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Original Article

Physiology Section

Pulmonary Functions in Patients with Subclinical Hypothyroidism

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ABSTRACT

Introduction: Hypothyroidism affects all organ systems of the human body including the respiratory system. Subclinical hypothyroidism is the earliest stage of hypothyroidism and has a high prevalence rate worldwide.

Aim: To assess the pulmonary function tests in female patients of subclinical hypothyroidism to find out lung function impairment if any.

Materials and Methods: The study comprised of 60 female participants (30 patients with subclinical hypothyroidism and 30 healthy controls) in the age-group of 20-40 years. Pulmonary function tests were performed by using computerised spirometer Helios 401 (RMS, Chandigarh). The parameters of the two groups were compared by student's t-test and $p<0.05$ was considered statistically significant.

Results: The patients of subclinical hypothyroidism showed a highly significant reduction in Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), Peak Expiratory Flow Rate (PEFR) values and their predicted percentages as compared to healthy controls ($p<0.001$), Forced Expiratory Flow 25%-75% ($FEF_{25-75\%}$) and its predicted value was also significantly lower in patients than in controls ($p<0.05$), but the difference in values of FEV_1/FVC% between two groups was not statistically significant ($p>0.05$).

Conclusion: Pulmonary functions are affected in the patients with subclinical hypothyroidism. Therefore, pulmonary functions should be evaluated in subclinical hypothyroid patients to detect early respiratory dysfunction.

Keywords: Lung, Pulmonary function tests, Respiratory system, Spirometer, Subclinical hypothyroidism

INTRODUCTION

Among the various metabolic and endocrine disorders, hypothyroidism is relatively common worldwide. Subclinical Hypothyroidism (ScH) represents the earliest stage of hypothyroidism and may be associated with adverse consequences. ScH is defined as an elevation in serum Thyroid Stimulating Hormone (TSH) above the upper limit of the reference range with normal free thyroxine (T_4) and triiodothyronine (T_3) concentrations and with few or no signs and symptoms of hypothyroidism [1].

Hypothyroidism is commonly caused by iodine deficiency, Hashimoto's thyroiditis, prolonged use of certain drugs like Rifampicin, Interferon, Lithium [2,3]. Subclinical hypothyroidism 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% [1] while different prevalence rates from Indian studies have been reported as 11.3% with 1: 3.7 male:female ratio [4], 8.02% [5] and 4.3-9% (7.5% in females and 2.8% in males) [6]. The prevalence showed a rising trend with age and was more in females (6-8%) than in males (3%) [2]. ScH can be reversible or it can progress to overt hypothyroidism. The annual risk of progression of subclinical hypothyroidism to overt hypothyroidism is 2-5% [1].

It has been reported in many studies that patients with ScH have increased frequency of hyperlipidemia, increased inflammatory markers, diabetes, hypertension and increased cardiovascular risk compared with the euthyroid population [7-9]. Pulmonary functions may get affected like other body systems in hypothyroidism but respiratory manifestations are generally not the major complaints. There are not many studies to report the influence of ScH on Pulmonary Function Tests (PFTs) [10,11]. The impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism [10,12]. Hence, the present study was aimed to assess the pulmonary function tests in female patients of subclinical hypothyroidism to find out lung function impairment if any.

MATERIALS AND METHODS

The present case-control study was carried out from July 2016-June 2017 in the Department of Physiology of MM Institute of Medical Sciences and Research, Mullana, Haryana, India. The study population comprised of 60 female participants of the age group 20-40 years and was divided into two groups. One group included 30 newly diagnosed patients of subclinical hypothyroidism from hospital OPD and was compared with another group of 30 BMI and age-matched healthy controls.

The patients with subclinical hypothyroidism (serum TSH >4.6 µIU/mL with normal T_3 and T_4 levels) were included as cases. The patients with a history of smoking, pregnancy, obesity, respiratory disease or any other disease affecting the respiratory system were excluded.

Approval of Ethics Committee of the Institution was obtained and Informed consent of participants was taken before conducting the study. After taking a detailed history, all participants were clinically evaluated and their BMI was also calculated. Thyroid function tests were done and evaluated in the Department of Biochemistry by using Chemiluminescent Immunoassay on the Advia Centaur XP supplied by Siemens (Munich, Germany).

The pulmonary functions were performed in the Department of Physiology by using portable computerised spirometer- Helios 401, version 1.3, Recorder and Medicare Systems (P) Ltd., (RMS), Chandigarh. The PFT parameters assessed were Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV_1), FEV_1/FVC, Peak Expiratory Flow Rate (PEFR), Forced Expiratory Flow 25%-75% ($FEF_{25-75\%}$) and their predicted values. The procedure was properly explained and demonstrated before the recordings. At least three satisfactory readings were recorded and the highest was taken as the representative value for a given individual.

STATISTICAL ANALYSIS

The continuous data was expressed as mean and standard deviation. The normality of quantitative data was checked by

measures of Kolmogorov-Smirnov tests of normality. Independent Student's t-test was used for comparison of two groups for the normally distributed data. All the statistical tests were two-sided and were performed at a significance level of α=0.05. Statistical analysis was conducted using IBM SPSS STATISTICS (version 22.0).

RESULTS

A total of 60 females (30 cases and 30 controls) who met the inclusion criteria were included in the study. The mean ages of 30 cases (subclinical hypothyroid patients) and 30 euthyroid controls were 28.37±6.88 and 29.50±7.75 years respectively. The two groups were comparable in age, weight, height and BMI i.e., p>0.05. Serum TSH levels were significantly higher in subclinical hypothyroid patients compared to control group (p<0.001) [Table/Fig-1]. The means of T_3 in cases and controls were 0.74±0.35 and 0.99±0.12 ng/mL respectively (p=0.023) and means of T_4 in cases and controls were 6.57±2.97 and 8.84±1.71 µg/dL respectively (p=0.034). Thus T_3 and T_4 levels were significantly different in two groups but were within normal range.

Parameters	Cases (n=30)	Controls (n=30)	p-value
Age (years)	28.37±6.88	29.50±7.75	0.552
Weight (Kg)	56.10±8.44	61.37±13.28	0.072
Height (m)	1.58±0.047	1.58±0.04	0.934
BMI (Kg/m^2)	22.40±3.02	24.51±5.08	0.056
TSH (µIU/mL)	12.72±28.30	1.66±0.66	<0.001**

[Table/Fig-1]: Baseline characteristics of the study participants in the two groups.
p≤0.05 considered as statistically significant* and p≤0.001 considered as statistically highly significant**

Reduction in FVC, FEV_1, PEFR values and their predicted percentages were statistically highly significant in cases compared to controls (p<0.001), $FEF_{25-75\%}$ and its predicted value was significantly lower in cases than controls (p<0.05) but the difference in values of FEV_1/FVC% between the two groups was not statistically significant (p>0.05) [Table/Fig-2].

PFT parameters	Cases (n=30)	Controls (n=30)	p-value
FVC (L)	1.70±0.46	2.07±0.29	<0.001**
FVC% Predicted	68.77±16.97	83.80±10.81	<0.001**
FEV_1 (L)	1.59±0.41	1.93±0.26	<0.001**
FEV_1% Predicted	79.60±19.00	96.80±12.33	<0.001**
FEV_1/FVC%	93.92±8.70	93.62±6.20	0.532
PEFR (L/sec)	3.35±1.07	4.44±1.06	<0.001**
PEFR% Predicted	51.83±16.39	68.67±16.61	<0.001**
$FEF_{25-75\%}$	2.28±0.78	2.76±0.79	0.022*
$FEF_{25-75\%}$ Predicted	78±27.94	93.50±24.17	0.025*

[Table/Fig-2]: Comparison of pulmonary function tests in the two groups.
PFT: Pulmonary function tests, p≤0.05 considered as statistically significant* and p≤0.001 considered as statistically highly significant**

DISCUSSION

Hypothyroidism can affect all organ systems and subclinical hypothyroidism can progress to overt hypothyroidism. The impairment of respiratory functions may be initiated at the subclinical state. In the presence of clinical manifestations, subclinical hypothyroid patients may require thyroid hormone replacement therapy [13].

The current study utilised simple and non-invasive spirometry method to evaluate respiratory parameters in female patients of subclinical hypothyroidism. Many researchers have found deranged pulmonary functions in patients with overt hypothyroidism, however in patients with subclinical hypothyroidism involvement of respiratory functions is still not very clear [3,14-16].

In the present study, subclinical hypothyroid patients showed a significant reduction in pulmonary function tests (FVC, FEV_1, PEFR, $FEF_{25-75\%}$ and their predictive values) indicating that pulmonary functions may get affected in subclinical hypothyroidism. The proportionate decrease in both FEV_1 and FVC resulted in no significant change in FEV_1/FVC ratio in the present study. 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 FEV_1 and $FEF_{25-75\%}$ suggest an obstructive pattern. Thus deterioration of pulmonary function tests in the study points to a mixed pattern of respiratory disorder. Similar to the present study Iyer SK et al., also found a mixed pattern of respiratory disorder in their study on hypothyroid patients which could be due to both parenchymal and non-parenchymal causes [17]. However, there are conflicting reports from different research studies.

Present results are consistent with results of Cakmak G et al., who also observed a significant reduction in FVC, FVC%, FEV_1, FEV_1%, PEFR, PEFR%, FEF_{25-75}, $FEF_{25-75\%}$ in patients with subclinical hypothyroidism [10]. In patients with overt hypothyroidism, Bhuvaneswari T et al., found decreased values of FVC, FVC%, FEV_1, FEV_1%, FEV_1/FVC, $FEF_{25-75\%}$ [3].

Roel S et al., found a significant reduction only in FVC and not in FEV_1, PEFR, $FEF_{25-75\%}$ values in hypothyroid patients [15], thus showing a restrictive pattern and Maiti SR et al., found a significant increase in values of FEV_1/FVC ratio and $FEF_{25-75\%}$ and suggested a mild restrictive pattern among hypothyroid patients [14].

Contrary to current findings, Koral L et al., found values of PFT within the normal range in patients of subclinical hypothyroidism. Thyroid hormone therapy was given to the patients to bring the TSH levels to a euthyroid state but researchers observed that PFT values were not significantly different before and after the treatment [11]. On the other hand, Bassi R et al., found better pulmonary functions in treated patients of hypothyroidism as compared to untreated newly diagnosed patients [18]. The possible advantages of treating subclinical hypothyroidism are described by Kek PC et al., as preventing its progression to overt hypothyroidism; decrease cardiovascular risk and therapy may reverse symptoms of mild hypothyroidism [6].

The study done by Swami G et al., found decreased pulmonary functions in hypothyroid patients who were already on thyroid hormone therapy and on doing pranayama for six months these patients showed significant improvement in FEV_1, Maximum Voluntary Ventilation (MVV) and Inspiratory Capacity (IC) and suggested that this beneficial effect of yoga could be due to improvement in respiratory muscle strength and increased air entry which increase oxygen concentration at tissue level [16].

The underlying pathophysiology in hypothyroid patients has been stated as multifactorial and various mechanisms causing respiratory derangements are attributed to impaired ventilatory drive, alveolar hypoventilation, decrease in respiratory muscle strength including diaphragmatic weakness, decreased lung elasticity and increased work of breathing [2,13,14,17-20].

The significant reduction in PFT values, found in subclinical hypothyroid patients in the present study, may be attributed to respiratory muscle weakness and defective ventilatory drive. Subclinical hypothyroidism 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.

LIMITATION

The large sample size and correlation of PFT parameters with TSH levels could have made the current study more robust. The

follow-up of study patients could have been done to find any change in pulmonary functions or TSH levels with respect to progression or recovery of their hypothyroid status.

CONCLUSION

The current study suggests the involvement of pulmonary functions in subclinical hypothyroidism as the values of pulmonary function tests were significantly lower in patients of subclinical hypothyroidism than those of healthy controls. The subclinical hypothyroidism represents the mildest and early form of hypothyroidism and thus may be associated with adverse consequences. The simple, portable and non-invasive spirometry can be considered as a means of evaluation of pulmonary functions in subclinical hypothyroid patients to detect early respiratory dysfunction to avoid complications. Further studies are warranted to establish a relation between pulmonary functions and TSH levels in subclinical hypothyroid patients.

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