly higher in the hypothyroids. TSH values were significantly higher in hypothyroids compared to euthyroids while FT<sub>4</sub> values were significantly lower in hypothyroids.

In our study, we observed a highly significant decreased FVC and FEV<sub>1</sub> in hypothyroid patients as shown in Table 2. FVC is maximally rapid expiratory vital capacity and its decrease has definite implication in lung diseases while FEV<sub>1</sub> is the volume of air exhaled in 1<sup>st</sup> second and it is the most reproducible and most useful measurement of lung function<sup>13</sup>. This is in accordance with the study conducted by Valjevac *et al*<sup>14</sup> who suggested that the cause for reduced respiratory function are decreased inspiratory muscle strength, hypoventilation, hypercapnia and it is related to the degree and duration of the thyroid disorders. Cakmak *et al*<sup>15</sup> observed a significant reduction in FVC, FEV<sub>1</sub>, FEF<sub>25%-75%</sub> and DLco in patients with subclinical hypothyroidism as compared to control. Bassi *et al*<sup>16</sup> reported a significant decrease in the lung functions between those not taking any treatment and those on thyroid hormone replacement therapy and they attributed the cause to be respiratory muscle weakness and decreased contractile strength due to low serum T<sub>4</sub>. Martinez<sup>17</sup> *et al* have confirmed that patients with hypothyroidism develop diaphragmatic dysfunction, which can vary from mild forms associated with reduced tolerance to physical effort to

very severe forms of diaphragmatic weakness which might even imitate diaphragmatic paralysis which can be attributed to low serum FT<sub>4</sub> values. Low thyroid hormone levels also decrease lung elastic tissue and increased work of breathing.

In the present study the FEV<sub>1</sub>/FVC ratio was found to be significantly increased in hypothyroid patients as compared to control. A reduced value is found in obstructive lung disorders while a normal or increased value is diagnostic of restrictive lung disease. This together with decreased FVC suggests that there is a mild restrictive pattern among the hypothyroid patients. Sharifi *et al*<sup>18</sup> reported a restrictive abnormality ranging from mild to moderate grade amongst the hypothyroid subjects which improved significantly on treatment. Similar restrictive pattern was found in 53% of hypothyroid patients by Sharon *et al*. Contrary to our findings, Siafakaset *al*<sup>7</sup> and Cakmak<sup>15</sup> found a decrease in FEV<sub>1</sub>/FVC ratio in hypothyroids compared to normal. Bassi *et al* in 2014<sup>16</sup> could not demonstrate any change in FEV<sub>1</sub>/FVC ratio.

FEF<sub>25%-75%</sub> is an average Forced Expiratory Flow rate over the middle 50% of the FVC and it is said to be more sensitive than FEV<sub>1</sub> for detecting early airway obstruction.<sup>13</sup> In the present study, we observed a significantly raised value of FEF<sub>25%-75%</sub>. Cakmak *et al* (2007)<sup>15</sup> reported a significant decrease in FEF<sub>25%-75%</sub> but Sharon *et al* (2014)<sup>19</sup> observed no significant decrease in FEF<sub>25%-75%</sub>. As this parameter reflects a slowing in terminal part of airways, our observation concludes that there is no small airway obstruction in hypothyroids. PEFR is highly dependent on patient effort as the patient must initially exhale as hard as possible to obtain reproducible data and it may not be the most suitable variable to detect the early deterioration of the

ventilatory functions. In our study, there was hardly any difference in PEFr between case and control. Sharon et al (2014)<sup>19</sup> also did not find any significant change in PEFr in hypothyroids but contrary to our findings, Koral et al (2006)<sup>20</sup>, Cakmak et al in (2007)<sup>15</sup> and Bassi et al in (2014)<sup>16</sup> found a significantly decrease in PEFr.

While considering the correlation studies, we have observed a negative correlation of TSH with FVC & FEV<sub>1</sub> and both were significant which means longer the duration of the disease, higher the TSH values and lesser are the lung parameters. Correlation of fT<sub>4</sub> and all lung parameter revealed a non-significant positive correlation, while no correlation was seen with PEFr (Table 3). Cakmak et al<sup>15</sup> in his study in 2007 also found a negative correlation between TSH and FVC in hypothyroids and a positive correlation between fT<sub>4</sub> and FVC and FEF<sub>25%-75%</sub>. Valjevac et al (2011)<sup>14</sup> also observed a significant negative correlation between TSH and FVC%. In 2012, Bassi et al<sup>16</sup> on his study on newly diagnosed hypothyroids found a highly significant negative correlation of TSH with FEV<sub>1</sub> and FEV<sub>1</sub>/FVC%. Sharon et al (2014)<sup>19</sup> also found a statistically non-significant negative correlation of TSH with FVC, FEV<sub>1</sub>, FEV<sub>1</sub>/FVC. They have also reported a positive correlation between fT<sub>4</sub> with all the lung parameters but none were statistically significant. Both inspiratory and expiratory respiratory muscles are weakened in hypothyroidism in a direct linear relationship to the thyroid hormone level and it is reversible with thyroxine therapy<sup>7</sup>. One of the major inspiratory muscles that are involved in hypothyroidism is the diaphragm.<sup>21</sup> This weakness can be very severe and associated with hypoventilation and hypercapnoea.<sup>22</sup> Analysis of changes in pulmonary function is complicated by

increased frequency of overweight in hypothyroid. In our study, we found a significant increase in BMI in hypothyroids but there was also a significant decrease in height without any significant alteration in weight. So the raised BMI could be due to decreased value of the height of the cases. Thus additive effects of obesity on spirometric parameters may be overruled. So, from our observation it can be said that in hypothyroidism, low fT<sub>4</sub> causes decrease in FVC and FEV<sub>1</sub> and it is suggested that alveolar hypoventilation and decreased inspiratory and expiratory muscle strength may be a possible explanation<sup>23,17</sup>

#### **Conclusion:**

The present study concludes that in hypothyroidism, low fT<sub>4</sub> causes decrease in FVC and FEV<sub>1</sub> and it is thereby suggested that alveolar hypoventilation and decreased inspiratory and expiratory muscle strength may be a possible explanation. If such a relationship between fT<sub>4</sub>, FVC and FEV<sub>1</sub> were found in a randomized controlled trial, it can be concluded that PFT can be used routinely as a screening test in all hypothyroid patients to detect early respiratory dysfunction. Further adequately powered properly designed studies are warranted to establish the antecedent outcome relationship in a biologically plausible background.

#### **Limitation of the study:**

The controls should have been taken from persons residing in the same locality as the patients, so that the environmental conditions affecting lung functions in controls would have been the same as the cases and the comparison of the PFT parameters between cases and controls would have been more justified. Also the PFTs could have been repeated after levothyroxine therapy to note whether changes are reversed or not.

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