Original Article

Prevalence of thyroid dysfunction in chronic obstructive pulmonary disease patients in a tertiary care center in North India

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Abstract

Introduction: Thyroid dysfunction can cause inspiratory and expiratory muscle weakness in patients with or without chronic obstructive pulmonary disease (COPD) Thyroid dysfunction in COPD results in increased frequency of exacerbation thus lead to poor quality of life. It may further increase cardiovascular disease risk thereby increasing mortality. **Aims and Objectives:** This study was conducted to evaluate the prevalence of thyroid dysfunction and hence that the quality of life of COPD can be improved **Materials and Methods:** This is a cross-sectional – prevalence study. The study was conducted over a period of 1 year from August 2015 to July 2016. The study group was consists of male and female COPD patients diagnosed with spirometry and severity was determined according to the global initiative for chronic obstructive lung disease classification criteria. The patients were enrolled in this study from medicine outpatient department (OPD), respiratory OPD and those admitted to indoor wards of Medicine Department. Patients were screened for thyroid dysfunction. **Results:** Out of 171 patients, thyroid dysfunction was present in 43 patients. All of them were hypothyroid. The prevalence of thyroid dysfunction was 25%. In Stage A it was 20.5%, Stage B 25.7%, Stage C 23.4%, and in Stage D 30.4%. Thyroid dysfunction was associated with more frequent exacerbation. **Conclusion:** Thyroid dysfunction is a common extrapulmonary manifestation in COPD patients. It is associated with frequent exacerbations which affect the quality of life in these patients. Early detection and proper management can improve the quality of life in these patients.

Keywords: Chronic obstructive pulmonary disease, exacerbation, thyroid dysfunction

Introduction

Chronic obstructive pulmonary disease (COPD) is a growing cause of morbidity and mortality worldwide and will be the third leading cause of death by 2020. According to the global initiative for chronic obstructive lung disease (GOLD), COPD is defined as a preventable and treatable disease with significant extrapulmonary effects that may contribute to its severity in individual patients.[1] Thyroid hormones play an important role in the regulation of thermogenesis and metabolism. Serum thyroid hormone levels change during systemic illnesses. Previous studies reported changes in thyroid hormone levels in respiratory diseases.[2] Hypothyroidism may also cause alveolar hypoventilation, decreased lung volumes, upper airway obstruction, depression in respiratory stimulus, and respiratory failure. Hypoxia and decreased ventilator response to hypercapnia have been demonstrated in patients with hypothyroidism.[3,4] Diaphragmatic dysfunction and myopathies can be seen in patients with hypothyroidism. Inspiratory and expiratory muscle strength is linearly related to the degree of hypothyroidism.[3,4] The myopathic manifestations may be related

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to the impaired expression of myosin heavy chains IIb or to impaired neuromuscular transmission.[5] Weakness correlates with the severity of hypothyroidism and is reversed by replacement therapy. Probably impaired muscle energy metabolism, resulting from a defect in glycogen breakdown or mitochondrial function and hypothyroid myopathy, contributes to the reduced exercise capacity in COPD patients. Hypoxia and hypercapnia cause destruction in sella turcica and pituitary gland dysfunction. During COPD, together with hypoxia, peripheral metabolism of thyroid function changes and thyroid hormone levels decrease in patients with very severe COPD. Several characteristics of COPD patients could potentially increase their likelihood of developing hypothyroidism or hyperthyroidism. Impaired thyroid function in COPD may present as subclinical hypothyroidism (ScH), overt hypothyroidism, and nonthyroidal illness syndrome.[6] It is well-known that severity of airway obstruction, hypoxemia, and systemic inflammation may predispose to not only nonthyroidal illness syndrome but also ScH and overt hypothyroidism.[7] Furthermore, hyperthyroidism may impair respiratory muscle function and exercise in COPD patients. In fact, both maximal inspiratory pressure and expiratory pressure decrease, with increasing severity of hyperthyroidism. Abnormalities in pulmonary function also may be observed because of decreased respiratory muscle performance, decreased lung compliance, and increased ventilator requirements.

Materials and Methods

Study population

This cross-sectional – prevalence study was carried out in a tertiary care center in North India over a period of 1 year from September 2015 to August 2016. The study group was consists of male and female COPD patients diagnosed with spirometry and severity was determined according to the GOLD classification criteria. The patients were enrolled in this study from Medicine OPD, Respiratory OPD, and those admitted to indoor wards of Medicine Department.

Inclusion criteria

All patients (men and women) age >40 years and <80 years diagnosed to have COPD by spirometry and given the consent for participation in the study.

Exclusion criteria

Individuals who did not give consent, patients with known chronic chest diseases other than COPD, patients with other diseases or illnesses that might affect thyroid functions, for example, endocrinal, metabolic, autoimmune disorders, etc., patients on any regular medication, other than the COPD drugs, that might affect thyroid functions, such as iodine-containing drugs, amiodarone and immunosuppressive drug, pregnant female.

Methodology

A detailed clinical history and physical examination carried out for every patient. In the clinical history, duration of COPD with a history of exacerbation and treatment were elicited. History of the presence of risk factors such as smoking, exposure to fumes (biomass), and the presence of any other chronic disease was inquired, history of previous thyroid dysfunction or treatment of thyroid dysfunction taken. Thereafter, the detailed physical examination was carried out. Complete hemogram, blood urea nitrogen, serum creatinine arterial blood gas analysis, pulmonary function test by spirometry, and X-ray chest posteroanterior-view FT3/FT4/thyroid stimulating hormone (TSH) was done.

Statistical tools employed

The statistical analysis was performed using SPSS (Statistical Package for Social Sciences) Version 15.0 Statistical Analysis Software, IBM corporation. The values were represented in number (%) and mean ± standard deviation (SD). Statistical formulas which were used are mean, SD, Chi-square test, analysis of variance, *post hoc* Tests (Tukey-honestly significant difference), and bivariate correlation. Level of significance is denominated by "*P*" value. Level of significance: $P > 0.05$ - not significant, $P < 0.05$ — significant, $P < 0.01$ - highly significant, and $P < 0.001$ is very highly significant.

Results

In this study, a total of 171 patients were enrolled after diagnosed as a case of COPD by spirometry. Age of patients ranged from 40 to 80 years. Mean age of the study population was 57.75 ± 9.81 years. Statistically, there was no significant association between age and COPD Stage. Majority of patients were male (73.7%) and male to female ratio of the study was 2.8:1. Maximum (32.7%) had two or more episodes of exacerbation followed by those having one episode not requiring hospital admission (24%). There were 22.2% who had no exacerbation history and 21.1% of patients had one exacerbation requiring hospital admission. Nearly 56.7% of the patients had the modified Medical Research Council (MMRC) disability score >2 and 43.3% had MMRC disability score 1–2. A total of 35 (20.5%) patients fulfilled the criteria of GOLD Stage A, 44 (25.7%) Stage B, 40 (23.4%) Stage C, and remaining 52 (30.4%) fulfilled the criteria for Stage D. A total of 43 (25.1%) patients had TSH levels above cutoff levels or had a history of treatment of hypothyroidism. None of the patients had TSH levels below cutoff level and T3/T4 levels above cutoff levels; hence, no case of hyperthyroidism was recorded. Overall prevalence of thyroid dysfunctions was 25% [Table 1].

Prevalence of thyroid dysfunction was 28.8% ($n = 13/45$) among females as compared to 23.8% ($n = 30/126$) among males, though the prevalence of thyroid dysfunction was higher in females than males yet this difference was not statistically significant.

Prevalence of thyroid dysfunction ranged from 8.6% (Stage A) to 32.7% (Stage D). The prevalence of thyroid dysfunction was higher in higher stages of COPD as compared to that in lower stages of COPD this difference was statistically significant ($P = 0.047$) [Table 2].

Prevalence of thyroid dysfunction among patients without exacerbation was 15.8%. It was 14.6% among those having one exacerbation without hospital admission. Maximum prevalence (38%) was among those having one exacerbation requiring hospital admission. The prevalence of thyroid dysfunction was 30.4% in those having two or more exacerbation episodes. Statistically, there was a significant difference in prevalence of thyroid dysfunctions among different degrees of exacerbations ($P = 0.034$) [Table 3 and Figure 1].

Discussion

In this study, the age of cases ranges between 40 and 80 years, with a mean of 57.75 ± 9.81 years. A similar study conducted on Indian population by Bhattacharyya *et al.* concluded that mean age of COPD patients was 65.32 ± 9.58 years which is comparable to our study.[8] In a study conducted by Yılmaz *et al.* the mean age of the patients was 62.1 ± 8.9 years. The finding of their study also correlates well with our observation.[9] 73.7% of the patients were male and male to female ratio of the study was 2.8:1. The reason for this difference is that in India, COPD is more prevalent among males due to a higher prevalence of smoking among males as compared to females. A similar study was conducted on Indian population by Jindal *et al.* concluded that the overall prevalence figures of COPD were 5% in men and 2.7% in woman (aged 35 or above.[10] In our study, 95 patients were current smoker or former smoker. In a study done by Gupta *et al.*, a total of 83 COPD patients were enrolled out of which 73 were male and 10 were female and depending on smoking history nonsmokers were 15, current smokers were 28 and former smokers were 40.[11] Au *et al.* studied that in comparison to current smokers, ex-smokers had a significantly reduced risk of COPD exacerbation after adjusting for age, comorbidity, markers of COPD severity and socioeconomic status (adjusted hazard ratio [HR] 0.78, 95% CI 0.75–0.87). The magnitude of the reduced risk was dependent on the duration of smoking abstinence (adjusted HR: Quit <1 years, 1.04; 95% CI: 0.87–1.26; 1–5 years 0.93, 95% CI: 0.79–1.08; 5–10 years 0.84, 95% CI: 0.70–1.00; ≥10 years 0.65, 95% CI: 0.58–0.74; linear trend <0.001).[12] Smoking cessation is associated with a reduced risk of COPD exacerbations, and the described reduction is dependent on the duration of abstinence.

Table 1: Prevalence of thyroid dysfunction (*n*=171)

Variable	Number of cases (%)
Thyroid dysfunction	43 (25.1)
Hypothyroidism	43 (25.1)
Hyperthyroidism	0

Table 2: Association of thyroid dysfunction with Global Initiative for Chronic Obstructive Lung Disease stage (*n*=171)

Stage	Total number	Positive for thyroid dysfunction (%)
Stage A	35	3 (8.6)
Stage B	44	10 (22.7)
Stage C	40	13 (32.5)
Stage D	52	17 (32.7)

χ^2=7.967 (df=3); *P*=0.047

Table 3: Association between thyroid dysfunction and exacerbation of chronic obstructive pulmonary disease (*n*=171)

Characteristic	Total number (*n*=171)	Number with thyroid dysfunction (*n*=43) (%)
No exacerbation	38	6 (15.8)
One not requiring hospital admission	41	6 (14.6)
One requiring hospital admission	36	14 (38.9)
Two or more	56	17 (30.4)

χ^2=8.594 (df=3); *P*=0.034

Maximum (32.7%) had two or more episodes of exacerbation followed by those having one episode not requiring hospital admission (24%). There were 22.2% who had no exacerbation history, and 21.1% had one exacerbation requiring hospital admission. A total of 56.7% had MMRC disability score >2 and 43.3% had MMRC disability score 1–2. The reason for this was that the maximum patients in our study were indoor patients.

A total of 43 (25.1%) patients had TSH levels above cutoff levels or had a history of treatment of hypothyroidism. None of the patients had TSH levels below cutoff level and T3/T4 levels above cutoff levels; hence, no case of hyperthyroidism was recorded. The overall prevalence of thyroid disorders in our study was found to be 25% [Table 1]. Prevalence of thyroid disorder was 28.8% (n = 13/45) among females as compared to 23.8% (n = 30/126) among males, though the prevalence of thyroid disorder was higher in females as compared to males yet this difference was not statistically significant.

Prakash *et al.* in 2014 conducted a study and 96 cases of acute exacerbation of COPD were analyzed, and he found that 62 (64.58%) patients had lower levels of T3, T4, and TSH.[13]

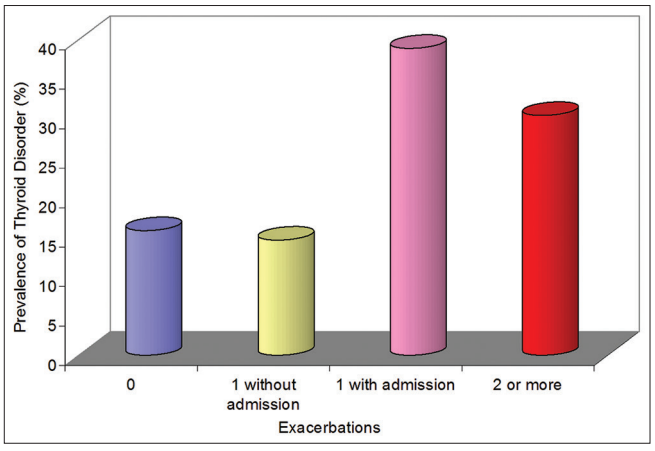

Figure 1: Association between thyroid dysfunction and exacerbation of chronic obstructive pulmonary disease (n = 171)

Singh *et al.* evaluated a total of 201 cases of COPD of which 130 (64.6%) were having thyroid disorders. Hypothyroidism was diagnosed in 119 (59.2%) cases and hyperthyroidism in 11 (5.4%) cases.[14] Prevalence of thyroid disorder was 8.6% (Stage A) 22.7% (Stage B), 32.5% (Stage C), 32.7% (Stage D) [Table 2]. The prevalence of thyroid dysfunction was higher in higher stages of COPD as compared to that in lower stages of COPD this difference was significant statistically ($P = 0.047$). Singh *et al.* evaluated a total of 201 cases of COPD of which 130 (64.6%) were observed to be having thyroid disorders. About 24.4% in stage I, 40.8% in stage II, 31.3% in stage III, and 3.5% in stage IV.[14]

Prevalence of thyroid disorder among patients without exacerbation was 15.8%. It was 14.6% among those having one exacerbation without hospital admission. Maximum prevalence (38.9%) was among those having one exacerbation requiring hospital admission. The prevalence of thyroid disorder was 30.4% in those having two or more exacerbation episodes. Statistically, a significant difference was observed in the prevalence of thyroid disorders among different degrees of exacerbations ($P = 0.034$) [Table 3].

Sarinc Ulasli *et al.*, did a study in which they studied 128 patients and showed that TSH values and exacerbation frequency have a positive correlation.[15]

Aras *et al.* in 2014 conducted a study and 21 patients within the exacerbation period of COPD were evaluated and found that 7 (33.33%) patients had free T3 levels below the normal values, and 3 (14.28%) patients had TSH levels below the normal values.[16]

Limitation of our study

The study was conducted in a single center. The number of patient enrolled in our study was small; hence, this study might need validation on a much larger scale for exact estimation of prevalence of thyroid dysfunction. Further, a prospective study may be needed to see the effect of thyroid dysfunction on COPD its effect on the duration of hospital stay and mortality and morbidity.

Conclusion

Thyroid dysfunction is present in a significant proportion of patients with COPD, especially in the severe form of COPD (GOLD Stage C and D). It results in frequent exacerbation of COPD which may results in an extra burden on patients both in the form of cost and in terms of quality of life. Thus, it is essential to focus on a comprehensive way of management of COPD and its comorbidities rather than primarily treating the pulmonary symptoms. Studies have shown that COPD patients with thyroid dysfunction have more dyspnea and a greater risk of hospitalization either due to acute exacerbations, or other complications. Thus, it may warrant extensive research to elucidate the exact mechanisms to understand the relationship between thyroid dysfunction and COPD.

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Conflicts of interest

There are no conflicts of interest.

References

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD) Global Strategy for the Diagnosis, Management, and Prevention of COPD (revised 2013).
2. Martinez FJ, Bermudez-Gomez M, Celli BR. Hypothyroidism. A reversible cause of diaphragmatic dysfunction. Chest 1989;96:1059-63.
3. Siafakas NM, Salesiotou V, Filaditaki V, Tzanakis N, Thalassinos N, Bouros D, *et al.* Respiratory muscle strength in hypothyroidism. Chest 1992;102:189-94.
4. Laghi F, Adiguzel N, Tobin MJ. Endocrinological derangements in COPD. Eur Respir J 2009;34:975-96.
5. Prakash YS, Gosselin LE, Zhan WZ, Sieck GC. Alterations of diaphragm neuromuscular junctions with hypothyroidism. J Appl Physiol (1985) 1996;81:1240-8.
6. Yen PM. Genomic and nongenomic actions of thyroid hormones. In: Braverman LE, Utiger RD, editors. The Thyroid: A Fundamental and Clinical Text. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 135-50.
7. Silva JE. Intermediary metabolism and the sympathoadrenal system in hypothyroidism. In: Braverman LE, Utiger RD, editors. The Thyroid: A Fundamental and Clinical Text. 9th ed. Philadelphia: Lippincott Williams & Wilkins; 2005. p. 817-23.
8. Bhattacharyya P, Paul R, Ghosh M, Dey R, Dey R, Barooah N, *et al.* Prevalence of osteoporosis and osteopenia in advanced chronic obstructive pulmonary disease patients. Lung India 2011;28:184-6.
9. Yılmaz D, Çapan N, Canbakan S, Besler HT. Dietary intake of patients with moderate to severe COPD in relation to fat-free mass index: A cross-sectional study. Nutr J 2015;14:35.
10. Jindal SK, Aggarwal AN, Gupta D. A review of population studies from India to estimate national burden of chronic obstructive pulmonary disease and its association with smoking. Indian J Chest Dis Allied Sci 2001;43:139-47.
11. Gupta B, Kant S, Mishra R, Verma S. Nutritional status of chronic obstructive pulmonary disease patients admitted in hospital with acute exacerbation. J Clin Med Res 2010;2:68-74.
12. Au DH, Bryson CL, Chien JW, Sun H, Udris EM, Evans LE, *et al.* The effects of smoking cessation on the risk of chronic obstructive pulmonary disease exacerbations. J Gen Intern Med 2009;24:457-63.
13. Prakash R, Harish M, Suryanarayana V, Padma Priya M. Evaluation of thyroid functions in chronic obstructive pulmonary disease. World J Med Sci 2014;11:57-8.
14. Singh L, Jain A, Agrawal A, Tandon R, Kumar H. A study of prevalence of thyroid disorders in chronic obstructive pulmonary disease patients at a tertiary care center in U.P. Int J Contemp Med Res 2016;3:1239-42.

15. Sarinc Ulasli S, Bozbas SS, Ozen ZE, Ozyurek BA, Ulubay G. Effect of thyroid function on COPD exacerbation frequency: A preliminary study. Multidiscip Respir Med 2013;8:64.
16. Aras G, Kanmaz D, Purisa S, Kadakal F, Yentürk E, Atabey F, *et al.* Are thyroid functions changing in patients with exacerbated COPD? Thyroid functions in exacerbated COPD. JAREM 2014;1:18-24.