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Research Article

MIXED PATTERN OF RESPIRATORY DYSFUNCTION IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM: A CASE-CONTROL STUDY

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ABSTRACT

Background: Subclinical hypothyroidism (SCH) is defined biochemically as a high serum thyroid-stimulating hormone (TSH) and normal serum free thyroxine (T4) and triiodothyronine (T3) concentrations. SCH influences cardiovascular system and metabolic parameters, and the effect on the respiratory system is controversial. The aim of this prospective observational case-control study was to evaluate the pulmonary function of patients diagnosed with SCH to find out lung function impairment if any.

Methods: The study comprised of 145 participants (70 patients with SCH and 75 healthy controls) in the age-group of 18-55 years. Pulmonary function tests were performed by using the computerized spirometer. 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 SCH showed a highly significant reduction in Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1) and their predicted percentages as compared to healthy controls (P<0.001). Forced Expiratory Flow 25-75 (FEF25-75) and its predicted value was also significantly lower in patients than in controls (P<0.05), but the Peak Expiratory Flow Rate (PEFR) and the difference in values of FEV1/FVC% values between two groups was not statistically significant.

Conclusion: Pulmonary functions were affected in the patients with SCH. A mixed pattern of respiratory dysfunction was seen in patients with SCH. Therefore, pulmonary functions should be evaluated in SCH patients to detect early respiratory dysfunction.

INTRODUCTION

Hypothyroidism is the most common endocrine disorders. Subclinical Hypothyroidism (SCH) represents the earliest stage of hypothyroidism. SCH is defined as an elevation in serum Thyroid Stimulating Hormone (TSH) above the upper limit of the reference range with normal free thyroxine (T4) and triiodothyronine (T3) concentrations and with few or no signs and symptoms of hypothyroidism [1]. The incidence of SCH varies between 4 and 10% depending upon the gender, age and population studied [2, 3]. SCH poses an enormous burden in India as the prevalence rates of SCH in India exceed those in the developed nations. Indian studies have been reported varying prevalence, which varies with geographical area and iodine status as 11.3% [4], 8.02% [5] and 21.5% [6]. The prevalence increases with age and is more common in females than males [6,7]. SCH can be reversible or it can progress to overt hypothyroidism. The annual risk of progression of SCH to overt hypothyroidism is 2-5% [1]. Etiologically, most cases of persistent SCH are due to autoimmune thyroiditis (AIT); however, germline loss of function mutations in the TSH receptor account for a small proportion of cases [8].

The consequences of SCH are variable at several levels and may depend on the duration and the degree of elevation of the serum TSH. 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 or mortality as compared with euthyroid population [9-12]. Pulmonary functions may get affected like other body systems in hypothyroidism but respiratory manifestations are generally not the major complaints. Since diagnosis depends on laboratory values in SCH, theoretically, no symptoms or signs are expected but still, patients may suffer from somnolence, weakness and fatigue

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[6,13,14]. Muscle strength is also affected in SCH. The decrease in muscle strength effects pulmonary functions accordingly [15-17]. There are not many studies to report the influence of SCH on pulmonary Function Tests [18-20]. The impairment of pulmonary functions may be considered as the indication for initiation of L-thyroxine at the subclinical stage of hypothyroidism [18,21]. Hence, the present study was aimed to assess the pulmonary function tests in patients of SCH to find out lung function impairment if any.

MATERIALS AND METHODS

This was a single center prospective observational case control study of adults with SCH. This study was carried out in the Department of Endocrinology and Department of Physiology of GMC Srinagar, Jammu and Kashmir, India. The study was approved by the institutional ethical committee.

Study Subjects

Total of 70 patients with diagnoses of SCH attending the outpatient department of Endocrinology, who fulfilled eligibility criteria were recruited in the study. We also recruited 75 randomly selected healthy Euthyroid controls standardized for age and gender for the comparison. This study was conducted over a period of 10 months from August 2018 to May 2019. Informed consent was obtained from all the recruited subjects. Information regarding various demographics characteristics was taken through well structured questionnaires from all subjects. Besides a detailed history, physical examination and biochemical workup which included baseline investigations complete blood count (CBC), blood glucose fasting (BGF), liver function test (LFT), lipid profile and Thyroid function test (TFT) were carried out.

Eligibility Criteria

Inclusion criteria included patients having age >18years and SCH was defined as biochemical evidence of elevated TSH levels (>4.3 to ≤ 10 mIU/ml) and normal fT3 and fT4 values.
Exclusion criteria include i) Hypertension, ii) Smokers, iii) Coronary artery disease, iv) Diabetes, v) Other chronic diseases like heart failure, respiratory disease, obesity or any other disease affecting the respiratory system were excluded, vi) Pregnancy.

TFT comprising of TSH, fT3 and fT4 levels was carried out by Electrochemiluminescence immunoassay (ECLIA) method using a fully automatic analyzer ECLIA 2010 (Roche Diagnostic Germany). The pulmonary functions were performed in the Department of Physiology by using portable the computerized spirometer- Helios 401, version 1.3, Recorder and Medicare Systems (P) Ltd. The pulmonary function test parameters assessed were Forced Vital Capacity (FVC), Forced Expiratory Volume in one second (FEV1), FEV1/FVC, Peak Expiratory Flow Rate (PEFR), Forced Expiratory Flow 25%-75% (FEF25-75%) and their predicted values. The procedure was properly explained and demonstrated before the recordings. At least three satisfactory readings were recorded and the mean 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. All the analyses were performed by the Statistical Package for Social Sciences (SPSS, Chicago, IL, USA, version 21.0).

RESULTS

A total of 145 patients (70 cases and 75 controls) who met the inclusion criteria were included in the study. Table 1 shows the baseline parameters of the study population. The mean ages of 70 cases (SCH patients) and 75 Euthyroid controls were 37.47±6.88 and 35.50±7.75 years respectively. The two groups were comparable in age, gender and BMI. Serum TSH levels were significantly higher in SCH patients compared to control group with TSH=10.72±4.30 and 3.66±0.88 respectively (P<0.001). The means fT4 in SCH and controls were 1.18±0.36 and 1.24±0.29 ng/dl respectively (P=0.269) and means fT3 in SCH and controls were 2.56±0.62 and 2.70±0.74 pg/ml respectively (P=0.221). Thus fT4 and fT3levels were comparative between two groups.

Table 1 Baseline parameters of study participants (SCH and Controls)

Parameters	SCH (n=70)	Controls (n=75)	*P*-value
Age (years)	37.47±6.88	35.50±7.75	0.108
Female Gender	46(66%)	50(67%)	0.898
Weight (Kg)	58.10±8.40	61.37±13.50	0.099
Height (m)	1.58±0.05	1.58±0.04	0.934
BMI (Kg/m2)	23.40±4.00	24.51±5.00	0.147
TSH (μIU/mL)	10.72±4.30	3.66±0.88	<0.001
fT4 (ng/dl)	1.18±0.36	1.24±0.29	0.269
fT3 (pg/ml)	2.56±0.62	2.70±0.74	0.221

*P-value <0.05 is considered statistically significant Categorical variables [n (%)] Continuous variables [mean ± SD] n = Number; SD = Standard deviation

Table 2 shows the comparison of pulmonary function tests between SCH and Controls. Reduction in FVC and FEV1 values and their predicted percentages were statistically highly significant in SCH compared to controls (P<0.001), FEF25-75 and its predicted value was significantly lower in SCH than controls (P<0.05) but the PEFR and difference in values of FEV1/FVC% between the two groups was not statistically significant.

Table 2 Comparison of pulmonary function tests between SCH and Controls.

Parameters	SCH (n=70)	Controls (n=75)	*P*-value
FVC (L)	1.84±0.46	2.07±0.35	<0.001
FVC%	68.70±16.60	83.80±10.70	<0.001
FEV1 (L)	1.59±0.41	1.93±0.26	<0.001
FEV1%	79.60±19.00	96.40±12.80	<0.001
FEV1/FVC%	93.52±8.40	92.88±6.50	0.563
PEFR (L/sec)	4.35±1.10	4.40±1.30	0.803
PEFR%	61.65±14.45	63.10±15.60	0.563
FEF25-75	2.42±0.65	2.76±0.75	0.004
FEF25-75%	82.70±27.40	94.00±24.30	0.007

DISCUSSION

Hypothyroidism can affect all organ systems and SCH can progress to overt hypothyroidism. The impairment of respiratory functions may be initiated at the subclinical state. In the presence of clinical manifestations, SCH patients may require thyroid hormone replacement therapy [22].

The current study utilized simple and non-invasive spirometry method to evaluate respiratory parameters in patients with SCH. Many researchers have found deranged pulmonary functions in patients with overt hypothyroidism, however in patients with SCH involvement of respiratory functions is still not very clear [23-25].

In our study, SCH patients showed a significant reduction in pulmonary function tests (FVC, FEV1, FEF25-75 and their predictive values) indicating that pulmonary functions may get affected in SCH. The proportionate decrease in both FEV1 and FVC resulted in no significant change in FEV1/FVC ratio and also PEFR was not significantly different. In our study, decreased values of FVC suggest a restrictive pattern and decreased values of FEV1 and FEF25-75% 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 [26]. However, there are conflicting reports from different research studies.

Our results are consistent with results of Cakmak G *et al*. [18] and Trigotra S *et al*. [20], they also observed a significant reduction in FVC, FVC%, FEV1, FEV1%, PEFR, PEFR%, FEF25-75, FEF25-75% in patients with SCH. Roel S *et al*., found a significant reduction only in FVC and not in FEV1, PEFR, FEF25-75% values in hypothyroid patients [24], thus showing a restrictive pattern and Maiti SR *et al*., found a significant increase in values of FEV1/FVC ratio and FEF25-75% and suggested a mild restrictive pattern among hypothyroid patients [23].

Contrary to current findings, Koral L *et al*., found values of pulmonary function test within the normal range in patients of SCH and L-thyroxine therapy did not improve pulmonary function test values from baseline (no significantly different before and after the treatment) [19]. The possible advantages of treating SCH 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 [27]. 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 yoga for six months these patients showed significant improvement in FEV1, Maximum Voluntary Ventilation (MVV) and Inspiratory Capacity (IC) and suggested that this beneficial effect could be due to improvement in respiratory muscle strength and increased air entry which increase oxygen concentration at tissue level [25].

The significant reduction in pulmonary function test values, found in SCH patients in the present study, may be attributed to respiratory muscle weakness. SCH is very common, thus all systems including the respiratory system should be clinically evaluated thoroughly. It is suggested 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.

CONCLUSION

The current study suggests the involvement of pulmonary functions in SCH as the values of pulmonary function tests were significantly lower in patients of SCH than those of healthy controls. The simple, portable and non-invasive spirometry can be considered as a means of evaluation of pulmonary functions in SCH patients to detect early respiratory dysfunction to avoid complications.

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