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Article

Evaluation of lung function by spirometric parameters and its association with serum TSH and serum fT4 in subclinical hypothyroidism in a tertiary care hospital serving rural population in West Bengal

Dr. Mainak Ghosh[1,*], Dr. Bosumita Sinha[2], Dr. Kausik Bandyopadhyay[3] and Dr. Bulbul Mukhopadhyay[4]

[1] Assistant Professor, Department of Physiology, Murshidabad Medical College & Hospital, Station Road, Berhampore, West Bengal-742101.
[2] Associate Professor, Department of Physiology, R.G. Kar Medical College & Hospital, 1, Khudiram Bose Sarani, Kolkata-700004, West Bengal.
[3] Assistant Professor, Department of Biochemistry, Murshidabad Medical College & Hospital, Station Road, Berhampore, West Bengal-742101.
[4] Professor & H.O.D., Department of Physiology, R.G. Kar Medical College & Hospital, 1, Khudiram Bose Sarani, Kolkata-700004, West Bengal.
* Correspondence: drmainak79@gmail.com

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Abstract: Introduction: Subclinical hypothyroidism is described as a condition where the patients' serum ft4 is within normal limit , but serum TSH level is raised . These patients have limited or no clinical features of hypothyroidism. It is to be mentioned here that clinical hypothyroidism is biochemically denoted as an elevated TSH level with a decreased serum fT4 level along with florid symptoms of hypothyroidism. There are numerous researches on how clinical hypothyroidism affects the respiratory system, but there are scanty numbers relating to subclinical hypothyroidism, which may also lead to remarkable deficits in lung function. Evaluation of the respiratory system in subclinical hypothyroidism is the prime target of this study . Spirometry was our method of choice here since it is less expensive, smoother, and more readily available than other respiratory function tests.

Aims and Objective: To measure the Expiratory Flow Volumes – FEV1, FVC, FEV1%, FVC%, FEV1:FVC% and rates- PEFR(L), PEFR%, FEF_{25-75} (L), FEF_{25-75} %, in subclinical hypothyroid patients and their correlation with serum TSH level and serum fT4 level.

Materials and Methods: The current study was a cross-sectional study with a case-control design conducted at the physiology department of a tertiary hospital situated in West Bengal surrounded by rural population. The selection of 100 subjects (50 cases and 50 controls) was based on age, BMI, inclusion and exclusion criteria. Serum TSH and fT4 levels were measured, and the pulmonary function tests were examined using the RMS Helios 401 Spirometer. The statistical study was conducted using Microsoft Office 2007's SPSS-17 and Excel. The Student Independent T-test and the Pearson's Two-Tailed Correlation Study were used for the analysis. The threshold for statistical significance was a P value of $\leq$ 0.05 and P value $\leq$ 0.001 was considered as statistically highly significant.

Results: The pulmonary function parameters in active control subjects and in subclinical hypothyroidism patients were measured by spirometry . It was noticed all the projected study parameters of pulmonary function test were lowered considerably in subclinical hypothyroidism in respect with the control group. The dissimilarities of the FVC, FVC%, FEV1, FEV1%, PEFR(L), PEFR%, FEV1/FVC, FEF_{25-75} (L) are statistically important ($p \leq 0.05$). In SCH , significant negative correlation persists between TSH and FVC(L), between TSH and FEV1(L) and between TSH and FEV1%. In SCH patients, FVC(L) , FVC%, FEV1% and PEFR(L) have significant correlation with fT4 value.

Conclusions: The present study depicts that subclinical hypothyroidism also may cause disorders of lung function along with disturbances of ventilation. Simple spirometry may be used to test patients for the widely prevalent subclinical hypothyroidism affecting a good number of common people. This will aid in prompt patient management.

Keywords: SCH; PFT; FEV1; FVC; PEFR; FEF_{25-75} (L); PEFR(L); PEFR%.

1. Introduction

Subclinical hypothyroidism is described as a condition where the patients' serum ft4 is within normal limit , but serum TSH level is raised . These patients have limited or no clinical features of hypothyroidism [1]. Prevalence rate in different studies in different states of India have been estimated as 11.3% with 1:3.7 male and female ratio [2]. As many as 2-5% is the risk of development of overt hypothyroidism from subclinical hypothyroidism [3]. Thyroid hormones T3 & T4 have influences on all organ system of human body. They have enormous role in maintaining the normal function of respiratory system due to their massive effect in body metabolism [4]. Hypofunction of thyroid hormones leads to a number of malfunction of respiratory system starting from mild breathing trouble to ventilatory failure [5]. It can cause respiratory function disorders and ventilatory disturbances [6].

Hypothyroidism may depress the central neural control mechanism of respiration and involves the strength of inspiratory and expiratory muscles which is directly had a link related to the thyroid hormone levels [7]. Diaphragm is the prime inspiratory muscle that is involved [8]. Both these factors influences the pulmonary functions ; the impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism [9].

We have checked the sub-clinical thyroid patients and evaluated the extent of lung function impairment by simple spirometry. Although respiratory disease symptoms may not frequently the main complaint voiced by patients , lung functions can also be tangibly impacted, just like other important body systems [10]. Due to the potential for myopathy, patients with SCH have been evaluated specifically for inspiratory and expiratory effects. Diaphragm is the important inspiratory muscles that is involved [11]. This weakness can be very severe and be accompanied by hypercapnia and hypoventilation. Therefore, Cakmak et al. [10] found that patients with subclinical hypothyroidism experience a significant reduction in pulmonary function . The indices of lung function were assessed by the authors in people with subclinical hypothyroidism and in a healthy control group, and they discovered significantly lower values for FEV1,FEV1%,FVC, and FVC%. In the population of this present study area, no definite study in sub-clinical hypothyroidism patients has been performed on assessment of correlation of pulmonary function parameters with serum TSH & serum f T4. Our aim is to perform the spirometric assessment of lung function in control group along with in SCH patients group, to compare between the two groups and to find out whether any suggestive correlation is present between the spirometric parameters and thyroid parameters i.e. serum TSH & fT4.

2. Material and methods

This cross-sectional study of case control design performed in Department of Physiology of Burdwan Medical College & Hospital on 50 healthy control subjects and 50 subclinical hypothyroid patients. The study population was picked from patients attending the medicine OPD Hospital from February-2010 & continuing till January-2011 . In this study group, 100 cases were picked -50 normal subjects & 50 cases of subclinical hypothyroidism between the 20 to 50 years age group with no smoking habits. In the study, 50 patients of subclinical hypothyroidism were chosen based on laboratory results showing a TSH > 6.16 IU/ml and a normal serum Ft4 level between 0.8 and 2 ng/dl in the same group. Controls with normal serum TSH levels of 6.16 IU/ml and fT4 levels were chosen. BMI of both groups was lower than 30kg/M2.

2.1. Inclusion criteria for selecting the patients

- Age between 20 to 50 yrs,
- Body Mass Index less than 30 kg/m2.

2.2. Criteria of Exclusion for selecting the patients

- History of smoking,
- Any localised disease of lung and respiratory tract,
- Any systemic disease affecting the respiratory system,
- Persons engaged in an occupation that may affect the respiratory system.

2.3. Study parameters

1. Serum TSH: estimated by 'Quantitative EIA method' using RFCL-manufactured commercial"ELISCAN - TSH"- kit .Test principle : quantitative EIA.TSH can be assayed in the range of 0.39-6.16 μIU/ml using 50 μl serum samples.
2. Serum free T_4 :by 'Quantitative EIA method' using RFCL-manufactured commercial "ELISCAN - fT_4"-kit.Test principle: competitive EIA.
3. Using the RMS Helios 401 Spirometer to measure spirometric variables including FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF 25-75 (L), PEFR(L), and PEFR%.

The Forced Vital Capacity is the maximum amount of air that can be forcedly expelled from a maximum inspiration (FVC). The most significant variables observed are their ratios (FEV1/FVC), which measure the highest amount of air expelled in the first second of a forced expiration from a position of complete inspiration. Other factors include Mean Expiratory Flow Rate, Peak Expiratory Flow Rate (PEFR), and FEF 25-75%, which represents the middle 50% of FVC.

2.4. Methods used for the study

First, it was important to conduct record analyses, objective examinations, and proper review reports for each topic involving two combined groups. Subclinical hypothyroidism and control group were separated following confirmation of thyroid stimulating hormone (TSH) and serum free thyroxin(fT_4) values. Then Pulmonary Function Test was performed in each control and patient of study population.

Pulmonary function tests are noninvasive tests that determine the functional status of the lungs. The tests measure lung volumes, capacites, rates of flow, and gas exchange. Spirometry is the most accurate pulmonary function test available since it measures the volume of air inhaled at specific times, followed by a strong and complete expiration and then a maximum inhalation. Here RMS Helios 401 Spirometer was utilized to measure spirometric variables including FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF 25-75 (L), PEFR(L), and PEFR%. Then spirometric study was acted with Computerised RMS Helios 401 Spirometer and the spirometric parameters ,i.e. FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF_{25-75} (L), PEFR(L), PEFR% were determined in both the group.

2.5. Statistical analysis

After the collection of data from 50 subclinical hypothyroid patients and from 50 healthy control subjects master figures were prepared for both the groups and were analyzed using SPSS software version 17 and Microsoft Excel software of MS-office 2007 software package in computer. For data analysis, Pearson's two-tailed correlation study and Student independent t - test were done . To measure the significance level, "p" values were calculated. SPSS-17 was used for analysis . A P value of ≤ 0.05 was taken as the threshold for statistical significance, whereas a P value ≤ 0.001 was considered as statistically highly significant.

3. Results

Table 1. Participant demographic information

		Control Group (n=50)	**Subclinical hypothyroidism (n=50)**
Age		36.78±4.52	37.22± 4.42
Gender	Female	31	38
	Male	19	12
existing symptoms	Yes	0	21
	No	50	29

According to Table 1, the average ages of the participants with subclinical hypothyroidism and the control group are 37.22± 4.42 and 36.78±4.52 years, respectively. Therefore, there isn't a big age gap between the groups.

Table 2. Participants' values for thyroid function

	Group in control (n=50)			**Subclinical hypothyroidism (n=50)**		
	Mean	Standard deviation	Standard error	Mean	Standard deviation	Standard error
Ft4(ng/Dl)	1.4	0.26	0.04	1.26	0.24	0.04
TSH (μIU/ml)	2.12	0.62	0.09	12.08	4.11	0.64

Table 2 shows the mean TSH and fT4 values of the participants in sub-clinical hypothyroidism and control group

Table 3. The spirometric means of subjects with subclinical hypothyroidism and the control group

	Subclinical Hypothyroidism (N=41)			**Control Group (N=50)**			**t-Stats**	**p-Value**
	Mean	**Standard Deviation**	**Standard Error**	**Mean**	**Standard Deviation**	**Standard Error**		
FVC (L)	3.17	0.24	0.04	3.57	0.35	0.05	-6.529	<0.001
FVC%	97.76	2.46	0.38	106.20	2.80	0.40	-15.314	<0.001
FEV1 (L)	2.96	0.21	0.03	3.41	0.35	0.05	-7.501	<0.001
FEV1 %	89.37	2.62	0.41	98.64	2.53	0.36	-17.047	<0.001
FEV1/FVC (%)	93.63	1.60	0.25	95.53	2.00	0.28	-5.018	<0.001
FEF25-75(L)	5.36	0.35	0.05	5.98	0.35	0.05	-8.321	<0.001
FEF25-75%	78.29	4.54	0.71	78.78	3.72	0.53	-0.552	0.583
PEFR (L)	5.28	0.34	0.05	5.94	0.39	0.06	-8.568	<0.001
PEFR %	77.78	4.35	0.68	79.50	3.56	0.50	-2.034	0.045

Spirometry values in the control group are greater than those in the subclinical hypothyroidism group, as seen in Table 3. The differences between FEF 25-75 (L), PEFR(L), FVC, FVC%, FEV1, FEV1%, FEV1/FVC, and others are highly significant. The t values and P values for the following variables are : FVC (t= -6.529, P0.001), FVC% (t= -15.314, p0.001), FEV1 (t= -7.501, P0.001), FEV1% (t= -17.047, P0.001), FEV1/FVC% (t= 5.018, P0.001), and value of FEF 25-75 (L), PEFR (L) . All the above-mentioned values are statistically significant . However, while the difference in FEF25-75% between these two groups does not achieve statistical significance (t= -0.552, p =0.583), the difference in PEFR% is significant (t= -2.034, p = 0.045).

Table 4. Correlation between spirometric parameters and serum TSH level in sub-clinical hypothyroidism.

Spirometric Parameters	**TSH**	
	Pearson Correlation Coefficient (r)	**p-Value**
FVC (L)	-0.521	0.000
FVC%	-0.284	0.072
FEV1 (L)	-0.502	0.001
FEV1 %	-0.356	0.022
FEV1/FVC (%)	0.146	0.364
FEF25-75(L)	-0.237	0.136
FEF25-75%	-0.025	0.877
PEFR (L)	-0.264	0.095
PEFR %	0.020	0.902

Table 4 points to the presence of significant negative correlation between TSH & FVC(L), TSH & FEV1 and between TSH & FEV1%. The other parameters do not have significant correlation with TSH value. It points to the fact that in case of subclinical hypothyroidism patients , significant negative correlation persists between TSH and FVC (L) (r = -0.521, p < 0.001), between TSH and FEV_1 (L) (r= -0.502 , p=0.001) and between TSH & FEV_1 % (r= -0.356 , 0.022). The other spirometric parameters do not have statistically significant ($p \leq 0.05$) correlation with TSH value .

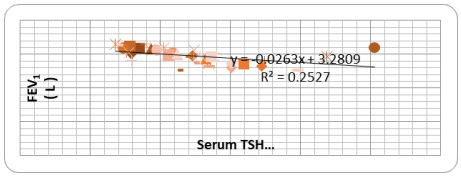

Figure 1. Correlation between TSH and FEV1 % values in the sub-clinical hypothyroidism

Figure 1 shows significant negative correlation persisting between serum TSH value and FEV1(L) [r= -0.502, $p \leq 0.001$].

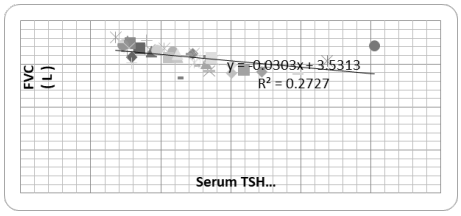

Figure 2. Correlation between TSH and FVC (L) values in the subclinical hypothyroidism patients

There is significant connection between serum TSH level and FVC(L) shown in Figure 2 (r0.521, p 0.001).

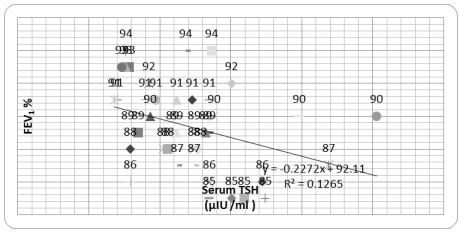

Figure 3. FEV1% and serum TSH levels are correlated in those with subclinical hypothyroidism

Figure 3 displays an inverse relationship between serum TSH levels and FEV1%, (r = -0.356, p= 0.022).

Table 5. Correlation between Ft4 value and Spirometry parameters in Subclinical hypothyroidism

Spirometric Parameters	**fT4**	
	Pearson Correlation Coefficient (r)	**p-Value**
FVC (L)	0.646	0.000
FVC%	0.462	0.002
FEV1 (L)	0.616	0.000
FEV1 %	0.462	0.002
FEV1/FVC (%)	-0.199	0.213
FEF25-75(L)	0.260	0.100
FEF25-75%	-0.032	0.840
PEFR (L)	0.374	0.016
PEFR %	-0.060	0.710

Table 5 shows the correlation between fT_4 value and spirometric parameters of subclinical hypothyroidism patients . It is obvious that FVC (L) , FVC % , FEV_1 (L) , FEV_1 % and PEFR (L) have significant positive correlation with fT4 value. The r value & the p value are (r=0.646 , $p \leq 0.001$) , (r = 0.462 , p =0.002) , (r = 0.616 , $p \leq 0.001$) , (r= 0.462 , p =0.002) and (r =0.374 , p = 0.016) respectively. The relations of fT4 and other spirometric parameters do not reach statistical significance ($p \leq 0.05$).

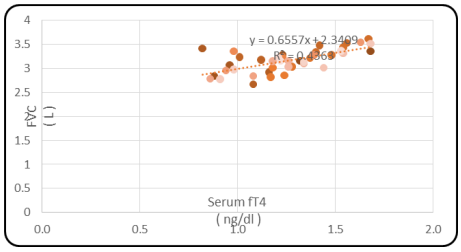

Figure 4. Correlation between fT_4 and FVC (L) values in the subclinical hypothyroidism patients

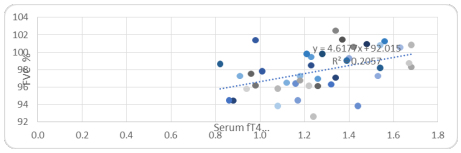

Figure 5. Correlation between serum fT_4 and FVC % values in the sub-clinical hypothyroidism patients

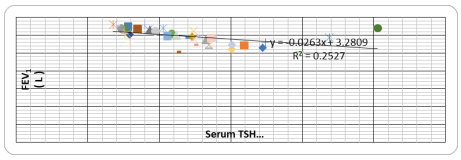

Figure 6. Correlation between serum fT4 and FEV1(L) values in the sub-clinical hypothyroid patients

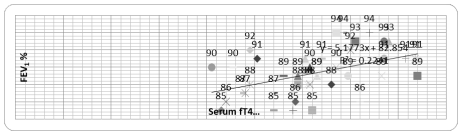

Figure 7. Correlation between fT_4 and FEV_1 % values in the sub-clinical hypothyroidism patients

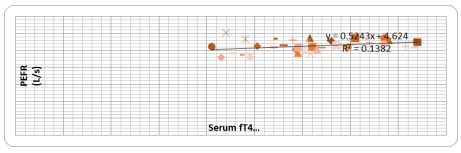

Figure 8. Correlation between fT_4 and PEFR(L) values in the sub-clinical hypothyroidism patients

Figures 4-8 show significant positive correlation between serum fT4 and FVC(L), FVC%, FEV1(L), FEV1% & PEFR respectively. In our study, 50 subclinical hypothyroidism patients and 50 healthy control subjects were selected.

1. Subclinical hypothyroid people have lower spirometric readings than the control group does. Only the difference in FEF 25-75% between these two groups fails to meet this requirement (p = 0.543), while the differences in FVC, FVC%, FEV1, FEV1%, FEV1/FVC, FEF25-75, PEFR, and PEFR% are all statistically significant (p 0.05).
2. In case of subclinical hypothyroidism patients , significant negative correlation persists between TSH and FVC(L) (r = -0.521 , $p \leq 0.001$), between TSH and FEV_1 (L) (r= -0.502, p=0.001) and between TSH & FEV_1 % (r= -0.356 , 0.022). The other spirometric parameters do not have statistically significant ($p \leq 0.05$) correlation with TSH value.
3. In subclinical hypothyroidism patients , FVC (L) , FVC % , FEV_1 (L) , FEV_1 % and PEFR (L) have significant positive correlation with fT4 value. The r value & the p value are (r=0.646 , $p < 0.001$), (r = 0.462 , p =0.002) , (r = 0.616 , $p < 0.001$) ,(r= 0.462 , p =0.002) and (r =0.374 , p = 0.016) respectively. The relations of fT4 and other spirometric parameters do not reach statistical significance ($p \leq 0.05$).

4. Discussion

Subclinical hypothyroidism depicts only initial changes in thyroid dysfunction. Even though hypothyroid patients may experience much impairment in respiratory function , pulmonary symptoms are rarely a serious issue. From mild dyspnea to deadly respiratory failure, the degree of pulmonary symptoms might vary [18]. The signs and symptoms of hypothyroidism include weakness of the inspiratory and expiratory muscles, insufficient alveolar ventilation as a result of depressed peripheral hypoxic and central hypercapnic ventilatory drives, and less than normal maximal ventilation capacity [19]. Both affects pulmonary functions. Accordingly, the impairment of pulmonary functions may be initiated at the subclinical stage of hypothyroidism [19]. These abnormalities indicate a restrictive lung disease and it is a clinical feature of hypothyroidism due to edema of the interstitial tissue and also due to respiratory muscle weakness as previously mentioned. In a study conducted in Egypt, the author assessed the maximal inspiratory and expiratory pressures to evaluate the strength of the inspiratory and expiratory muscles in patients with hypothyroidism and an equal number of controls who had normal thyroid function (n = 30). In comparison to the control group, both inspiratory & expiratory pressures were lower and statistically significant in hypothyroidism patients, which may indicate that the respiratory muscles are weaker in this condition [20]. In a study by Cakmak et al., patients with subclinical hypothyroidism were evaluated by their spirometric parameters . There were 60 healthy volunteers, 120 people with subclinical hypothyroidism, and 87 people with symptomatic hypothyroidism in this study. All of the observed spirometric measurements except for the forced vital capacity differences were smaller in the control group (FVC). When subclinical hypothyroidism was included, spirometric values were higher in the control group, and there was a statistically significant difference between the two groups in terms of FVC, FVC%, FEV1, and FEF25%-75% (P 0.05) in the control group. FEV_1/FVC ratio was comparable across all the three groups (i.e., clinical hypothyroidism, subclinical hypothyroidism and healthy controls). These findings are suggestive of restrictive pulmonary defect. If we can start treatment in subclinical hypothyroidism patients at very initial stage, it may slower the development of clinical hypothyroidism. By definition, theoretically in subclinical hypothyroidism no or minimal symptoms /clinical features are found. However, in our study, a sizable proportion of patients (58%) experienced one or more of the symptoms, including muscleache, weakness, somnolence, etc. It was also observed that, in line with the findings of Cakmak et al. [21], those clinical observations are also accompanied by anomalies in spirometry values. Lung function is moderately reduced in people with subclinical hypothyroidism, according to Cakmak et al. In our study, we also have noted the appreciable difference of the values of FVC, FVC%, FEV1, FEV1% between the subclinical hypothyroidism and the control group of healthy subjects and the differences are statistically significant. Cakmak et al. [21] detected a significant positive correlation between ft4 and FVC and FVC%. In our study, we also noted significant negative correlation between serum TSH and FVC(L) [r= -0.521, P $\leq$ 0.001], and FEV1(L) [r= -0.356, P=0.022], and FEV1% [r=-0.356, 0.022] in subclinical hypothyroidism group of cases. FVC(L), FVC%, FEV1(L), FEV1% also have significant positive correlation with fT4 level.

5. Conclusion

For comparison and contrast purposes, we assessed the pulmonary function of patients with subclinical hypothyroidism and a healthy control group in the current study. Spirometric values are higher in patients with subclinical hypothyroidism than in the control group. There are statistically significant alterations in the FVC, FVC%, FEV1, FEV1%, and FEV1/FVC (p 0.05). The relationship between TSH and FVC(L), FEV1(L), and FEV1% is persistent and significantly negative for patients with subclinical hypothyroidism. Furthermore, fT4 values have strong positive correlation with FVC(L), FVC%, FEV1(L), and FEV1% (p 0.05). Thus to conclude , our study shows that subclinical hypothyroidism may cause disorders of respiratory function and disturbances of ventilation . Simple spirometry, a non-invasive screening technique, may be used to find potential individuals who show no or minimal clinical signs and symptoms due to the presence of subclinical hypothyroidism in the general population. And thus doing so, we could help them with timely patient management. According to the study, subclinical hypothyroidism may even cause pulmonary function to be disturbed. Simple spirometry can identify people who are at risk of developing overt clinical hypothyroidism because subclinical hypothyroidism is common in the general population. Additionally, it aids in the timely treatment of those individuals.

Ethical Compliance

The study was approved by Institutional Ethics Committee of Burdwan Medical College & Hospital, having a memo no. BMC/PG/167(56) dated 14/01/2010.

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Conflicts of Interest: The authors declare no conflict of interests.

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