



PULMONARY FUNCTION TEST IN PATIENTS WITH SUBCLINICAL HYPOTHYROIDISM: A STUDY FROM EASTERN INDIA

Sutar S. B

Senior Resident, Department of Medicine, SLN Medical College, Odisha

Mishra S.*

Senior Resident, Department of Neurology, SCB Medical College, Odisha
*Corresponding Author**ABSTRACT**

Context: Subclinical hypothyroidism (SCH) is defined by an elevated Thyroid stimulating hormone (TSH) level in presence of normal serum free T4 concentration. Thus serum TSH measurement is the necessary test for diagnosis of mild thyroid failure.

Aims: Evaluation of the pulmonary function by spirometry in patients of SCH, correlate the pulmonary function with fT3, fT4, TSH level and assess any change in pulmonary function in patients of SCH following treatment.

Settings and Design: Prospective case control study from December 2014 to November 2016 in tertiary medical college of eastern India

Methods and Material: 70 patients and 35 age sex matched controls were included in the study. The main outcome measures of the study were based on a comparison of spirometric findings of subclinical hypothyroidism with the control group and change in spirometric parameters after 3 months follow up with levothyroxin replacement.

Statistical analysis used: The statistical comparisons were done by SPSS software version 20. P value was considered significant if <0.05.

Results: The study population 90% were females and 10% males. The mean TSH of the patients with subclinical hypothyroidism was 11.49±8.44 and that of the control group was 3.22±0.79, it was statistically significant. Forced expiratory volume in 1 second of subclinical hypothyroidism patients was significantly lower than control group. The mean FEV1/FVC% was higher in subclinical hypothyroidism as compared with control. After 3 months of thyroid hormone replacement the TSH level was normalised. With improvement of TSH all the respiratory parameters improved significantly.

Conclusions: Though mild restrictive pattern of respiratory function abnormality occurs in subclinical hypothyroidism, it cannot be ignored. Hence they should be evaluated and clinical approaches should be taken accordingly at the earliest.

KEYWORDS : Subclinical Hypothyroidism, Spirometry, Restrictive lung disease, levothyroxin

INTRODUCTION:

Subclinical hypothyroidism is defined by an elevated TSH level in presence of normal serum fT4 concentration. Serum TSH has a log linear relationship with circulating thyroid hormone levels (a 2 fold change in free thyroxin will produce a 100 fold change in TSH). Thus serum TSH measurement is the necessary test for diagnosis of mild thyroid failure when the peripheral thyroid hormone levels are within normal laboratory range.¹

The entity may present with mild symptoms of hypothyroidism (like fatigue, cold intolerance, consistent weight gain) impaired wellbeing and quality of life, impaired cognitive function, mood disturbance and increase of TSH.² The progression to clinical hypothyroidism is evident in 17% of cases.³ Hypothyroidism affects the lung function in various ways by depressing ventilatory drive resulting in alveolar hypoventilation, respiratory muscle weakness due to skeletal muscle weakness because of skeletal muscle myopathy and obesity causing moderate reduction in vital capacity and lung volumes.⁴

Spirometry is the most common of the pulmonary function tests measuring lung function, specifically the amount (volume) and/or speed (flow) of air that can be inhaled and exhaled. Though there are many literatures regarding the effect of hypothyroidism on pulmonary function but few studies revealing the influence of subclinical hypothyroidism on pulmonary functions are found. Hence this study is undertaken to evaluate the effect of subclinical hypothyroidism on pulmonary function. Simple spirometry for pulmonary function test is a cheap, simple and non-invasive method has been performed on the patients with subclinical hypothyroidism in order to determine if respiratory functions are affected or not.

SUBJECTS AND METHODS:

Study was done in a referral tertiary medical college of eastern india Patient from December 2014 to October 2016 .The study group consists of 70 patients who came to our hospital having Serum fT4 level between 0.8 to 1.8ng/dl, Serum fT3 level between 2.4 to 4.2 pg/dl and TSH level >4.2 mIU/L with /without mild symptoms of hypothyroidism like fatigue, cold intolerance, consistent weight gain, depression. They were considered as subclinical hypothyroid and were eligible in this prospective follow-up study. 35 age, sex and BMI matched healthy individuals were taken as control. Patients with known thyroid disorder under treatment, BMI>30kg/m², with history

of smoking, pregnancy, known respiratory disorders like COPD, Bronchial asthma, Interstitial lung disease (ILD), bronchiectasis etc ,Neuromuscular disorder and Patients with other systemic disorders affecting the function of respiratory system were excluded from the study.

Blood samples were collected from the patients for estimation of serum glucose, serum creatinine, TSH and fT4, fT3. Serum fT3, fT4 levels were assessed by chemiluminescent competitive enzyme immunoassay method with immulite 2000 of BIODPC. Serum TSH analysis was performed by Enzyme Chemiluminescent Immunometric Assay method with same analyser. Spirometric analysis was performed by computerised spirometer-Helios 401/701. All respiratory parameters including forced vital capacity FVC, FVC%, forced expiratory volume FEV1, FEV1%, FEV1/FVC, forced expiratory flow, FEF25-75, FEF 25-75%, peak expiratory flow PEF, PEF% assessed The assessment of predictive values for spirometric parameters was predicted as per the guidelines of American Thoracic Society (1995). Data collection was done in a case record format. The investigation results including blood tests and spirometry findings were also recorded. All patients were followed up for 3months. The composite primary endpoints of this study were to evaluate the pulmonary function by spirometry in patients of subclinical hypothyroidism, correlate the pulmonary function with TSH level and assess any change in pulmonary function in patients of subclinical hypothyroidism following treatment.

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Statistical Analysis: We used SPSS version 20.0 (SPSS Inc., Chicago, IL) for statistical analysis. For the purpose of present analysis, patients were divided into 2 groups based on spirometry: group 1, with normal spirometry and group 2, abnormal spirometry and compared with control group. Continuous variables were presented as mean \pm SD and categorical variables were presented as number of patients and percentage. Baseline characteristics of the 2 groups were compared using the χ^2 test or the Fisher exact test for categorical variables and the Student unpaired t test for continuous variables, as appropriate. Paired t-test method was used to compare outcome.

RESULTS:

The comparisons of baseline characteristics of participants are shown in Table 1. In this study, 90% were females suggesting subclinical hypothyroidism is common in females. TSH value in subclinical hypothyroidism is statistically higher in patients as compared with control group (table-1). Among 70 patients 52(74.3%) patients were having normal spirometry whereas 18 (25.7%) patients were having abnormal values in spirometry. Table -2 shows the presentation of different symptoms among patients having normal and abnormal spirometry. From table-2 its evident that 90% of the patients with subclinical hypothyroidism were asymptomatic and 10% of patients had symptoms like somnolence (2%), depression (6%) and combined (2%) among this group. But in case of patients having abnormal spirometry, had fatigability (51%) and depression (17%), somnolence (11%), weight gain (5%), asymptomatic (5%) and combined symptoms (11%).

In this study from table-1, out of most common spirometric abnormality was mild restrictive pattern i.e decreased FVC% and FEV1% and increased FEV1/FVC%. In the cohort of high TSH value the alteration of respiratory parameters were more marked than low TSH value group. To study the spirometry parameters between SCH and control, Fisher's exact test was performed using a contingency table (table 3) and the p value were calculated to be 0.0001 which were significant. To compare the spirometric parameters before and after treatment among subclinical hypothyroidism, we found significant improvement of spirometric parameters with 3month levothyroxin replacement. (table 4). Significant comparisons are marked bold.

DISCUSSION:

Literature research reveals many studies regarding the effects of clinical hypothyroidism on respiratory and cardiovascular systems. Subclinical hypothyroidism is a common phenomenon seen more often in women with increasing age. The prevalence in women is 6-8% and 3% in men³. In this study, from table -1 there was 90% (63 out of 70) female and 10% male patients had subclinical hypothyroidism. So our study shows women dominate the cohort like literature epidemiologies. Usually minimal symptoms or findings are expected in subclinical hypothyroidism. Fatigue is observed in subclinical hypothyroidism may be because of muscle dysfunction.^{5,9}

In this study out of 70 subclinical hypothyroidism patients, only 26% (18 out of 70) patients had abnormal spirometry findings. Among them most common spirometric abnormality was mild restrictive pattern i.e. decreased FVC% and FEV1% and increased FEV1/FVC%. This was in accordance with the study conducted by Valjevac et al¹¹ 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 in hypothyroidism. Cakmak et al¹² observed a significant reduction in FVC, FEV1, FEF25%-75% and diffusing capacity of lung for carbon monoxide (DLCO) in patients with subclinical hypothyroidism as compared to control. our study is aligned with the previous studies.

In the present study the FEV1/FVC ratio was found to be same in both groups. 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 subclinical hypothyroid patients. Sharifi et al¹³ reported a restrictive abnormality ranging from mild to moderate grade amongst the hypothyroid patients which improved significantly on treatment. FEF25% -75% is an average Forced Expiratory Flow rate over the middle 50% of the FVC and it is said to be more sensitive than

FEV1 for detecting early airway obstruction.¹⁰ In the present study, it was observed that there was not significantly decreased value of FEF25%-75% in patients of SCH. Cakmak et al (2007)¹² reported a significant decrease in FEF25%-75% but Sharon et al (2014)¹⁴ observed no significant decrease in FEF25%-75%. As this parameter reflects a slowing in terminal part of airways, in present study observed that there is no small airway obstruction in subclinical hypothyroids as evidenced by FEF 25%-75% in subclinical hypothyroidism and control group were respectively 95.61 \pm 29.42 and 98.09 \pm 28.12.

SCH patients had abnormal pre-treatment values in FEV1 (1.89 \pm 0.32), FVC (2 \pm 0.00), or FEV1/FVC (92.44 \pm 8.14) and these parameters like FVC (2.44 \pm 0.51), FEV1(2.17 \pm 0.38), FEV1/FVC (83.17 \pm 3.46) levels changed significantly after they became euthyroid. Also pre-treatment values of FVC%(75.17 \pm 6.33), FEV1%(82.75 \pm 6.70), and FEV1/FVC %(115.78 \pm 9.36) were significantly normalized after treatment with levothyroxin. Limited studies exist against which these findings can be compared. In this study of subclinical hypothyroidism patients, 26% cases had mild restrictive pulmonary function test which significantly changed with thyroid hormone replacement.

CONCLUSION:

Neuromuscular abnormalities and impaired respiratory functions are frequently observed in many studies in clinical hypothyroidism, but the effect of subclinical hypothyroidism on respiratory function remains controversial as there are few numbers of studies concerning this aspect. The effect of subclinical hypothyroidism on several organ systems is well known, whereas its effect on respiratory function is not fully understood. SCH may progress to the overt one but it is hypothesized that the impairment in respiratory function may have started at the subclinical state. In this study it was observed that there was significant decrease of FVC, FEV1 and PEFr values in patients of subclinical hypothyroidism. However on follow up of these patients with levothyroxin replacement for three months both these parameters were improved, which suggested that there was some effect of SCH on respiratory function. Though mild restrictive pattern of respiratory function abnormality occurs in subclinical hypothyroidism, it cannot be ignored. Hence they should be evaluated and clinical approaches should be taken accordingly at the earliest. Since this study is done in small number of cases and not all, but some had mild restrictive lung function abnormality, further more studies are required to establish the effect of subclinical hypothyroidism on respiratory function.

Limitations of the study:

- 1) small sample size.
- 2) Only spirometry parameters of PFT was taken for this study while other components of PFT like DLCO, DLCO/VA, Pimax, Pemax, not performed
- 3) The controls taken from persons residing in same locality as the patients so that the environmental conditions affecting lung functions in controls would have been the same as the cases.

REFERENCES:

1. Cooper DS. Subclinical hypothyroidism. *N Engl J Med*. 2001;345(4):2602-65
2. Larsen PR, Davies TF. Williams Textbook of Endocrinology. In: Larsen PR, Kronenberg HM, Melmed S, Polonsky KS. Hypothyroidism and thyroiditis. 10th ed. Philadelphia, Pennsylvania Saunders; 2003; pp 423-56.
3. Kek PC, Ho SC, Khoo DH. Subclinical thyroid disease. *Singapore Med J* 2003;44: 595-600.
4. Sifatakis NM, Salesiotou V, Filaditaki V, Tzanakis N, Thalassinou N, Bouras D. Respiratory muscle strength in hypothyroidism. *Chest* 1992; 102: 189-94.
5. Reuters VS, Buescu A, Reis FA, Almeida CP, Teixeira PF, Costa AJ, et al. *Arq Bras Endocrinol Metabol* 2006; 50: 523-31.
6. Rajagopal KR, Abbrecht PH, Derderian SS, Pickett C, Hofeldt F, Tellis CJ, et al. Obstructive Sleep Apnea in Hypothyroidism. Washington, DC; Bethesda, Maryland; and Denver, Colorado. *Ann Intern Med* 1984; 101: 491-4.
7. Jameson JL, Weetman AP. Disease of thyroid Gland. In: Braunwald E, Fauci AJ, Kasper DL, Hauser SL, Longo DL, Jameson JL. Harrison's Principles Of Internal medicine. 15th ed. New York: McGraw-Hill, 2001; pp 2060-2084.
8. Biondi B, Palmieri EA, Lombardi G, Fazio S. Effects of subclinical thyroid dysfunction on the heart. *Ann Intern Med* 2002;137: 904-14.
9. Biondi B, Palmieri FA, Lombardi G, Fazio S. Subclinical hypothyroidism and cardiac function. *Thyroid* 2002; 12:505-510.
10. Hyatt Robert E, Scanlon Paul D, Nakamura Masao. In: Interpretation of Pulmonary Function Tests 2nd ed. 14
11. Valjevac S, Hadzovic-Dzuvo A, Valjevac A, Kucukalic -selimovic E, Lepara O. Assessment of lung dysfunction with spirometry in patients with thyroid Disorders. *Acta inform med* 2011; 19(1): 16-8.
12. Cakmak G, Saler T, Saglam Z, Yenigen M, Demir T. Spirometry in Patients with clinical and subclinical hypothyroidism. *Tüberkulozve Toraks Dergisi* 2007; 55(3): 266-70.
13. Sharifi F, Amari A. The effect of levothyroxine on pulmonary function tests of hypothyroid patients. *Int J Endocrinol Metab* 2005;1: 48-51
14. Roel S, Punyabati O, Prasad L, Salam R, Ningshen K, Shimray AJ, et al. Assessment of Functional Lung Impairment in Hypothyroidism. *IOSR. Journal of Dental and Medical Sciences* 2014;13(9):4-7