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Assessment of pulmonary function by spirometry in hypothyroid children and adolescents

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ABSTRACT

Background and objectives. Hypothyroidism affects the function of the respiratory system. Although this effect has been thoroughly studied in adults, it has not been extensively studied in children and adolescents. The aim of this study was to evaluate the pulmonary function in hypothyroid children and adolescents and its correlation with thyroid hormone levels.

Methods. A case-control study was conducted with 65 subjects, aged 7–16 years. They were classified into three groups: the control (euthyroid) group (1st group, n = 25), the treated hypothyroid group (2nd group, n = 25), and the newly diagnosed hypothyroid group (3rd group, n = 15). Spirometry and thyroid function tests were performed for all participants.

Results. All groups were comparable in terms of age, gender, and body mass index (BMI). Forced vital capacity percentage (FVC%) was significantly higher in the euthyroid group compared to the treated and newly diagnosed hypothyroid groups (p-value <0.05; p-value <0.001, respectively) and in the treated group compared to the newly diagnosed group (p-value <0.001). The percentage of forced expiratory volume in one second (FEV1%) was significantly lower in the 3rd group compared to the 2nd and 1st groups (p-value <0.01; p-value <0.001, respectively). The correlations of FVC% and FEV1% with thyroid-stimulating hormone (TSH) levels were significantly negative (p-value <0.00; p-value <0.05, respectively). Conversely, the correlation of FVC% with free thyroxine (fT4) levels was significantly positive (p-value <0.05).

Conclusion. Hypothyroidism reduces pulmonary function in hypothyroid children and adolescents. The reduction in spirometric parameters improves with thyroxine therapy.

Keywords: Basrah, children and adolescents, hypothyroidism, pulmonary function, spirometry

INTRODUCTION

Hypothyroidism is a common endocrine disease in children and adolescents. The pathogenesis of the disease is either congenital or acquired [1-3]. Early detection and prompt therapy reduce the consequences of the disease, especially and most important mental retardation in this age group. Hypothyroidism affects about 0.1% of people aged 11–18 years [4]. Risk factors include insufficient dietary iodine intake, female gender, and coexistence of autoimmune disorders [5,6].

Thyroxine (T4) and triiodothyronine (T3) regulate body basal metabolic rate (BMR), and affect skeletal and nervous system growth as well as the function of various body systems [7]. Pulmonary function is adversely affected in hypothyroidism, resulting in symptoms ranging from mild dyspnea to respiratory failure [8-10]. Thyroid hormones are essential for the development of the pulmonary system and secretion of alveolar surface tension-lowering surfactant [11-14]. Alveolar hypoventilation occurs in hypothyroidism, and obstructive sleep apnea syndrome as well as pleural effusion may occur in hypothyroid patients [15-18]. Moreover, reduced hypoxic and hypercapnic have induced hyperventilation [19].

The low performance of respiratory muscles in hypothyroidism is improved by thyroxine replacement therapy [20,21]. Reduced muscle performance

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occurs secondary to atrophy of type 2 muscle fibers (fast-twitch fibers), reduced mobilization and deposition of glycosaminoglycan in interstitial fluid, decreased contractility of proteins involved in muscle contraction, and reduced activity of the ATPase enzyme in myosin heads [22,23]. In addition, diffusing lung capacity is reduced in hypothyroidism [24]. Studies on hypothyroid patients have revealed altered pulmonary function parameters and a restrictive or combined (restrictive and obstructive) pulmonary pattern [25,26]. However, some studies have indicated an obstructive pulmonary pattern [27,28].

Evaluation of pulmonary system function is frequently conducted in adults by measuring spirometric parameters. Although spirometry can assess pulmonary function in children, it is rarely requested by physicians [29,30]. Therefore, pulmonary function in this age group has not been well studied. The aim of this study was to highlight the effect of hypothyroidism in children and adolescents on pulmonary function by measuring spirometric parameters, illustrating their correlation with T4 and T3 serum levels, and determining the type of pulmonary defect and the effect of T4 replacement therapy on pulmonary function tests in hypothyroid patients of this age group.

MATERIALS AND METHODS

Study design

Hypothyroid patients in this case-control study were collected from Al-Faiha Specialized Diabetes, Endocrine, and Metabolism Center (FDEMC), Basrah, Iraq, from January 2023 to November 2024. Meanwhile, control (euthyroid) individuals were relatives of the patients or staff at the College of Pharmacy, Basrah. Seventy participants (male and female) aged 7–16 years were included in this study. The participants were categorized into three groups depending on serum levels of TSH and free T4 (fT4) [27]:

1. **The control (euthyroid) group:** Included 25 apparently healthy individuals (nine males and 16 females). Their serum TSH was 0.4–4 mIU/L and fT4 was 0.9–1.7 ng/dL.
2. **The treated hypothyroid group:** Included 25 hypothyroid patients (six males and 19 females) on thyroxine therapy.
3. **The newly diagnosed hypothyroid group:** Included 20 newly diagnosed hypothyroid patients (four males and 11 females) with serum TSH > 5.5 mIU/L and fT4 < 0.89 ng/dL.

Hormonal assay

Thyroid hormone levels were measured enzymatically by ELISA (Roche Diagnostics, Hitachi High Technologies Corporation, Japan).

Pulmonary function test

Pulmonary function was assessed using the MIR Spirolab 4 (Medical International Research, Italy). The test was performed in the morning (8–11 a.m.) in a sitting position. Each test was repeated at least three times, and the best result was recorded, printed, and analyzed. Patients with a history of respiratory diseases (obstructive or restrictive), chronic systemic illness, smoking, or drug intake interfering with the test results were excluded from the study.

Statistical analysis

Continuous data were presented as mean ± SD and analyzed using the Statistical Package for the Social Sciences (SPSS), version 26. Differences among the means of the groups were tested using one-way analysis of variance (ANOVA) with Bonferroni correction. Categorical data were presented as frequencies and percentages, and the chi-squared test (χ^2 test) was used for group comparisons. Correlations between spirometric parameters and serum TSH and fT4 levels were analyzed using the bivariate correlation test. A p-value ≤0.05 was considered statistically significant.

RESULTS

The results in Table 1 show that age, gender distribution, height, weight, and BMI did not significantly differ among the studied groups (p-value >0.05). Total serum TSH was significantly higher (p-value <0.05) in the treated and newly diagnosed hypothyroid groups compared to the control group and in the newly diagnosed group compared to the treated hypothyroid group. Meanwhile, fT4 was significantly lower in the newly diagnosed group compared to the treated hypothyroid group. However, the difference was not significant between the control and treated groups.

Table 2 shows that forced vital capacity (FVC) and forced expiratory volume in one second (FEV1) did not significantly differ among the studied groups (p-value >0.05). However, FVC% was significantly higher in the control group compared to the treated and newly diagnosed hypothyroid groups (p = 0.03 and p <0.001, respectively) and higher in the treated group compared to the newly diagnosed hypothyroid group (p <0.001). Similarly, FEV1% was significantly higher in the control group compared to the newly diagnosed group (p <0.001). FEV1% in the control group (87.6 ± 12.6%) was not significantly different from that in the treated group (80.2 ± 11.4%; p-value > 0.05), but it was significantly higher than that in the newly diagnosed group (67.7 ± 17.1%; p-value <0.001). Moreover, FEV1% was significantly higher in the treated group compared to the newly diagnosed group (p-value <0.05).

TABLE 1. Characteristic of participants (mean ± SD)

Parameter	Control (1st) group n=25	Treated hypothyroid (2nd) group n=25	Newly diagnosed hypothyroid (3rd) group n=15	p-value
Age (year)	12.6±2.4	13.6±2.2	13.5±1.9	[a]p=0.353 [b]p=0.613 [c]p=1.000
Gender Male Female	 9 (36%) 16 (64%)	 6 (24%) 19 (76%)	 4(26.7%) 11(73.3%)	[a]p=0.538 (0.875) [b]p=0.73 (0.372) [c]p=1.000 (0.651)
Height (cm)	138.4±12.0	144.7±10.9	143.1±9.4	[a]p=0.602 [b]p=0.147 [c]p=1.000
Weight (kg)	41.4±12.8	44.8±14.1	41.9±8.4	[a]p=1.000 [b]p=1.000 [c]p=1.000
BMI (kg/m^2)	20.4±3.2	20.9±4.2	21.2±3.6	[a]p=1.000 [b]p=1.000 [c]p=1.000
Serum TSH (mU/L)	1.94±0.63	3.97±1.9	17.7±3.7	[a]p=0.004 [b]p<0.001 [c]p<0.001
Serum fT4 (µg/dl)	1.26±0.32	1.29±0.24	0.69±0.25	[a]p=1.000 [b]p<0.001 [c]p<0.001

ANOVA, Post hoc test with Bonferroni correction for continuous data and Chi-square for categorical data (gender): BMI= body mass index, TSH= thyroid-stimulating hormone, fT4= free thyroxine. [a]p, [b]p, and [c]p

Indicates the difference between 1st and 2nd, 1st and 3rd, and 2nd and 3rd groups, respectively. A significant difference was considered if p-value ≤0.05.

TABLE 2. Results of spirometry in hypothyroid and euthyroid children and adolescents (Mean ± SD)

Parameter	Control (1st) group n=25	Treated hypothyroid (2nd) group n=25	Newly diagnosed hypothyroid (3rd) group n=15	p-value
FVC (L)	2.32±0.84	2.34±0.61	1.89±0.68	[a]p=1.000 [b]p=0.229 [c]p=0.194
FVC %	91.4±10.5	82.4±9.9	67.3±16.6	[a]p=0.03 [b]p<0.001 [c]p<0.001
FEV1(L)	1.93±0.58	2.00±.0.52	1.66±.0.61	[a]p=1.000 [b]p=0.408 [c]p=0.186
FEV1 %	87.6±12.6	80.2±11.4	67.7±17.1	[a]p=0.158 [b]p<0.001 [c]p=0.016
FEV1/FVC%	85.3±9.5	85.8±10.4	88.3±12.5	[a]p=1.000 [b]p=1.000 [c]p=1.000
PEF (L/sec)	3.49±0.77	3.43±0.84	3.96±1.0	[a]p=1.000 [b]p=0.301 [c]p=0.196
PEF%	76.2±19.7	64.4±16.5	72.7±21.7	[a]p=0.097 [b]p=1.000 [c]p=0.559
FEF (25-75) (L/sec)	2.3±0.58	2.57±0.96	2.77±0.93	[a]p=0.769 [b]p=0.254 [c]p=1.000
FEF% (25-75%)	87.4±23.1	77.0±18.7	83.7±27.2	[a]p=0.325 [b]p=1.000 [c]p=1.000

ANOVA, Post hoc test with Bonferroni correction: FVC=forced vital capacity, FEV1=forced expiratory volume in one second, PEF= peak expiratory flow, FEF (25-75%) = forced expiratory flow in mid expiration. [a]p, [b]p, and [c]p Indicates the difference between 1st and 2nd, 1st and 3rd, and 2nd and 3rd groups, respectively. A significant difference was considered if p-value ≤0.05.

Other spirometric parameters [FEV1/FVC ratio, peak expiratory flow (PEF), PEF percentage (PEF%), mid-forced expiratory flow (FEF25–75), and FEF25–75 percentage (FEF25–75%)] did not significantly differ among the studied groups (p-value >0.05).

The second and third groups had significantly more abnormal spirometry results [12 (48.7%) and 13 (86.7%), respectively] than the first group [4 (16%)] (p-value <0.05; p-value <0.001, respectively). Additionally, abnormal spirometry results were significantly higher in the third group compared to the second group (p-value < 0.05) (Table 3).

TABLE 3. Pattern of spirometry in hypothyroid and euthyroid children and adolescents

Diagnosis		Control (1st) group n=25	Treated hypothyroid (2nd) group n=25	Newly diagnosed hypothyroid (3rd) group n=15	p-value
Normal spirometry		21(84%)	13 (52%)	2 (13.3%)	
Abnormal spirometry	Restrictive	4 (16%)	10 (40 %)	12 (80%)	[a]p=0.032 [b]p<0.001 [c]p=0.02
	Obstructive	0 (0%)	1 (4%)	0 (0%)	
	Combined	0 (0%)	1(4%)	1 (6.7%)	
	Total	4 (16%)	12(48.7%)	13 (86.7%)	

Fisher's exact test: ap, bp, and cp Indicates the difference between 1st and 2nd, 1st and 3rd, and 2nd and 3rd groups, respectively. A significant difference was considered if p-value ≤ 0.05.

The results in Table 4 demonstrate a significant negative correlation between FVC% and FEV1% and TSH levels (r = -0.562, p-value <0.001; r = -0.372, p-value <0.05, respectively), whereas FVC% showed a significant positive correlation with free T4 levels (r = 0.352, p-value <0.05).

FVC% was significantly lower in the newly diagnosed and treated groups compared to the euthyroid group, and this reduction was not accompanied by a significant reduction in FEV1/FVC%, suggesting a restrictive pulmonary defect pattern. These findings are comparable to the results of other studies conducted on adults with hypothyroidism [25,26,35,36]. Bhandari et al. [37] observed a reduction in FEV1 and FVC in adults with hypothyroidism. While Sivaranjani and Chaitra [38] observed a reduction in FEV1 and FEV1/FVC in adults with hypothyroidism, Abdulhussein et al. [39] reported a significantly reduced FVC only.

The percentage of normal spirometry results was significantly higher in the control group compared to

TABLE 4. Correlation of spirometric parameters with TSH, and fT4 in hypothyroid children and adolescents

		FVC%	FEV1%	FEV1/FVC%	PEF%	FEF% (25-75%)
TSH	r	-0.562	-0.372	0.188	0.148	0.215
	p-value	<0.001	0.018	0.246	0.362	0.182
freeT4	r	0.352	0.274	-0.078	-0.121	-0.196
	p-value	0.026	0.087	0.633	0.456	0.255

Bivariate correlation test: TSH= thyroid-stimulating hormone, fT4= free thyroxin, r=correlation coefficient. A significant difference was considered if p-value ≤0.05

DISCUSSION

Hypothyroidism is an endocrine disorder that affects various systems in the body and presents with a variety of signs and symptoms. This study examined the effect of hypothyroidism on pulmonary function in adolescents and children using spirometry. The groups examined showed no significant differences in age, sex, weight, height, and BMI distribution, signifying that the groups were well-matched (Table 1). The gender bias seen in this study may be attributed to genetic and gender-related factors influencing the production of thyroid autoantibodies [31,32]. Low fT4 levels in newly diagnosed hypothyroid patients result in elevated TSH levels because fT4 inhibits pituitary secretion of TSH through a negative feedback mechanism [33,34].

both the newly diagnosed and treated groups. Additionally, the treated group showed a higher percentage of normal spirometry than the newly diagnosed hypothyroid group. Although the percentage of normal spirometry improves with thyroxine replacement therapy, it remains lower in the treated group than in the control group. This may be attributed to insufficient dosing or inaccurate use of thyroxine, which is indicated by the higher TSH levels in the treated group compared to the control group, as shown in Table 1.

The most commonly observed abnormality was the restrictive pattern on spirometry, reported in 40% of the treated group and 80% of the newly diagnosed group, as shown in Table 3. Studies conducted

on adults also reported a restrictive pulmonary pattern on spirometry. Roel et al. reported a restrictive pulmonary defect in 52% of adult patients with hypothyroidism, while Abdulhussein et al. reported a restrictive pulmonary defect in 30% of adult patients with hypothyroidism [39,40]. It seems that pulmonary fibrosis underlies the restrictive pulmonary defect [41]. Van Tuyl et al. attributed the reduction of pulmonary ventilation in hypothyroidism to reduced pulmonary compliance and surfactant production due to the deposition of mucopolysaccharides in the lung [42].

The production of surfactant by type 2 pneumocytes is enhanced by thyroid hormone, and its deficiency leads to infant respiratory distress syndrome due to immature lungs [11,43,44]. Roel et al. suggested that respiratory muscle weakness and alveolar hypoventilation are the cause of low spirometric parameters in hypothyroid patients [40]. Maiti et al. [45] found that FVC% and FEV1% were significantly negatively correlated with TSH levels, while FVC% was positively correlated with fT4. Valjevac et al. [36] reported that FVC was negatively correlated with TSH, while Roel et al. [40] did not report any correlation between spirometric parameters and thyroid hormone levels.

CONCLUSION

Pulmonary function in children and adolescents is adversely affected by hypothyroidism, primarily presenting as a restrictive pattern, which can be detected using spirometry. Thyroxine therapy helps improve deteriorated respiratory function.

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