

# Thyroid Stimulating Hormone and Hemoglobin Status in Patients Suffering from Chronic Obstructive Pulmonary Disease

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## Abstract

**Introduction:** Chronic obstructive pulmonary disease (COPD) is a respiratory disease characterized by chronic airflow limitation due to the destruction of lung parenchyma and airways. COPD is associated with several extrapulmonary manifestations that could be the expression of the systemic inflammatory state of COPD.

**Materials and Methods:** Serum thyroid stimulating hormone (TSH) assay and hematologic investigations such as hemoglobin, hematocrit, blood indices and peripheral smear examination were performed in 50 patients with COPD and 51 healthy age-matched volunteers (control group).

**Result:** The study result showed that a significant proportion of COPD patients had an imbalance in TSH level in blood and majority were suffering from a normocytic normochromic type of anemia.

**Conclusion:** COPD is associated with an imbalance in TSH level in blood. Although COPD was thought to cause polycythemia, the current study showed that a significant proportion of patients have normocytic normochromic type of anemia.

**Key words:** Anemia, Chronic obstructive pulmonary disease, Hemoglobin, Thyroid stimulating hormone

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is the chronic inflammatory airways diseases with partially or fully irreversible airflow obstruction.<sup>1</sup> Altered endocrine function can worsen the clinical manifestations of COPD through several mechanisms.<sup>2</sup> Several characteristics of COPD patients could increase their likelihood of developing altered thyroid hormone level in blood. Only few studies and data are available on the prevalence of thyroid diseases among patients suffering from COPD.<sup>3</sup> Thyroid dysfunction has been influential known effects on respiratory system, including upper airway obstruction,

respiratory muscle weakness, sleep apnea, alveolar hypoventilation, and pleural effusion.<sup>4</sup> Anemia seems to be a common feature in COPD, although its real prevalence remains to be determined. Recent data support that; low haemoglobin (Hb) concentrations can also have a detrimental impact on mortality in COPD patients.<sup>5</sup>

## MATERIALS AND METHODS

This study was accomplished by examining the COPD patients attending medicine outpatient department and pulmonary clinic of the tertiary referral hospital at coastal Karnataka. Informed, written consent from the patients and control group were taken, before including them to this study. Ethical Clearance from the College Ethics Committee has been obtained.

### Subjects

A total of 50 patients were selected randomly as the subjects (Group 1) who came to the hospital during a period from June 2013 to June 2014.

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Detailed medical history was taken, followed by physical examination and chest X-rays (postero-anterior view) in order to establish the diagnosis of COPD.

Criteria for selection of study group (Group 1) are as follows:

#### Inclusion Criteria

Diagnosis of COPD based on current Global Initiative for Chronic Obstructive Lung Disease guidelines.

#### Exclusion Criteria

- Patients with known chronic chest diseases other than COPD
- History of malignancy or hematologic disorder
- Those had clinical or diagnosed evidence of thyroid disease or previous thyroid surgery
- History of gastrointestinal or other hemorrhage
- History of chronic alcoholism and liver disease
- We also excluded patients with anemia related vitamin B12 and folate deficiency or other chronic disorders by taking thorough clinical history and physical examination.

Control group (Group 2) consisted of 51 apparently healthy individuals. The control group was recruited with their voluntary consent from the outpatient clinic of other departments who came for minor ailments or minor surgical procedures. Detailed medical history, through physical examination were also done on Group 2 as on Group 1 before selection.

Venous blood samples for hormonal assay were collected into plain blood collection tube, following an overnight fast. Using mini Vidas biomerieux analyzer, thyroid stimulating hormone (TSH) level was measured. Meanwhile hemoglobin (Hb), hematocrit and blood indices were estimated by collecting blood in ethylene diamine tetraacetic acid anticoagulant and test performed using lab life hematology three-part differential premier analyzer. Peripheral smears were prepared from each sample and reported after staining with leishman's stain.

TSH level of 0.25-5  $\mu$  IU/ml is taken as normal reference range for both the sexes. Hb level of 13.5-16 g/dl for male whereas, 12.5-15 g/dl for female is taken as normal reference limits, and if Hb is less than its lower reference limit for the sex of the individual, then it is considered as anemia.

Statistical analysis was performed using the SPSS computer package version 20.0. The mean  $\pm$  standard deviation (SD) was used for quantitative variables. Independent samples *t*-test was applied, to assess the differences in means

of quantitative variables between patients and controls. *P*-value and confidence intervals were calculated. *P* < 0.05 was considered as statistically significant.

## RESULTS

Mean age of the sample was  $52.7 \pm 5.75$  SD years. In study group (Group 1) 40 patients were male and 10 were female. majority of the patients (66%) were ex-smokers and they were clinically stable at the time of inclusion to study (Table 1), 35 patients had been clinically stable for at least 3 months and 15 had clinical signs of COPD exacerbation. 80% were male and 20% were female. In the control group (Group 2) 19.6% gave a history of smoking, 35.3% were male and 64.7% were female (Table 1). Significant thyroid hormonal abnormalities were detected among established moderate to the severe COPD patients. The mean  $\pm$  SD of TSH, in the focus population, was  $1.04 \pm 0.41$   $\mu$  IU/ml (Table 2).

The mean  $\pm$  SD of Hb, in the study population was  $10.07 \pm 0.72$  g/dl (Table 3). Out of 50 patients (Group 1), 35 showed decreased Hb in blood, of which 32 were the normocytic normochromic type and 2 were macrocytic anemia and one was the dimorphic type of anemia. Nine patients showed polycythemia and rest with Hb within normal reference range.

**Table 1: Characteristics of patients and control group**

Characteristics	COPD patients	Control
Sex		
Male	40/50	18/51
Female	10/50	33/51
Smoking (%)		
Yes	66	19.6
No	34	80.4

COPD: Chronic obstructive pulmonary disease

**Table 2: Comparison of thyroid stimulating hormone level in COPD patients and control population**

TSH	COPD patients	Control
TSH in $\mu$ IU/ml		
Range	1.64	3.64
Mean $\pm$ SD	$1.04 \pm 0.41$	$1.89 \pm 0.82$

COPD: Chronic obstructive pulmonary disease, SD: Standard deviation

**Table 3: Comparison of Hb level in blood in COPD patients and control population**

Hb	COPD patients	Control
Hb in g/dl		
Range	3.60	3.90
Mean $\pm$ SD	$10.07 \pm 0.72$	$12.92 \pm 0.96$

COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, Hb: Hemoglobin

Statistical analysis showed  $P$ -value were  $P < 0.05$  for both TSH and Hb and were considered statistically significant.

TSH was within normal limits in both groups however, in the study group (Group 1) the values were toward upper normal limits when compared to their values in the control group (Group 2).

## DISCUSSION

COPD was estimated to become the third leading cause of death and fifth leading cause of disability by the year 2020.<sup>6</sup> Abnormalities in thyroid hormone regulation are encountered frequently in non-thyroidal diseases.<sup>7</sup> Since thyroid hormones regulate the metabolic rate, impaired thyroid function is associated with respiratory workload.<sup>8</sup> The thyroid hormone augments metabolic rate by enhancing mitochondrial oxidation.<sup>9</sup> There is also a significant relationship between TSH levels and COPD exacerbation frequency which suggests that the detection of impairment in thyroid function can decrease exacerbation number and improve the quality of life in COPD patients.<sup>10</sup> Study conducted by El-Yazed *et al.* showed that COPD is associated with the impairment of thyroid gland function with increased mean values of free T3 in these patients but with no significant change in TSH level. Whereas in our study, there was a significant change in TSH level in COPD patients compared to control group.<sup>11</sup>

Study by Madhuri *et al.* showed that Mean serum TSH was within normal limits but had lower values than controls in COPD patients, in the present study we got the similar findings with respect to TSH level in blood.<sup>8</sup>

As far as Hb level in blood is concerned, it has since long been known that COPD causes polycythemia secondary to erythrocytosis caused by hypoxia present in advanced cases of COPD.<sup>12</sup> Contrary to common thinking, recently some studies have shown that some COPD patients had anemia rather than erythrocytosis.<sup>13,14</sup> However, the prevalence of anemia in COPD remains unclear and varies widely. This variability depends on the population under study (stable COPD or patients hospitalized for acute exacerbation), the tools to identifying anemic subjects, and the definitions used for anaemia.<sup>15</sup> It occurs relatively frequently in COPD patients and is related to the presence of inflammation; it is an understudied issue in COPD, but may be of great importance in this disease.<sup>16</sup> Inadequate Hb levels could aggravate tissue hypoxia, worsen dyspnea, and limit exercise tolerance in COPD patients.<sup>17,18</sup> Anemia of chronic disease is an immune disorder with an inflammatory component, which is seen in numerous chronic diseases. Inflammatory cytokines interfere with the normal

process of erythropoiesis by exerting various effects on pathogenesis of this form of anaemia.<sup>6</sup> It has considered that COPD is a disease likely to be associated with anemia of chronic disease or anemia of inflammation.<sup>13</sup> The underlying mechanisms of this type of anemia is complex, could be attributed to dysregulation in iron homeostasis, production of erythropoietin and impaired proliferation of erythroid progenitor cells.<sup>6</sup>

Study conducted by El-Korashy *et al.* showed that almost half of patients with COPD have anemia which is in accordance with our study.<sup>19</sup>

Study by Attaran *et al.* also showed that anemia is an underestimated issue in COPD and occurred relatively frequently in these patients.<sup>14</sup>

In our study, we have highlighted the incidence of TSH imbalance and anemia in COPD patients and were based on hypothesis that correction of TSH imbalance and anemia in COPD may improve the outcome and quality of life in COPD patients. Another study with a larger sample size is required for better determination of the correlation between TSH, anemia and COPD. Furthermore, extensive studies are also required to identify the exact underlying mechanism of TSH imbalance and cause of anemia in COPD patients.

## CONCLUSION

COPD is associated with an imbalance in TSH level in blood. Although COPD was thought to cause polycythemia, the current study showed that a significant proportion of patients have the normocytic normochromic type of anemia. Further studies with larger sample sizes are required for better determination of these correlations and to confirm our conclusions.

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