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Research Article

Cognitive Impairment in Chronic Obstructive Pulmonary Disease: A Cross-Sectional Study at A Tertiary Care Centre

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Abstract
COPD is characterized by a progressive and irreversible airway obstruction and lung inflammation that is diagnosed using spirometry, and more specifically an $FEV_1/FVC < 0.70$. Cognitive impairments in COPD patients are manifested in the changes in the attention, memory, and executive functions and are caused by hypoxic damage to neurons. The purpose of this research was to establish the proportion of patients with COPD who have cognitive impairment and the relationship between the two. The study was carried out between December 2018 and December 2019 and involved 95 COPD patients. Information gathered included socio-demographic and behavioral factors, spirometry and arterial oxygen saturation. The results showed that the prevalence of MCI was 32 percent among the participants. 6 percent of COPD patients, and its prevalence rises in proportion to the disease's progression ($p<0.001$). Since cognitive impairment is related to poor health and survival in COPD patients, it is necessary to detect and raise awareness about it.

Keywords: Chronic Obstructive Pulmonary Disease, Cognitive Impairment, Spirometry, Arterial Oxygen Saturation, Mild Cognitive Impairement.

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INTRODUCTION

COPD (Chronic Obstructive Pulmonary Disease)is a common respiratory disease with features of irreversible airflow obstruction and chronic inflammation in the lungs. The condition is usually identified using spirometry, and the FEV_1/FVC post bronchodilator ratio is less than 0.7 confirming the diagnosis[1]. India, the largest democratic country in the world, which is experiencing the process of globalization and industrialization, has a highly heterogeneous population with different sociodemographic characteristics and cultural attitudes. A recent cross-sectional questionnaire survey conducted across the country projected the COPD prevalence to be 3.49% in India, with rates ranging from 1.1% in Mumbai to 10% in Thiruvananthapuram[2]. Also, the mortality rate due to COPD in India is over 500,000 per year, which is four and a half times the total of the USA and Europe.

Globally, the World Health Organization (WHO) estimated that there were 251 million cases of COPD in 2016, and 3.17 million deaths in 2015[3]. More than 90% of COPD mortalities happen in LMICs(Low and Middle Income Countries), and India and China contribute to 66% of global COPD mortality because of the large population size[3]. In India, COPD prevalence is estimated to be between 6.5% and 7.7% according to McKay et al.[4]. COPD used to be more prevalent in men than in women, but the prevalence rate is almost equal in both sexes due to the rising use of tobacco products by women in developed nations and indoor air pollution in developing nations.

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COPD patients have other diseases that affect them, like as cardiac diseases, diabetes mellitus, hypertension and psychological diseases[9]. Of these, cognitive impairment is a significant and clinically relevant complication that impacts patients' social and mental health. Cognitive dysfunction in COPD patients can be from mild to moderate and severe and can involve attention, concentration, memory, information processing, and executive functions. This impairment has a detrimental effect on the quality of life and the disease, its treatment, and functioning [10,11]. COPD and cognitive impairment are related in a way that is not fully understood yet. COPD is defined by a gradual decline in FEV1, an increase in end expiratory lung volume, hypoxemia, hypercapnia, pulmonary hypertension and cor pulmonale[12]. These changes can cause progressive hypoxia, increased blood viscosity, pulmonary vascular resistance, and reduced cerebral blood flow, which in turn cause neuronal damage and cognitive impairment. However, cognitive impairment in COPD is underrecognized and poorly managed in clinical practice, although it is a significant clinical concern [13,14].

The objectives of this study were to establish the proportion of the COPD patients with cognitive impairment and to compare the level of cognitive impairment between the COPD patients of different severity. From December 2018 to December 2019, 95 patients diagnosed with COPD were included in the study. The socio-demographic and behavioral information were gathered by a semi-structured questionnaire. The cognitive status of the patients was evaluated by the Mini-Mental State Examination (MMSE) that was adapted for the studied population. This paper brings to light the problem of cognitive impairment in COPD patients and stresses the need for its inclusion in COPD treatment. The incorporation of cognitive assessments into the daily practice of COPD management is beneficial for patients.

Aim

The aim of this study were to assess the prevalence of cognitive impairment in COPD patients at a tertiary care centre and to determine the association between the extent of cognitive impairment and the severity of COPD in the study sample.

Objectives

To estimate the proportion of COPD patients attending a tertiary care center who have cognitive impairment over a period of one year.

To find the association between cognitive impairment and the severity of COPD in the study group.

To determine arterial oxygen saturation levels in COPD patients with cognitive impairment.

REVIEW OF LITERATURE

Mechanics of Ventilation

Respiration is the process of the exchange of gases between the atmosphere and lungs through the respiratory tracts with the help of pressure differences generated by the contraction of the diaphragm and chest muscles. Pulmonary ventilation is the process of change in the lung's gas content during the process of breathing in and out. Two primary forces are involved in ventilation: It is the action of the inspiratory muscles and the elastic recoiling of the lungs during the filling of the lungs with gases, and the movement of gases from the region of higher pressure to the region of lower pressure. To understand the mechanics of ventilation, three pressures must be looked at.

Atmospheric Pressure: The pressure exerted by the air outside the body.

Intraalveolar Pressure (Intrapulmonary Pressure): The pressure within the alveoli.

Intrapleural Pressure: The pressure within the pleural cavity (15).

Respiratory Volumes and Capacities are crucial for assessing pulmonary function. They are measured using a spirometer, which quantifies the air volumes involved in breathing. The primary lung volumes include:

Tidal Volume (TV): Approximately 0.5 L of air moved in or out of the lungs with each breath.

Inspiratory Reserve Volume (IRV): About 3.3 L of additional air that can be inhaled with maximum effort.

Expiratory Reserve Volume (ERV): Approximately 1 L of air that can be expelled beyond the tidal volume.

Residual Volume (RV): About 1.2 L of air remaining in the lungs after maximal exhalation (18).

Factors such as age, sex, body build, and physical conditioning affect lung volumes and capacities. Typically, lung capacity peaks in early adulthood and declines with age (19).

2.2. Physiology of Ventilation

Partial pressure of CO2 (PACO2) is influenced by the balance between CO2 diffusing from pulmonary blood and CO2 being eliminated via alveolar ventilation (20). During exercise or non-steady-state conditions, variations in CO2 output may occur due to impaired tissue CO2 clearance and regional differences in lung CO2 concentration (21,22).

CO2 transport in blood occurs mainly in three forms: dissolved in plasma, as bicarbonate, and as carbamino compounds. About 70% of CO2 is transported as bicarbonate, a reaction catalyzed by carbonic anhydrase in red blood cells. The accumulation of $HCO3^-$ is balanced by a chloride shift to maintain electrical neutrality (23). CO2 binding to hemoglobin is influenced by the oxygenation state of the hemoglobin, with deoxygenated hemoglobin having a greater CO2 carrying capacity (24).

2.3. Pathophysiology in COPD

COPD is primarily caused by cigarette smoking in Western countries and environmental pollution in developing nations (25). The toxic agents from smoking and pollution injure airway epithelium, leading to inflammation and structural changes. In

some smokers, inadequate repair processes contribute to chronic airflow obstruction, even after cessation of smoking (26).

Oxidative stress in COPD is driven by external sources like cigarette smoke and internal production of oxidants due to bronchial inflammation. Antioxidant systems like glutathione and the heme oxygenase (HO)-1 pathway are compromised in COPD, contributing to disease progression (27). Protease-antiprotease imbalance also plays a significant role, with proteases degrading lung matrix components and contributing to emphysema (28).

Neutrophils increase oxidative stress and protease activity, while macrophages release oxidants and growth factors that perpetuate inflammation and structural changes in the lungs (29). The presence of dendritic cells and B-lymphocytes in COPD adds to the complexity of the immune response, with potential implications for novel therapeutic strategies (30, 31).

2.4 COPD Diagnosis and GOLD 2018 Guidelines

COPD diagnosis involves clinical evaluation and spirometry testing according to the presence and nature of the patient's symptoms. According to GOLD 2018, COPD is characterized by persistent respiratory symptoms and reduced lung capacity caused by airway and/or alveolar inflammation and destruction from significant exposure to toxic substances (36). Diagnosis is made based on the presence of symptoms like dyspnea, cough, and or sputum production. Spirometry confirmation is obtained by demonstrating a FVC<FEV1 ratio of less than 0. 70, which signifies obstructive airflow limitation. (36).

2.5 COPD and its Severity

Assessing COPD severity involves understanding the difference between the 'severity of illness' and the 'severity of disease.' Disease severity encompasses the risk of death and overall disability, while illness severity focuses on the patient's suffering and functional impairment (61). COPD severity assessment combines various markers, including respiratory symptoms, medication use, hospitalization history, and home oxygen use (62). A study by Bednarek et al. found that many COPD patients had moderate to severe airflow limitation, with only a small percentage previously diagnosed (63). The impact of disease severity on exacerbations is significant, with frequent exacerbations leading to substantial health and economic burdens (65). Spirometry, measuring airflow limitation, remains a critical tool for assessing COPD severity, though clinical judgments without spirometry may lead to underestimation of severity (69)(70). In the Birmingham COPD Cohort study, patients with low SpO2 levels were more likely to be ever-smokers and obese, highlighting the importance of monitoring oxygen levels in managing COPD (70).

MATERIALS AND METHODS

Study Design

This research uses a cross-sectional descriptive study among COPD patients attending the outpatient department of Respiratory Medicine at Pushpagiri Institute of Medical Science and Research Centre. The study is carried out in the Department of Physiology and the Department of Respiratory Medicine of the same college in Thiruvalla.

Study Period and Study Population

Data collection for the study was conducted from December 2018 to December 2019.

The study population included only patients having COPD who were attending the outpatient department of Respiratory Medicine. The subjects had to fulfill some criteria for inclusion and signed a consent form. The sample consisted of 95 patients, 45 to 80 years of age.

Inclusion and Exclusion Criteria

The study included COPD patients aged 40 and older from the outpatient department of Respiratory Medicine, who provided informed consent. It specifically targeted individuals aged 45 to 80. Exclusions were made for those unwilling to consent, individuals with psychiatric disorders, and those with a history of cerebrovascular accidents. This selection aimed to ensure a representative and relevant patient population.

Sample Size

The sample size was determined from the formula derived from Leslie et al., given the percentage of COPD patients with cognitive impairment as per Fekri et al. (44.82%). Using 95% confidence level and absolute precision of 10%, the sample size was estimated to be 95. The formula used for this calculation is: n = (1. 96)2 * 0. 5 * (1- 0. 5) / 0. 10^2 = 95. 04.

$$n = \frac{Z^2(1-\alpha/2) \times P(1-P)}{d^2}$$

where $P = 44.82\%$. The resulting sample size was 95.

Study Tools

The survey questionnaire was conducted with the help of a semi-structured questionnaire that included questions on socio-demographic and behaviour aspects. The Mini Mental State Examination (MMSE) was used to evaluate the patients' cognitive function. Spirometry was used to assess the pulmonary function whereas the oxygen saturation levels in the blood were assessed using pulse oximeter.

Method of Data Collection

A detailed explanation of the study procedures was provided. Data on socio-demographic and behavioural variables were collected via a semi-structured questionnaire. Cognitive function was assessed using a pilot-tested, interviewer-administered MMSE questionnaire. Spirometry values and arterial oxygen saturation levels were measured using standard techniques.

Study Variables

Cognitive Impairment: Assessed using MMSE scores, categorized as:

No Cognitive Impairment: 24-30

Mild Cognitive Impairment: 18-23

Severe Cognitive Impairment: 0-17

Severity of COPD: Determined by post-bronchodilator FEV_1 values:

GOLD 1 (Mild): $FEV_1 \geq 80\%$ predicted

GOLD 2 (Moderate): $50\% \leq FEV_1 < 80\%$ predicted

GOLD 3 (Severe): $30\% \leq FEV_1 < 50\%$ predicted

GOLD 4 (Very Severe): $FEV_1 < 30\%$ predicted

Arterial Oxygen Saturation: Measured using pulse oximetry.

Operational Definition

Cognitive impairment in COPD patients is defined and categorized based on MMSE scores as follows:
Mild Cognitive Impairment: MMSE score between 18 and 23
Severe Cognitive Impairment: MMSE score between 0 and 17
No Cognitive Impairment: MMSE score between 24 and 30

Data Analysis

The quantitative data will be analyzed by using mean, standard deviation, median, and range for the measurement data whereas qualitative data will be analyzed by using frequency and percentage. "The prevalence of patients with cognitive impairment will be described by point estimates and 95% confidence intervals. Spearman's Rank Correlation Coefficient will be used to determine the correlation between spirometric values and the scores of cognitive impairments". Kruskal-Wallis one way analysis of variance will be applied to compare the mean oxygen saturation level across the groups of cognitive impairment. Chi-square tests will be conducted to compare the socio-demographic characteristics of the participants and the presence of cognitive impairment. Here, a p-value of < 0. The value of 05 will be considered statistically significant.

ANALYSIS AND RESULTS

4.1 Sociodemographic Characteristics

The participants in the study were aged between 45 and 80 years, with a mean age of 62.9 ± 6.8 years. Most of the participants (70.5%) were between the ages of 55 and 69 years. The study population was predominantly male, comprising 84.2% of the sample. Most participants (86.3%) had achieved at least a middle school education. In terms of habits, 77.9% of participants were smokers, and 70.5% consumed alcohol either daily or occasionally. Additionally, 72.6% of participants did not use tobacco.

Table 1: Sociodemographic Characteristics of Participants

Characteristic	Frequency	Percent
Age		
<50	3	3.2
50-54	9	9.5
55-59	19	20.0
60-64	23	24.2
65-69	25	26.3
≥70	16	16.8
Gender		
Female	15	15.8
Male	80	84.2
Educational Status		
High School	42	44.2
Middle School	40	42.1
Primary School	13	13.7
Alcohol Consumption		
No	28	29.5
Yes	67	70.5
Tobacco Chewing Status		
No	69	72.6
Yes	26	27.4

Using the MMSE score, 32.6% of the participants were found to have mild cognitive impairment, while the remaining 67.4% had normal cognitive function.

Table 2: Cognitive Impairment in Participants

Cognitive Impairment	Frequency	Percent
Mild	31	32.6
No Cognitive Impairment	64	67.4

4.2 Chronic Obstructive Pulmonary Disease (COPD)

The severity of COPD among participants was classified as mild (11.6%), moderate (43.2%), severe (26.3%), and very severe (18.9%) (Table 7). The duration of COPD among participants ranged from 1 to 35 years, with a mean duration of 7.2 ± 6.1 years. Most participants (76%) had COPD for less than 10 years (Table 8). The oxygen saturation (SpO_2) levels of the participants varied between 84% and 99%, with a mean of 94.3 ± 3.3% (Table 9). This range of oxygen saturation levels indicates a diverse degree of disease impact on respiratory function.

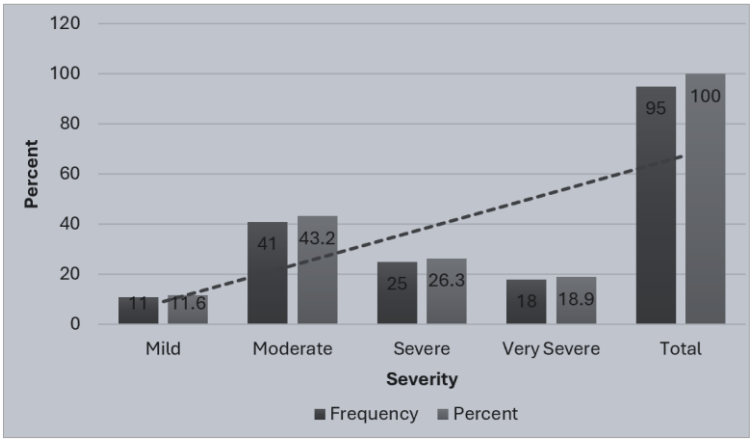


Figure 1: Severity of COPD in Participants

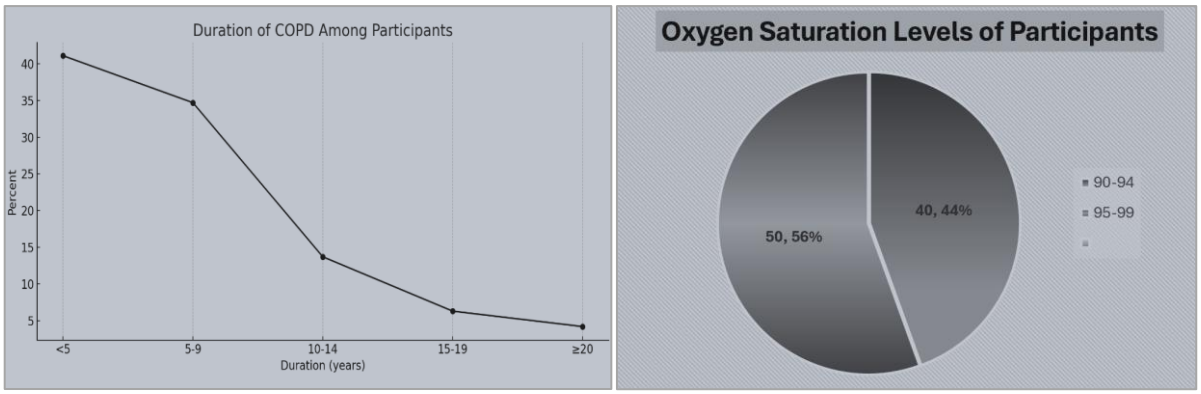
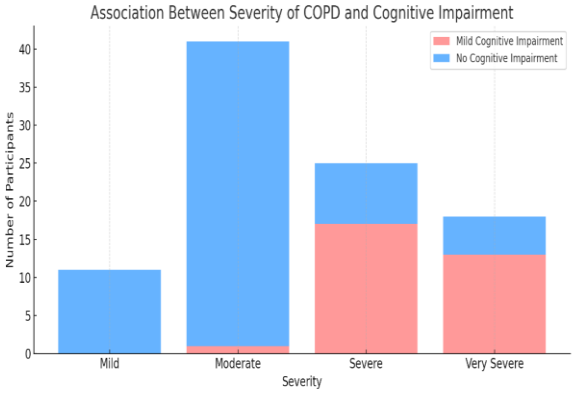
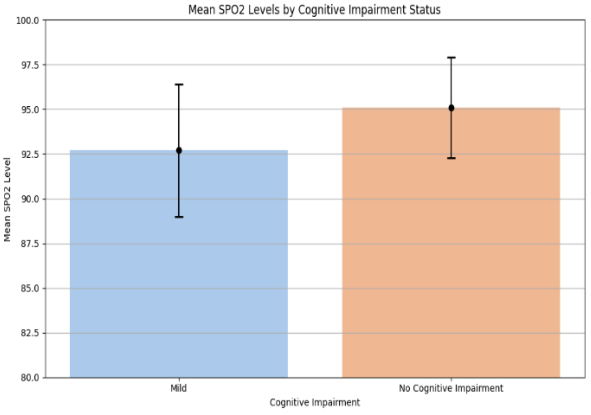


Figure 2: Duration of COPD and Oxygen Saturation Levels of Participants

Association Between Cognitive Impairment and COPD Severity, Duration, and Oxygen Saturation Levels

It was established that cognitive impairment is related to various aspects of Chronic Obstructive Pulmonary Disease (COPD). The relationship between the severity of COPD and mild cognitive impairment was highly significant with a $p < 0.001$.Specifically, none of the participants with mild COPD exhibited mild cognitive impairment, while 2.4% of those with moderate COPD had mild cognitive impairment. In contrast, 68.0% of individuals with severe COPD and 72.2% of those with very severe COPD presented with mild cognitive impairment, as indicated by a chi-square value of 49.39 ($p < 0.001$). Participants with longer durations of COPD had a higher median duration of illness compared to those without cognitive impairment. Those with mild cognitive impairment had a mean duration of 9.32 years (± 6.1 years) and a median duration of 8.0 years, while those without cognitive impairment had a mean duration of 6.2 years (± 5.8 years) and a median duration of 4.0 years.





The median SPO2 level for individuals with mild cognitive impairment was 94.0, significantly lower than the median level of 96.0 for those without cognitive impairment ($p = 0.001$). The mean SPO2 for participants with mild cognitive impairment was 92.7 (± 3.7), while it was 95.1 (± 2.8) for those without cognitive impairment.

DISCUSSION

COPD is a severe lung disease with a permanent reduction in the flow of air and its impact on organs other than the lungs remains poorly investigated. The purpose of this investigation was to determine the rate of cognitive dysfunction in COPD patients and to establish its link to the disease and other variables. The results suggest that the COPD patients have a high degree of cognitive impairment with 32. 6% of our sample affected, which is close to the 32. 8% observed elsewhere. This prevalence is rather high, particularly in light of Villeneuve et al. 's reported 36% prevalence and Dodd et al. 's even higher 77% prevalence among hypoxemic patients. This work shows a causal relationship between COPD and cognitive impairment with the percentage of patients with MCI rising as the severity of the disease advances. Specifically, 72. Two percent of the patients with very severe COPD and 68% of the patients with severe COPD had MCI, while only 2% of the patients with mild/moderate COPD had MCI. 4% of the patients fell under the moderate severity, while none of the patients had a mild severity. These findings are similar to Torres-Sanchez et al., who reported increased prevalence of CI in relation to the severity of COPD. On the other hand, Thakur et al. did not observe any correlation between the COPD severity and cognitive dysfunction, and concluded that the cognitive impairment is directly associated with the low baseline oxygen levels. This study also indicates arterial oxygen saturation and cognitive dysfunction relationship the median SPO_2 was significantly lower at 94 % in the MCI group compared to the 96 % in the no MCI group (p = 0. 001).

CONCLUSION

The current study also has findings that could be used to support the hypothesis of this study that severity of COPD, low oxygen levels, and cognitive decline are associated. It also examines the effect of education on the cognitive and the associated deterioration and finds that smoking is a risk factor. The findings of the research suggest the need to assess and treat cognitive impairment in COPD patients. The results show that roughly one third of the participants had been previously diagnosed with at least one chronic disease. The findings of the study indicated that MCI in COPD patients was 6% based on the MMSE. The study also reveals the link between the severity of COPD and MCI; patients with severe COPD had poorer cognitive function. In addition, the results reveal that the median oxygen saturation levels were lower among patients with MCI compared to the patient with normal cognition. With regard to sociodemographic characteristics, education was not a risk factor for cognitive decline while smoking was identified as a risk factor for MCI; the rate of MCI was higher among smokers than the non-smoker group. Cognitive impairment significantly reduces the HRQoL and the prognosis of the COPD patients. Because this condition is not very well-known, early diagnosis is critical. Future research should focus on the search for more effective tools for the assessment of cognitive dysfunction in patients with COPD, as well as the effect of supplementary oxygen therapy and smoking cessation on COPD patients' cognition.

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