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RESEARCH ARTICLE

PREVALENCE OF THYROID DYSFUNCTION IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE: A SINGLE CENTRE STUDY

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ABSTRACT

Introduction: COPD is defined as a disease state characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible and associated with multiple episodes of exacerbations. Thyroid dysfunction can be one such cause of acute worsening. Any thyroidal illness if present and leading to increased complication/exacerbation will go unnoticed and result in increased morbidity and mortality. **Aims and Objectives:** To determine thyroid function in COPD patients, to see if there is difference in thyroid function in COPD patients with different mMRC, Spirometry and GOLD stages. **Methodology:** Thyroid function tests and spirometry were conducted on 174 chronic obstructive pulmonary disease patients and compared with mMRC score, GOLD category and Spirometry stages. The statistical analysis was done using SPSS (Statistical Package for Social Sciences) Version 15.0 statistical Analysis Software. Appropriate tests were applied. **Results:** The most common thyroid disorder found in the study was hypothyroidism (16.1%) and subclinical hyperthyroidism was found in 15(8.6%) patients. No cases of overt hyperthyroidism or non-thyroidal illness were seen. The prevalence of hypothyroidism was significantly higher in cases compared to controls. Prevalence of thyroid disease increased as the severity of COPD increased. It is also seen that the prevalence of thyroid disease in patients with high risk of exacerbation is 20.8% as hypothyroidism and 12.3% as subclinical hypothyroidism which is significantly higher (p value = 0.006) to 8.8% and 3.3% in low risk group respectively. **Conclusion:** Thyroid dysfunction can be one of the major reasons for morbidity in COPD patients. The study shows a high prevalence of thyroid dysfunction in COPD patients especially the ones with more severe disease. Hence routine application of thyroid function test in COPD patients must be done.

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is currently the fourth leading cause of death in the world (Lozano, 2012) but is projected to be the 3rd leading cause of death by 2020. Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by persistent respiratory symptoms and airflow limitation that is not fully reversible (Longo, 1998). *COPD* includes emphysema and chronic bronchitis3. Causes of COPD are manifold and include tobacco smoking, indoor air pollution, long term occupational exposure of chemical agents and fumes, genetic factors such as severe hereditary deficiency of alpha -1 antitrypsin deficiency, older age and childhood infections as the major ones (Global Initiative for Chronic Obstructive Lung Disease, 2019).

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Having knowledge about the causes can help in preventing COPD but once COPD has developed it becomes necessary to understand the pathophysiology behind the exacerbations as they are the major cause of frequent hospitalization of COPD patients and invariably serve as the final nail in the coffin of the struggling COPD patients. Exacerbations fundamentally reflect acute worsening of expiratory flow limitation, and there is evidence for both increased airway inflammatory activity and worsening airway obstruction as plausible explanations (O'Donnell, 2006). It is reasonable to assume that worsening airway inflammation is the primary inciting event of COPD exacerbations and may be caused by bacteria, viruses, or environmental pollutants, including cigarette smoke. Thyroid dysfunction can be one such cause of acute worsening of expiratory flow limitation in the absence of airway inflammation (Tantucci, 2013). Different patterns of thyroid disorder in COPD patients have been described in various

studies. Some say that hypothyroidism is more prevalent (Chaudhary, 2018) whereas others find non thyroidal illness as most common pattern (Karadag, 2007); while few others ended up with hyperthyroidism[8] as the significant leading pattern there also are studies showing no thyroid illness[9] at all. The actual prevalence of the concurrent thyroid illness in patients with COPD remains uncertain. Hence any thyroidal illness if present and leading to increased complication/exacerbation will go unnoticed and result in increased morbidity and mortality. It is of due importance to find out thyroid dysfunction very early in COPD patients and treat the same in order to lessen the burden of the morbidity and frequent hospitalization. In order to be able to do this we need to find out the true prevalence of thyroid dysfunction in COPD patients so as to ascertain that applying a screening thyroid function test is beneficial.

MATERIALS AND METHODS

This is a cross sectional study conducted on 174 chronic obstructive pulmonary disease patients visiting the outpatient department and/or admitted to medicine wards of Maharana Bhupal government hospital, RNT Medical College Udaipur during September 2017 to September 2019. Adetailed clinical history, history of exacerbations, History of presence of risk factor and presence of any other chronic disease was inquired. A detailed physical examination was carried out which include general and systemic examination. All subjects underwent Spirometry in presence of medical personnel. Data from the highest amount of flow- volume curve Forced Vital Capacity (FVC) and Forced Expiratory Volume in 1 Second (FEV1) were used for calculations using the computerized spirometer Helios 702.

Inclusion Criteria: All patients of COPD (presenting with symptoms of chronic cough, dyspnea and/or sputum production and who show post bronchodilator FEV1/FVC<0.7) and willing to undergo assessment of thyroid function and be part of the study and not qualifying the exclusion criteria.

Exclusion Criteria

- Individuals who did not give consent for the study.
- Patients with known chronic chest diseases other than COPD.
- Patients with other diseases or illnesses that might affect thyroid functions e.g., 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 drugs.
- Pregnant female.

OBSERVATIONS AND RESULTS

A total of 174 COPD patients and 50 matched controls were enrolled in the study during the study period of 2 year from September 2017 to August 2019.In our study the age of cases ranges between 37 and 80 year, with a mean of 61.13±8.54 year for cases and 60.89±9.0 for controls. Maximum number (47.1%) of patients were in age group 61-70 year followed by those aged below 50 year (14.4%), 51-60 year (25.3%) and >70 year (13.2%). Of the total 174 patients of COPD 145 were male constituting 83.3% of all the study subjects and 29 were females being 16.7% of the total study subjects. The control group was comparable with 88% males and 12% female (p = 0.423). Most patients in the study belonged to the rural area. The study had 75.3% rural patients and 24.7% urban patients. Out of the 174 patients included in the study, 143 patients were current smoker or had a history of smoking constituting 82.2% of the total patients. Only 31 patients (17.8%) did not smoke ever. It is found that there is higher risk of exacerbation among smokers as compared to non-smokers. (odds ratio = 2.45, p = 0.018) (Table 1). Frequency wise distribution of the study patients into four groups based on exacerbation history found that 106(60.92%) patients qualified as high risk for exacerbation (one exacerbation requiring hospitalization or two or more exacerbations in the past one year). Only 68 (39.1%) patients belonged to the low risk for exacerbation group (one or less exacerbation in the last one year). As per the mMRC (modified Medical Research Council) dyspnea scores the patient distribution showed maximum patients (29.3%) with mMRC score of 1 followed by 22.4% patients with mMRC score 2.Only 8.1% patients had mMRC score of 4.All the patients were divided into four groups as per their spirometry staging with 33.91% qualifying as stage 3 being the group with maximum patients and stage 1 had the lowest number of patients with 18.4% of the total.

Table 1: Various parameters studied in study population

Parameters	Values /No./%
No. patients	174
Age	61±8.69
Male	145(88%)
Female	29(12%)
Smokers	143(82.2%)
Non smokers	31(17.8%)
Rural	131(75.3%)
Urban	43(24.7%)

Table 2: Distribution of smokers in various stages of COPD

	Stage 1 No. (%)	Stage 2 No. (%)	Stage 3 No. (%)	Stage 4 No. (%)	P value
Smoking	24(75.0)	32(78.05)	51(86.44)	36(85.71)	0.441
Non smokers	8(25.0)	9(21.95)	8(13.56)	6(14.29)	
Total	32(100)	41(100)	59(100)	42(100)	

Table 3. Prevalence of thyroid dysfunction (n=174)

		Subject		
Variable		Cases No. (%)	Control No. (%)	P value
Hypothyroidism	Subclinical	7(4.0)	1(4.0)	0.008
	Overt	21(12.1)	0(0)	
Hyperthyroidism	Subclinical	15(8.6)	1(2.0)	0.1
	Overt	00	00	
Euthyroid		131(75.3)	46(92.0)	
Total		174(100)	50(100)	

Table 4. Comparing results of this study with other studies

Study	Thyroid status	
	Hypothyroidism	Hyperthyroidism (including subclinical forms)
Present study	16.1	8.6
Kumar et al. (2013)	13.2	4.9
Lalit Singh et al. (2016)	59.2	5.2
Shyam Chand Chaudhary et al. (2018)	25.1	0
Prabhu et al. (2019)	67	0
Western studies (Sevinc Sarinc Ulasli, 2013; Ali Eman, 2016; Okutan, 2004)	0	0

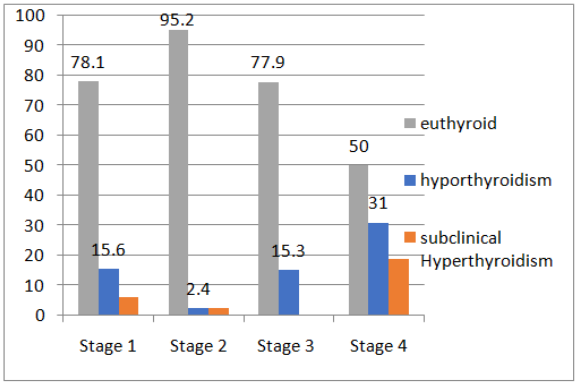

Chart 1. Prevalence of thyroid dysfunction according to stage

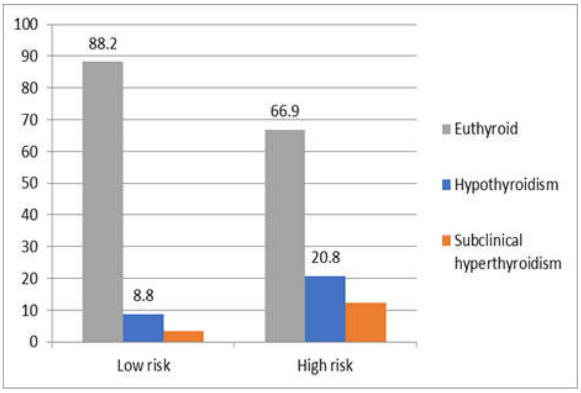

Chart 2. Prevalence of thyroid dysfunction according to exacerbation risk

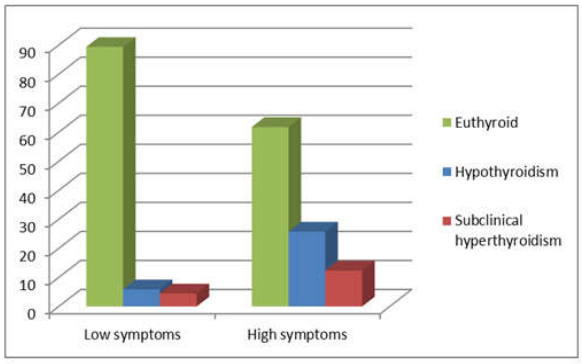

Chart 3. Prevalence of thyroid dysfunction according to symptom severity (n= 174)

The cases were equally distributed with respect to smokers and non-smokers and no significant difference was found in stages among the two (p value = 0.441). Thus, the cases appear to be well matched in regards to smoking. The most common thyroid disorder found in the study was hypothyroidism (16.1%) which was significantly higher compared to the control group (p=0.008).Subclinical hyperthyroidism was found in 15(8.6%) patients but the prevalence was not significant compared to control (p = 0.1).No cases of overt hyperthyroidism or non-thyroidal illness were seen in either groups (Table 3). It is seen that hypothyroidism (subclinical and overt) is more prevalent in stage 4 patients (13%). Similarly, hyperthyroidism is also more prevalent in stage 4 COPD. The association is significant (p = <0.001). It is seen that the prevalence of thyroid disease in patients with high risk of exacerbation is 20.8% as hypothyroidism and 12.3% as subclinical hypothyroidism which is significantly higher (p value = 0.006) to 8.8% and 3.3% in low risk group respectively.

The prevalence of hypothyroidism is significantly (p<0.001) higher in patients with high symptoms group compared to those of low symptoms group.

DISCUSSION

The disability associated with COPD is quite high and exacerbations add another level of difficulty in the lives of such patients. So, any attempt to find the associated factors and correct them could be very effective in treating a COPD patient. Thyroid function derangements have great impact on metabolic rate, ventilation mechanics and cardiovascular system's performance. So early identification of such a derangement in COPD patients could be of immense value in improving patients' symptom severity and further exacerbations. Present study was carried out with this aim of finding the actual prevalence of thyroid disease in patients of COPD in the medicine and respiratory medicine department of RNT medical college (inpatient as well as outpatient). Most of our patients hailed from the rural areas (75.28%). This is in accordance with Toshita Kalkana's study[14] which reasons out the cause as exposure to biomass combustion fuels inside the home, which lead to hazardous indoor air effluents that are associated with an increase of COPD and is worse in the rural areas where houses are more poorly ventilated. Out of 174 patients in our study 143 (82.18%) patients were smoker and 31 (17.82%) were non-smoker. This show the odds of having a smoking history in COPD patients are very high. Patient distribution on the basis of exacerbation risk shows that in the present study there were 96 patients in high risk group while 68 patients belonged to low risk group. Shyam Chand Chaudhary[6] *et al* study had 91 with low risk and 100 with high risk patients. The difference is due to all of their patients being inpatient ones while we also included the outpatient visitors who have a milder disease (Table 2). All the patients were divided into four groups as per their spirometry staging for evaluation of thyroid dysfunction across various stages. In this study 59(33.91%) patients belonged to stage 3 being the group with maximum patients and stage 1 had the lowest number of patients with 32(18.4%) of the total. There are 41(23.56%) and 42(24.14%) patients of stage 2 and stage 4 respectively.

The finding is comparable to Shyam Chand Chaudhary[6] *et al* study. The most common thyroid disorder found in patients of COPD as observed in this study is hypothyroidism with 16.1% of total patients 8.6% patients have sub clinical hyperthyroidism. No cases of overt hyperthyroidism or non-thyroidal illness were seen (Table 3). In a study done by Kumar H *et al*[15] in Bikaner in 2016 on 456 patients revealed the prevalence of hyperthyroidism and hypothyroidism to be 5.9% and 13.2% respectively which is comparable to the present study with a slightly higher prevalence in ours. T Sobhy *et al*[12] did not find any case of thyroid dysfunction in the COPD patients nor did H.A. Abo El-Yazed *et al*[8] and other international studies. Whereas Indian studies reported high number of thyroid diseases for instance Lalit singh *et al*[13]reported that 59.2% (119) of his study patients had hypothyroidism, 5.5% (11) had hyperthyroidism and mere 35.3% (71) of the patients were normal. Similarly, Shyam Chand Chaudhary *et al* found 25.1% (43 patients) having hypothyroidism (overt or subclinical). None of their patients had hyperthyroidism or non-thyroidal illness. Prabhu *et al*[14] study results showed the prevalence of thyroid dysfunction in the form of hypothyroidism was observed in 67 out of 100 COPD study subjects and he did not report any case of

hyperthyroidism or non-thyroidal illness (Table 4). The possible reason for finding no cases of thyroid diseases in COPD patients in western studies was probably due to exclusion of all previously diagnosed thyroid diseases and better health facilities leading to early diagnosis of the thyroidal illness. Even this study excludes previously diagnosed thyroid diseases but still finds 16.1% of patients having hypothyroidism and 8.6% patients having subclinical hyperthyroidism. This could be due to less frequent contact with health facilities in younger age and hence the longer lag period in the diagnosis of thyroid disease. This also evident from other Indian studies (Chaudhary, 2007; Vijayaragavan, 2019) where the thyroid disease prevalence was higher. In this study it is seen that most of the COPD patients discovered to have thyroid dysfunction belonged to spirometry stage 4 (very severe disease). This is in agreement to studies done by Shyam Chand Chaudhary *et al*. (2018) Lalit Singh *et al* and Prabhu *et al*. (2019) (Chart 1). This study also finds that thyroid diseases were significantly higher in patients with higher risk of exacerbation and with higher symptom severity (Chart 2 and 3). Studies done by Madhuri *et al*. (2013), Ulasli *et al*. (2013) and H.A. Abo El-Yazed *et al*. (2013) are in similar agreement except that their studies had values towards upper normal limit and no overt disease.

Conclusion

Thyroid dysfunction can be one of the major reasons for morbidity in COPD patients. The study shows a high prevalence of thyroid dysfunction in COPD patients especially the ones with more severe disease. Hence routine application of thyroid function test in COPD patients must be done. This becomes more significant in view of the large difference noted in prevalence among other studies. The prevalence database is incomplete at most centres of the country and the few studies done suggest a higher prevalence of thyroid dysfunction in COPD patients, so a recommendation to carry out further studies at varied centres to assess prevalence for the local population is also given.

Conflict of interest: Nil

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