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# The Effect of Hypothyroidism on Pulmonary Function in School-age Children

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**Abstract:** *Background:* Hypothyroidism is a relative public health problem in pediatric, associated with increased morbidity due to multisystemic impairment including deleterious changes in lung function. *Objective:* The aim of this study is to assess lung function in children affected by hypothyroidism. In addition to, comparison lung function between clinical and subclinical hypothyroidism. *Materials and Methods:* An Observational Comparative Cross-Sectional study was conducted in 40 patients with newly diagnosed hypothyroidism and 40 healthy children aged 6-14 years. They are selected from Endocrinology and General Pediatric Clinic, Tishreen University Hospital between August 2020 and August 2021. Weight and height were measured and body mass index BMI was calculated. Blood samples were taken and TSH, FT4 were measured. *Results:* A total of 80 children, 30 males (37.5%) and 50 females (62.5%) with mean age  $10.4 \pm 2.1$  years were included in the study. Out of the 80 children, 40 (50%) were euthyroidism, 20 (25%) were with subclinical hypothyroidism, and 20 (25%) were with clinical hypothyroidism. BMI was higher in patients with clinical hypothyroidism compared to other groups with significant difference ( $p: 0.04$ ). A statistically significant decrease in FEV1, FVC, and increase in FEV1/FVC were seen in children with clinical hypothyroidism compared to other children ( $p: 0.0001$ ). Significant negative correlation was seen between TSH and FEV1 ( $r: -0.36$ ,  $p: 0.02$ ), FVC ( $r: -0.64$ ,  $p: 0.0001$ ), and positive correlation with FEV1/FVC ( $r: 0.44$ ,  $p: 0.004$ ). Positive correlation was found between FT4 and FEV1 ( $r: 0.88$ ,  $p: 0.04$ ), FVC ( $r: 0.49$ ,  $p: 0.001$ ) and negative correlation with FEV1/FVC ( $r: -0.43$ ,  $p: 0.006$ ).

**Keywords:** Hypothyroidism, Pulmonary Function, Body Mass Index

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## 1. Introduction

Hypothyroidism is among the most common disturbance of thyroid function. It can result from either primary thyroid disease or secondary to hypothalamic-pituitary disease [1]. Acquired hypothyroidism develops typically during late childhood, and is most commonly caused by autoimmune destruction. Hypothyroidism can manifest with different signs and symptoms and has a wide range of presentations from subclinical hypothyroidism to overt form [2].

Clinical hypothyroidism is defined by the presence of elevated levels of TSH, low concentrations of free T4 (FT4) with various clinical manifestations [3]. Subclinical hypothyroidism is characterized by TSH levels above the upper limit of reference range with normal concentrations of FT4. It occurs in less than 3% of children and adolescents [4].

The main thyroid hormones secreted by the thyroid gland are thyroxine (T4) (80%), and, to a lesser extent, triiodothyronine (T3) (20%) [1].

These hormones are very important to growth, energy metabolism, and control of body temperature, among other metabolic processes; nearly, all metabolically active cells require thyroid hormones for function. [5].

So because of the wide spectrum of physiological effects of these hormones, comes the importance of early diagnosis and treatment of hypothyroidism to improve the outcome [6].

Respiratory system is one of the systems affected by hypothyroidism. The pathophysiological mechanism through which hypothyroidism could lead to alterations is unknown. Major changes that occur in hypothyroidism include a

decrease in ventilator drive and respiratory muscle myopathy, and deposition of mucopolysaccharides in pulmonary interstitium and decreased pulmonary compliance [7].

There are significant changes in spirometry include mildly lower forced vital capacity (FVC), lower forced expired flow, and carbon monoxide diffusing capacity may be low [8]. These changes may be explained by the following: both respiratory system and thyroid gland are linked functionally to cellular oxidative metabolism, and thyroid hormones may play a role in maturation of lung structure and surfactant system [9].

Pulmonary function tests provide an objective, quantifiable measures of lung function. Spirometry measures lung volume and flow on the basis of forced expiration following maximum inspiration to reach the total lung capacity [10]. Pulmonary function of hypothyroidism patients has been investigated in previous studies in adults with different results. Absence of local studies in children prompted us to carry out this study. Therefore, the objectives of the study were to: 1: determine the effect of acquired hypothyroidism on pulmonary function tests. 2: compare lung function between patients with clinical and subclinical hypothyroidism.

## 2. Patients and Methods

### 2.1. Study Population

After approval by local research ethics committee, an Observational Comparative Cross-Sectional study was conducted in 40 patients with acquired hypothyroidism and 40 healthy children aged 6-14 years seen at Endocrinology and General Pediatric Clinic, Tishreen University Hospital over a period of one year from August 2020 to August 2021.

*Inclusion Criteria were as follows:* Children aged 6-14 years old with newly diagnosed hypothyroidism, and age – matched healthy group.

*Non – Inclusion Criteria:* Patients with diseases that might affect pulmonary functions e.g., cardiovascular disease, neurological disorders, asthma, cystic fibrosis, muscular dystrophy. Patients on regular medication that might affect pulmonary functions such as corticosteroids and beta-blockers agents.

Patients were classified according to the BMI as follows: normal weight with  $BMI \geq 5$  p and  $< 85$ p, overweight with  $BMI \geq 85$  p and  $< 95$  p, obese with  $BMI \geq 95$  p and  $< 99$  p [11].

Serum levels of thyroid-stimulating hormone (TSH) and Free thyroxin (FT4) were analyzed, and patients were classified depending on these levels as follow: euthyroidism, subclinical hypothyroidism, and clinical hypothyroidism. For every child, FEV1 (forced expiratory volume), FVC (forced vital capacity), FEV1/FVC ratio were recorded by using spirometry type VITALO GRAPH. Patients were classified according to spirometry results:

*Normal:* normal value of FVC ( $> 80\%$  of the predicted normal), and normal value of FEV1 ( $> 80\%$  of the predicted normal).

*Obstructive type:* reduced FEV1 ( $< 80\%$  of the predicted normal), reduced FVC, FEV1/FVC ratio reduced ( $< 70\%$  of the predicted).

*Restrictive type:* reduced FEV1 ( $< 80\%$  of the predicted normal), reduced FVC ( $< 80\%$  of the predicted normal), FEV1/FVC normal.

*Combined type:* reduced value of FEV1, FVC, and FEV1/FVC. [12]

### 2.2. Statistical Analysis

Statistical analysis was performed by using IBM SPSS version20. Basic Descriptive statistics included means, standard deviations (SD), median, Frequency and percentages. Chi-square test was used to study the relation between categorical variables. One way Anova was used to compare between the three groups. Pearson's correlation coefficient was used to measure the association between quantitative variables. P value  $< 0.05$  was considered as statistically significant.

## 3. Results

The study included a group of 40 healthy children (16 males, 24 females), 20 patients with clinical hypothyroidism (6 males, 14 females), and 20 patients with subclinical hypothyroidism (8 males, 12 females), p: 0.7. No significant difference was found between the groups in terms of age and gender. BMI was significantly higher in patients with clinical hypothyroidism (p: 0.04). FVC was significantly lower in clinical hypothyroidism group ( $87.3 \pm 2.8$ ) compared to subclinical hypothyroidism group ( $96.9 \pm 5.1$ ) and euthyroid group ( $107.5 \pm 6.5$ ), p: 0.0001. FEV1 was significantly lower in clinical hypothyroidism group ( $90.2 \pm 3.2$ ) compared to subclinical hypothyroidism group ( $94.6 \pm 5.1$ ) and euthyroid group ( $100.8 \pm 4.3$ ), p: 0.0001. FEV1/FVC was significantly higher in patients with clinical hypothyroidism compared to other groups (p: 0.0001), table 1.

**Table 1.** Demographic characteristics of the study population.

Variable	Euthyroid	Clinical	subclinical	p value
Sex				
Male	16 (40%)	6 (30%)	8 (40%)	0.7
Female	24 (60%)	14 (70%)	12 (60%)	
Age (year)	10.14 $\pm$ 2.1	11.12 $\pm$ 1.8	10.70 $\pm$ 2.2	0.2
BMI (kg/m <sup>2</sup> )	44.30 $\pm$ 17.6	57.26 $\pm$ 27.06	44.54 $\pm$ 28.6	0.04
Function				
FVC	107.5 $\pm$ 6.5	87.3 $\pm$ 2.8	96.9 $\pm$ 5.1	0.0001
FEV1	100.8 $\pm$ 4.3	90.2 $\pm$ 3.2	94.6 $\pm$ 5.1	0.0001
FEV1/FVC	93.6 $\pm$ 5.1	102.9 $\pm$ 3.5	97.4 $\pm$ 6.3	0.0001

We studied the relationship between TSH and lung function. we found that with increasing TSH, there was a significant decreasing in FEV1 (r: -0.36, p: 0.02), and FVC (r: -0.64, p: 0.0001), with a significant increasing in FEV1/FVC (r: -0.44, p: 0.004).

**Table 2.** Correlation between TSH levels and pulmonary function tests.

	Pearson correlation (TSH)	P value
FEV1	-0.36	0.02
FVC	-0.64	0.0001
FEV1/FVC	0.44	0.004

We studied the relationship between FT4 and lung function. we found that with decreasing FT4, there was a significant decreasing in FEV1 (r: 0.18, p: 0.04), and FVC (r: 0.49, p: 0.001), and a significant increasing in FEV1/FVC (r: -0.43, p: 0.006).

**Table 3.** Correlation between FT4 levels and pulmonary function tests.

	Pearson correlation (FT4)	P value
FEV1	0.18	0.04
FVC	0.49	0.001
FEV1/FVC	-0.43	0.006

## 4. Discussion

Acquired hypothyroidism is a common and treatable disease. If untreated, the condition may have devastating effects in human body systems, so that early diagnosis and treatment is crucial to prevent complications.

This study showed a significant decreasing in FEV1 and FVC, with increasing in FEV1/FVC ratio in children with clinical hypothyroidism suggesting presence of restrictive type of lung disease, Although the values were within the normal range, we can explain this that the children were newly diagnosed with hypothyroidism, so it is possible that these values decrease with exacerbation of hypothyroidism.

Marked inverse associations existed between TSH and both FEV1 and FVC, with positive correlation with FEV1/FVC. Positive correlation was found between FT4 and both FEV1 and FVC, with negative correlation with FEV1/FVC.

These changes may be explained by the effects of low levels of FT4 on lung function in children with clinical hypothyroidism. Reduced respiratory muscle strength (diaphragm and intercostal muscles) lead to reduced FVC.

Reduction in lung function parameters in hypothyroidism may be improved by thyroxine therapy [13].

Many studies have been conducted in adults, while there are no studies in children. among these studies:

Valjevac *et al.*, (2011) demonstrated that hypothyroidism cause significant decrease in FEV1 and FVC, with presence of negative correlation between TSH and FVC, and positive correlation between FT4 and FVC [14].

Gulay *et al.*, (2013) showed significant lower values for FVC, FEV1 in patients with hypothyroidism (clinical, subclinical), normal values for FEV1/FVC ratio, suggesting presence of restrictive type [15]. That was similar to our findings in which lung disease was of restrictive type.

In contrast to our study, Sivaranjani *et al.*, (2019) demonstrated that hypothyroidism cause significant decrease in FEV1 and FEV1/FVC ratio, suggesting obstructive type of lung involvement. There was no significant correlation between TSH or FT4 with FVC, FEV1, FEV1/FVC [16]. It may be explained by the difference of anatomy of respiratory

system between children and adult.

## 5. Conclusion

The current study demonstrated that both clinical and subclinical hypothyroidism lead to pathological alterations in pulmonary function in children. These changes were clear in clinical hypothyroidism patients. Although the measured values were within the normal range, but they are lower as compared with controls, the reason may be its detection in initial stage of the disease, where the cross-sectional study does not allow to follow up the patients over time.

We found a negative relationship between TSH and FEV1, FVC. And a positive relationship between FT4 and these values, which indicates a decrease in lung function according to the severity of hypothyroidism.

## Declarations

### Competing of Interests

All the authors do not have any possible conflicts of interest.

### Ethical Consideration

After discussing the study with the parents, all of them gave a complete and clear informed consent to participate in the study. This study was performed in accordance with the Declaration of Helsinki.

### Availability of Data and Materials

Most of the data was in the article, and other data can be asked from the corresponding author.

### Author Contributions

All authors performed the measurements and wrote the article. Literature review was done by Dr. Rahaf Sleman, and all authors performed analytic calculations and performed the numerical simulations.

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