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RESEARCH ARTICLE

Pulmonary function tests in thyroid disorders

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ABSTRACT

Background: Worldwide thyroid diseases are one of the most common endocrine disorders. India is also no exception. Thyroid disorders affect all organ systems leading to decreased quality of life and long-term morbidity. The altered levels of thyroid hormone also affect respiratory system. They lead to disorders of respiratory function and disturbances in ventilation. **Aims and Objectives:** This study was aimed to explore the respiratory disease pattern in thyroid dysfunction (both hyperthyroid and hypothyroid). **Materials and Methods:** After taking clearance from institutional ethical committee, we undertook this case–control observational study. A total of 105 participants were included in the study, 60 euthyroid controls and 45 patients of thyroid disorder (hypothyroid = 30 and hyperthyroid = 15). Convenient sampling technique was used for the study, and simple random sampling technique was used for selecting control groups. Patients were then assessed for thyroid profile. Thyroid-stimulating hormone (TSH), fT3, and fT4 were measured by mini-VIDAS. Once diagnosed with thyroid disorder, these patients were subjected to a battery of pulmonary function test (PFT). We measured the PFT parameters of both cases and controls by SPIRODOC (Spiro PRO6.6 spirometry standard mode, version no. A23-OW-06145). Differences between the study group and controls were examined using SPSS version 19.0. The statistical analysis included one-way ANOVA with Tukey's Honest Significant Difference *post hoc* test. Pearson's correlation was calculated among various parameters. $P < 0.05$ was considered statistically significant with confidence interval of 95%. **Results:** The forced expiratory volume in 1(FEV1)/forced vital capacity (FVC) in euthyroids, hypothyroids, and hyperthyroid was 82.83 ± 1.09, 83.76 ± 2.80, and 83.3 ± 1.77, respectively. FVC in euthyroids was 3.29 ± 0.66, in hypothyroids 2.70 ± 0.52, and in hyperthyroids 2.97 ± 0.48. A restrictive pattern was found in hypothyroid patients whereas we could not find any significant difference in pulmonary functions of hyperthyroid patients when compared with euthyroids. We found a positive linear relation between FEV1 and TSH for both hyperthyroid and hypothyroids ($r = 0.54$ and $r = 0.19$, respectively). **Conclusion:** Our study shows a restrictive pattern with FEV1/FVC raised in hypothyroid whereas we could not find any statistically significant differences in PFT in hyperthyroid patients.

KEY WORDS: Thyroid Function; Pulmonary Function Tests; Hyperthyroid; Hypothyroid

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INTRODUCTION

Worldwide thyroid diseases are one of the most common endocrine disorders. India is also no exception. A study has shown that estimated 42 million people globally have suffered from the disease.[1] When the thyroid hormones produced by gland are less either due to structural or functional impairment,

resultant is a clinical state called as hypothyroidism. There is a wide range of symptoms ranging from subclinical condition with normal T3 and T4 levels with mildly elevated thyroid-stimulating hormone (TSH) to myxedema, end-organ effects, and multisystem failure.[2-6] The disease could be due to autoimmune inflammation of thyroid or goiter or excessive secretion of TSH from anterior pituitary gland. Hyperthyroidism is increased secretion of T3 and T4 with depressed levels of TSH. Its common causes are Graves' disease, toxic nodular goiter, and toxic adenoma. The prevalence of hypothyroidism is 11%[2] whereas that of hyperthyroidism is 1.3%[7].

Thyroid disorders affect all organ systems leading to decreased quality of life and long-term morbidity. The altered levels of thyroid hormone also affect respiratory system. They lead to disorders of respiratory function and disturbances in ventilation. There are studies which show restrictive pattern in hypothyroidism, whereas studies such as Iyer *et al*.[8] had found a mixed pattern of respiratory disease. We took this study to explore the respiratory disease pattern in thyroid dysfunction (both hyperthyroid and hypothyroid). There are very few studies which have compared euthyroids, hypothyroids, and hyperthyroids in one study and this is the novelty of our study.

MATERIALS AND METHODS

After taking clearance from the Institutional Ethical Committee, we undertook this case–control observational study. The study was conducted in the Department of Physiology and Department of Medicine, Subharti Medical College and associated Chhatrapati Shivaji Subharti Hospital, Meerut. The study period extended from November 2016 to June 2018, and a total of 105 participants were included in the study, 60 euthyroid controls and 45 patients of thyroid disorder (hypothyroid = 30 and hyperthyroid = 15), and the written informed consent was taken from all the participants in both Hindi and English. Participants in the study group were recruited from patients attending medicine outpatient department, and controls were recruited from hospital and college employees and people residing in the campus. Convenient sampling technique was used for the study, and simple random sampling technique was used for selecting control groups. The inclusion criteria included freshly diagnosed untreated hypothyroid and hyperthyroid males and females in the age group of 18–60 years. Patients who were on treatment for thyroid disease, anemic, smokers, and pregnant had cardiopulmonary disease, diabetes, hypertension, etc., were excluded from the study. After a thorough history and clinical examination, these patients were then assessed for thyroid profile. TSH, fT3, and fT4 were measured by mini-VIDAS. Once diagnosed with thyroid disorder, these patients were subjected to a battery of pulmonary function test (PFT). We measured the PFT parameters of both cases and controls by SPIRODOC (Spiro PRO6.6 spirometry standard mode, version no. A23-OW-06145). Each participant performed three trials (with at least two reproducible and acceptable maneuvers) of all parameters according to the American Thoracic Society recommendations.[9] The parameters included were forced vital capacity (FVC), forced expiratory volume in the 1st (FEV1) second, FEV1/FVC ratio, and peak expiratory flow rate (PEFR).

All values were expressed as mean ± standard deviation (SD). Differences between the study group and controls were examined using SPSS version 19.0. The statistical analysis included one-way ANOVA with Tukey's honest significant difference *post hoc* test. Pearson's correlation was calculated among various parameters. $P < 0.05$ was considered statistically significant with confidence interval of 95%.

RESULTS

One-way ANOVA shows no significant difference in age and height ($P = 0.2366$ and $P = 0.0915$, respectively). Weight (kg) and body mass index (BMI) (kg/m^2) showed significant difference among all the three groups ($P = 0.0003$ and $P = 0.0085$, respectively), and *post hoc* by Tukey–Kramer test showed significant difference [Table 1]. One-way ANOVA shows significant difference TSH, fT3, and fT4 in among all the three groups ($P = 0.0000$ for all the parameters), and *post hoc* by Tukey–Kramer test showed significant difference [Table 2]. One-way ANOVA showed no significant difference in FEV1/FVC and PEFR in all the three groups ($P = 0.0779$ and $P = 0.6844$, respectively). FVC and FEV1 showed significant difference among all the three groups ($P = 0.0003$ and $P = 0.0006$, respectively), and *post hoc* by Tukey–Kramer test showed significant difference when hypothyroid was compared with euthyroid [Table 3].

DISCUSSION

When we compared the three groups, euthyroid, hypothyroid, and hyperthyroid, we found that age and height

Table 1: Anthropometric and general measurements in control group and study groups

Parameters	Euthyroid (*n*=60)	Hypothyroid (*n*=30)	Hyperthyroid (*n*=15)	*P*	F/df
Age (years)	33.47±7.08	34.5±8.38	30.33±9.16	0.2366	1.4619/2,102
Weight (kg)	55.55±4.81	59.73±10.67*	50.4±6.47***$^{\#\#\#}$	0.0003	8.7489/2,102
Height (cm)	153.47±5.32	156.3±7.71	156.13±7.31	0.0915	2.4482/2,102
BMI (kg/m^2)	21.10±1.93	22.87±4.11**	20.12±4.24$^{\#\#}$	0.0085	4.9931/2,102

Values are mean±SD. *Comparison with controls and $^{\#}$comparison between hypothyroid and hyperthyroid. *P<0.05, **P<0.01, ***P<0.001, $^{\#\#}P$<0.01, $^{\#\#\#}P$<0.001. BMI: Body mass index, SD: Standard deviation

were comparable in the three groups (mean age ± SD was 33.47 ± 7.08, 34.5 ± 8.38, and 30.33 ± 9.16 years, respectively and mean height ± SD was 15.47 ± 5.32, 156.63 ± 7.71, and 156.13 ± 7.31 cm, respectively). However, these differences were not statistically significant ($P = 0.23$ for age and 0.09 for height) [Table 1]. When weight and BMI were compared between the three groups and also between the two groups, we found a statistically significant difference ($P < 0.001$).

The TSH levels in euthyroid were 2.92 ± 0.97, in hypothyroids were 27.41 ± 18.88, and in hyperthyroids were 0.43 ± 0.34. The fT3 in euthyroids was 5.32 ± 0.97, whereas in hypothyroids, it was 1.11 ± 0.53 and in hyperthyroids, it was 22.27 ± 9.78. fT4 levels also differed significantly among the three groups (euthyroid = 11.76 ± 1.89; hypothyroid= 7.67 ± 2.15; and hyperthyroid= 46.3 ± 19.80). All the three groups differed significantly in thyroid profile, ($P = 0.00$) and also, the difference was statistically significant when hypothyroids were compared with euthyroids, hyperthyroids with euthyroids, and between hypothyroids and hyperthyroids [Table 2].

Our study shows a restrictive pattern with FEV1/FVC raised in hypothyroid as compared to controls (83.76 ± 2.80 vs. 82.83 ± 1.09) and a decreased FVC in hypothyroids as compared to controls (2.70 ± 0.52 vs.3.29 ± 0.66, $P < 0.001$) [Table 3]. FEV1 is also less in comparison to control with $P < 0.05$. Our study is in accordance with Martinez *et al*.[10] and Ladenson *et al*.[11] and Valjevac *et al*.[12] who also found statistically significant difference in the pulmonary function parameters. Cakmak *et al*.[13] observed a significant reduction in FVC, FEV1, FEV1%, and forced expiratory flow 25–75 in patients with subclinical hypothyroidism as compared with control participants. Sharifi and Amari[14] reported about 87% of restrictive abnormality ranging from mild-to-moderate grade among the hypothyroid participants which improved significantly on treatment.

There are numerous effects of hypothyroidism on the respiratory system. The frequently encountered symptoms are fatigue and dyspnea on exertion, but we rarely found these symptoms in the absence of primary respiratory pathology. Valjevac *et al*.[12] in their study on hypothyroidism showed restrictive changes that were reversible after treatment with levothyroxin. It has been shown that muscle strength is reduced in hypothyroidism and improves with treatment. The attributed this to both myopathy and neuropathy.[12] The changes observed in our spirometry findings can be explained on the basis of researches by some investigators which suggest that respiratory center depression, interference of neural conduction or neuromuscular transmission to the respiratory muscles, and respiratory muscles diseases in hypothyroidism may cause alveolar hypoventilation which may affect central ventilator control and can impair ventilation. Hypothyroidism is also associated with reduced surfactant phospholipids, phosphatidylglycerol, and phosphatidic acid along with increase in surface active lipids phosphatidylserine and phosphatidylinositol in alveolar epithelium. All these decrease alveolar septation and reduce lung compliance and surfactant adsorption. Deposition of mucopolysaccharide in the lungs may cause fibrosis and alveolar wall thickening with loss of elastic tissue and this may increase the work of breathing. All these changes may reduce ventilator lung functions. The decreased value of FVC and FEV1 and increased value of FEV1/FVC in untreated hypothyroids patients as compared to healthy controls can be attributed to low serum T4 which may cause respiratory muscle weakness and decreased contractile strength. Low thyroid hormone levels also decrease lung elastic tissue and increase the work of breathing.

Very few authors such as Iyer *et al*.[8] had found a mixed pattern of respiratory disorder and have attributed it to parenchymal and non-parenchymal causes. The reported cases of this pattern are only 3.5%–4%.[8]

Table 2: Thyroid function test in control group and study groups

Parameters	Euthyroid (*n*=60)	Hypothyroid (*n*=30)	Hyperthyroid (15)	*P*	F/df
TSH	2.92±0.97	27.41±18.88***	0.43±0.34***###	0.0000	66.0271/2,102
fT3	5.32±0.97	1.11±0.53***	22.27±9.78***###	0.0000	170.4263/2,102
fT4	11.76±1.89	7.67±2.15***	46.3±19.80***###	0.0000	147.8880/2,102

Values are mean±SD. *Comparison with controls and #comparison between hypothyroid and hyperthyroid. ***P<0.001, ###P<0.001.
TSH: Thyroid-stimulating hormone, SD: Standard deviation

Table 3: PFT in control group and study group

Parameters	Euthyroid	Hypothyroid	Hyperthyroid	*P*	F/df
FVC	3.29±0.66	2.70±0.52***	2.97±0.48	0.0003	8.6704/2,102
FEV1	2.88±0.56	2.43±0.34*	2.64±0.56	0.0006	7.9290/2,102
FEV1/FVC	82.83±1.09	83.76±2.80	83.3±1.77	0.0779	2.6178/2,102
PEFR	16.56±78.05	6.25±0.37	6.53±0.58	0.6844	0.3806/2,102

Values are mean±SD. *Comparison with controls and #comparison between hypothyroid and hyperthyroid. *P<0.05, ***P<0.001.
PFT: Pulmonary function test, FVC: Forced vital capacity, FEV1: Forced expiratory volume in 1, PEFR: Peak expiratory flow rate, SD: Standard deviation

We compared the pulmonary function parameters between the hyperthyroid and euthyroid controls. The mean value of FVC in hyperthyroid was 2.97 ± 0.48. Although FVC of hyperthyroid showed a lower mean value in comparison to control 2.97 ± 0.48 versus 3.29 ± 0.66, this was statistically non-significant. FEV1 was also found to be lower in hyperthyroid (mean value = 2.64 ± 0.56) as compared to controls 2.88 ± 0.56, but this difference was also found to be non-significant statistically. The mean value of FEV1/FVC in hypothyroid was 83.3 ± 1.8, whereas in euthyroid, it was 82.8 ± 1.1, and this difference in mean values was found to non-significant statistically. Hence, to summarize, we could not found any statistically significant differences in PFT in hyperthyroid patients.

We found a positive linear relation between FEV1 and TSH for both hyperthyroid and hypothyroids (r = 0.54 and r = 0.19, respectively). Valjevac *et al*.[11] found negative linear relation between FEV1 and TSH. TSH for both hyperthyroids and hypothyroids (r = −0.01 and r = −0.388, respectively).

Valjevac *et al*.[12] found no correlation on comparing FEV1/FVC and hypothyroid (r = −0.011). Similar finding was also found in our study (r = −0.0002). When they compared FEV1/FVC and TSH in hypothyroids, they found a negative linear relation (r = −0.302) and we found a positive linear relation (r = 0.32).

Limitation of Study

Smaller sample size was the limitation of this study, and we also could not see the effect of treatment on pulmonary functions in these patients. We would recommend to do this study with a larger sample size and to measure pulmonary functions both before and after the treatment.

CONCLUSION

We found a restrictive pattern of pulmonary functions in hypothyroids whereas we could not find any significant changes in hyperthyroid patients.

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