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Cognitive Impairment Among COPD Patients. Hospital - Based Comparative Cross - Sectional Study

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Abstract

Background

Chronic obstructive pulmonary disease (COPD) is a term for conditions, including chronic bronchitis and emphysema that block the flow of air in the bronchi and trachea. Cognitive impairment is the major public health problem worldwide particularly among people with COPD. However, little is known about the association between COPD and cognitive impairment among adults.

Objective

To assess the prevalence of cognitive impairment and associated factors among chronic obstructive pulmonary disease patients attending hospitals of Bahirdar, Ethiopia, 2020.

Materials and methods

Comparative cross-sectional study was conducted among 110 COPD patients who were under follow-up in chronic clinics of hospitals of Bahirdar city and 110 age, sex, and educational level matched healthy individuals (controls) coming to the hospital by using a consecutive sampling technique. A Proportional sample size allocation formula was used to allocate study participants in each hospital of Bahirdar city. The data collection tools were a structured questionnaire,

Spirometer, stadiometer, Mini-mental state examination tool, Pulse Oximeter, and Glucometer. Descriptive analysis was made to describe the data. Besides logistic regression, one-way ANOVA and independentt-test were used to determine the association between dependent and independent variables. Variables with p < 0.05 were considered statistically significant.

Results

The present study revealed that the prevalence of cognitive impairment among COPD patients is 51.8 % and among healthy controls 18.2%. Having COPD is 4.48 times the risk for cognitive impairment than non-COPD groups [AOR=4.48(CI (2.6-8.9), p <0.001]. A mild form of cognitive impairment is the most common severity form of cognitive impairment among COPD patients. COPD patients aged 70 and above have a 5.8 risk of being cognitively impaired [AOR= 5.8, 95% CI (1.15, 27.2), p = 0.01] than age groups of 50 and lower. Other factors which significantly affects the occurrences of cognitive impairment among COPD patient are oxygen saturation (2.13 (1.42-4.32)), the severity of COPD (3.99 (1.37-9.0)), educational status (2.3 (1.07-5.5).

Conclusions and recommendations

The present finding suggests that COPD could be a major risk factor for cognitive impairment. Also, the severity of COPD is significantly associated with cognitive impairment. Moreover, age and educational status could be potential contributors to cognitive impairment.

This pointed out that routine screening for cognitive impairment should be done among COPD patients. And also further research investigation at a larger scale is recommended.

Keywords

Cognitive impairment, COPD, MMSE, cognitive function, Hospitals of Bahirdar, Comparative crossectional study.

Introduction

Chronic obstructive pulmonary disease (COPD) is the name given for conditions, including chronic bronchitis and emphysema that blocks the flow of air in the bronchi and trachea (1). It is an irreversible and progressive obstructive airway disease characterized by airflow limitation (2). At present, it is the third leading cause of death worldwide, but the World Health Organization (WHO) projects that COPD will become the first-leading cause of death within 15 years (1, 3). COPD is diagnosed by using a Spirometer showing airflow limitation that is the ratio of FEV1 and FVC is less than 0.70 that is not completely reversible with a bronchodilator (4). Most of the COPD is attributable to cigarette smoking but air pollution and long-standing tuberculosis and asthma may be responsible for the cause of COPD (1, 5).

COPD has been highly associated with other comorbid conditions with resulting in serious morbidity and mortality; those comorbid conditions include diabetes mellitus, hypertension, and cognitive impairment may be due to in one way hypoxemia and hypercapnia resulting from long-lasting airflow limitation and in another way maybe by the direct effects of cigarette smoking which is the most common initiating factor for COPD (6, 7). Cognitive function is the mental act of appreciating, obtaining, and using knowledge or information, through thinking, experience, and the senses, by which human behavior can be adjusted to new situations and/or preferences changed. It includes different cognitive processes which can be separated into six elementary

neuropsychological domains including attention/concentration, learning and memory, visuospatial and motor function, language, social cognition/emotions, and executive functions (7, 8, 9).

The shared disastrous effect of COPD is impairment of cognitive function which could be defined as a misunderstanding or inability to memorize something further than what is estimated in normal age (9,10,11). CI affects one-third of the general older adults worldwide. Even if cognitive impairment (CI) is common in older individuals, it is not restricted to a specific age group and all age groups are susceptible to cognitive decline (10, 12). CI in COPD is believed to be caused by many conditions and it is associated with disease comorbidities and severity (12, 13). The cognitive impairment among COPD is mainly due to hypoxemia, inflammation, cigarette smoking, and vascular comorbidities (7). The age-associated decline in cerebral perfusion, COPD-associated hypoxemia, and the interaction of aging and COPD is responsible for CI (12).

The dysfunction in Cognitive function among COPD increases the assistance requirement in different aspects of daily living, treatment adherence, and effectual self-management (7, 14). The most commonly impaired cognitive domain in patients with COPD is verbal memory, attention, and learning (14). Cognitively impaired COPD patients had a poor quality of life. It mainly happens in severe COPD with hypoxemia but researchers also conclude that CI can be present in mild forms of COPD and non-hypoxemic individuals (4, 7, 12). COPD is highly prevalent and causing higher proportions of morbidity and mortality, impacting both the rural and urban populations of Ethiopia (15).

The presence of CI comorbidity in COPD is associated with a significantly increased burden of COPD related morbidity, mortality especially by causing deteriorations in health-related quality of life, reducing physical activity, increasing the frequency of hospital admission, and reducing adherence to treatment by causing such effects it makes patients vulnerable for other disease burdens (16,17,18). CI is an important self-sufficient forecaster of mortality in COPD patients (19). Cognitive impairment is a significant concern for the elderly because it can decrease quality of life and, in advanced stages, also causes functional debility (1, 17,20).

The prevalence of COPD-related disability is high in patients with cognitive impairment (20, 21). When they come together COPD and CI have an additive effect on respiratory-related and all-cause hospitalizations and death (22). The coexistence of COPD and cognitive impairment is associated with a rate of death nearly three times as great as the sum of risks associated with having each condition alone (23,24,25). CI is a significant determinant of death and other health-related problems in chronic obstructive pulmonary disease patients (25, 26).

Timely recognition, diagnosis, and management of CI in patients with COPD are very relevant clinically (27, 28). Despite these problems, the screening for coexisting cognitive deficits that may interfere with the successful progress of COPD treatment is yet neglected (29, 30,31, 32). Related researches are scarce in Africa and not done in Ethiopia.

Methods

Study area and period

The study was conducted in hospitals of Bahirdar city. Bahirdar city is the administrative center for the Amara regional state and it is located 576 Km

North West of Addis Ababa, the capital city of Ethiopia. According to the 2007 census, there are total populations of more than 221,991 inhabitants in Bahirdar city. There are three public and three private hospitals in the city. The public hospitals include; Felege-Hiwot Referral Hospital, Tibebe-Ghion Specialized Hospital, and Adisalem General Hospital. Felege-Hiwot Referral Hospital is one of the Referral Hospitals in the region and it is a center of referral for the West-Gojjam, South-Gondar, Beinshagul-gumuz region, and some part of the East Gojjam zone. The private hospitals in Bahirdar city include; Adinas General Hospital, Gambi Teaching General Hospital, and Dream-Care General Hospital. All the hospitals serve around 7,000,000 peoples in their catchment.

Study design

A hospital-based comparative cross-sectional study design was conducted.

Population

Source population

The source populations were all COPD patients attending the hospitals of Bahirdar city.

For Non-COPD groups, all ages, sex, and educational status matched non-COPD individuals attending the hospitals of Bahirdar.

Study population

All COPD patients attending the hospitals of Bahirdar city during the study period were the study population.

For Non-COPD groups, all ages, sex, and educational status matched non-COPD individuals attending hospitals of Bahirdar during the study period.

Eligibility criteria

Inclusion criteria

All COPD patients attending hospitals of Bahirdar city were included in the study

Individuals who were able to take mini-mental state examinations.

For Non-COPD groups, individuals with no acute and chronic diseases that may affect cognitive function were included in the study. Attendants of critically ill patients were taken as control based on their consent.

Exclusion criteria

Severely ill individuals

Patients with

- Established diagnosis of psychiatric disorders, dementia, Alzheimer's disease, Parkinson's disease, and Brain tumor.
- Established diagnosis of chronic medical disorders like AIDS, Congestive heart failure, and chronic liver disease.
- Established diagnosis of hypothyroidism and hyperthyroidism
- Individuals with DM and hypertension.

Sample size determination

The Sample size was determined by using the double population proportion formula with the assumption of P1 = 50% because of the absence of previous researches done in Ethiopia and P2 =31.4% (33)**,** a confidence level of 95%, and power of 80%.

$$n = \frac{(r+1)\,(Z\alpha/2+Z\beta)^2\,p\,(1-p)}{r\,(p1-p2)^2} = 105\ (34)$$

Where;

n = minimum sample size, p1= proportion of COPD with cognitive impairment, p2=proportion of controls with cognitive impairment, Zβ= standard normal variate for power, Zα=standard normal variate for a level of significance, p1-p2= effect size, P= pooled proportion, which is the average proportion (p1+p2)/2, r =ratio of a number of participants of cases to controls (1 in this case).

✓ Therefore, the final sample size for both COPD and healthy controls was **220.**

Sampling procedures

A consecutive sampling technique was used to employ study participants. Patients with COPD who are on follow-up were consecutively interviewed and sampled. Proportional sample size allocation formula was used to allocate study participants in each hospital of Bahirdar city. Healthy controls with matched age, sex, and educational status and who was attending the hospital during the study period were also interviewed as shown in **(Fig-1)** below**.**

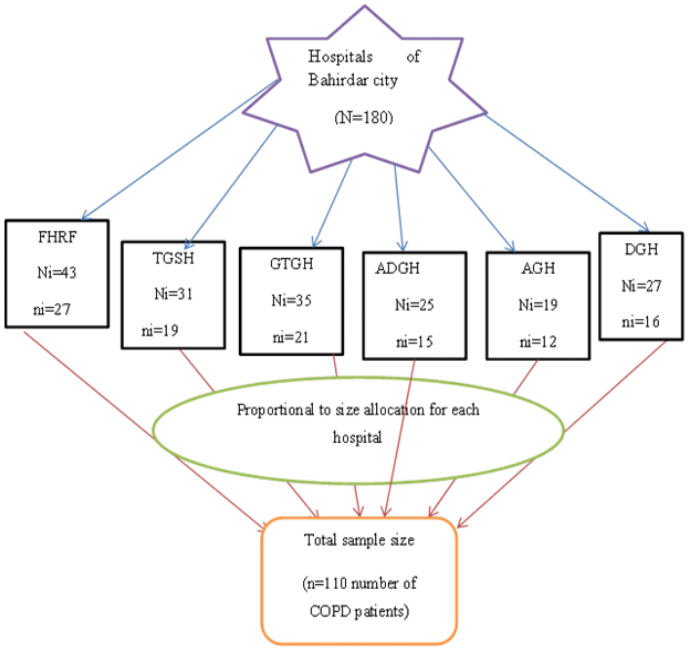

Fig 1. Schematic representation of sampling procedures for COPD patients attending hospitals of Bahirdar, Ethiopia, 2020(n=220).

Where N=the total number of COPD patients attending hospitals of Bahirdar city between September 2nd and November 4th of 2019 obtained by document review, Ni= the total number of COPD patients attending in each hospital of Bahirdar city and ni=the sample that will be drawn from each hospital. FHRF=Felege-Hiwot Referral Hospital, TGSH=Tibebe Gyon Specialized Hospital, DGH=Dream Care General Hospital, ADGH=Adinas General Hospital, AGH=Adisalem General Hospital, GTGH=GAMBI Teaching General Hospital.

Variables

Dependent variables

Cognitive impairment

Independent variables

Age, sex, religion, educational status, occupational status, residence, monthly income, marital status, physical activity, cigarette smoking, khat chewing, alcohol consumption, COPD, duration of COPD, the severity of COPD, oxygen saturation, history, and number of exacerbations, BMI.

Operational definitions and definition of terms

Cognitive impairment

A person has problems in the recall, orientation, registration, attention and calculation, language, and praxis (7, 32).

MMSE is a commonly used 30 - point scale for

assessing cognitive function. Cognitive impairment is when;

- 21 or below for participants with an educational level of 8th grade or lower.
- Below 23 for participants with the educational level of high school to preparatory (9-12 grades).
- 24 or below for participants with the educational level of college and above.
- Mild cognitive impairment- A MMSE score of 20-24/30
- Moderate cognitive impairment- A MMSE score of 10-19/30
- Severe cognitive impairment- A MMSE score of 0-9/30
- No cognitive impairment- A score of 25-30/30 on MMSE (35).

NB-the severity of cognitive impairment given above works for those individuals with educational level of college and above. For other categories first, it should be adjusted.

Hypoxemia: - when the blood oxygen saturation is less than 90 % (1).

Mild COPD: - Mild **COPD** with an FEV1 about 80 percent or more of normal.

Moderate COPD: - Moderate COPD with an FEV1 between 50 and 80 percent of normal.

Severe COPD: - with an FEV1 between 30 and 50 percent of normal (1, 2).

Underweight: - A person having a BMI of <18.5Kg/m2

Overweight: - A person having a BMI of >24.9Kg/m2

Obese: - A person having a BMI of >30Kg/m2 (36).

Substance use: – Use at least one of the substances (alcohol, khat, cigarettes) in an individual's lifetime (37)

Data collection tools and procedures

A pretested structured questionnaire which is adopted with little modification from a study done in Egypt was used (32). The questionnaire has four parts including Sociodemographic related questions, a 30 point standardized MMSE tool which is used to measure the cognitive status of an individual. The interview took place in the appropriate place according to the standard. A digital spirometer (Spiro-lab, Italy) was used to assess the severity status of COPD. The examination was taken place at an appropriate place according to the standard. During the spirometer examination, the examiner wear a face mask washed their hands, and mouthpiece was used for each study participant. Pulse Oximeter (GE B30 Medical system, Germany) was also used to measure the peripheral blood oxygen saturation level. Stadiometer was used to measure the weight and the height of the study participant and BMI was calculated with the formula weight/height2. The measurement was done by a clinical nurse who works at a chronic disease clinic after the participants removed all heavy clothing and shoes (32).

Data management and analysis

The data collectors were trained psychiatrists and BSc nurses. Daily monitoring of the data collection was undertaken. Daily checking of the completeness of the questionnaire was made. The collected data were entered into Epi data version 3.1 and it was exported into SPSS version 20 for analysis. An Independent two-sample t-test was used to compare the mean of the cases and controls. ANOVA was performed to compare cognitive impairment among different COPD groups. After assumptions were made binary Logistic regression analysis was undertaken. Variables that are significantly associated with the occurrence of cognitive

impairment with p <0.25 were entered into multiple logistic regression and variables with p <0.05 were considered statistically significant.

Ethical consideration

Ethical clearance was obtained from the Institutional Review Board of Jimma University, institute of health. Participants were informed about the objective of the study and informed consents were obtained from each study participant.

Results

Sociodemographic and anthropometric characteristics of the study participant

In this study, a total of 220 study participants were involved. The mean age of the study participant was 63.4±10. The mean age of the controls and cases does not have a statistically significant difference which is 63.8±10.9 and 63±8 respectively (t=0.21, p=0.823). About 63.6 % (140) were males. Around 60% of the study participants were urban resides. About 86.4% (190) of the study participants were orthodox in religion. Of all, 58.2 % of the study participants were married. Around 35.9 % of the study participants were farmers. There is no statistically significant difference between COPD and control groups related to age, sex, and educational status. The mean BMI of the study participant was 24.6±3.2 and there is a statistically significant difference among cases and controls that is 26.7±3.2 and 22.6±1.5 respectively with (p =0.001). Regarding the physical activity status of the study participants, 23.6 % of the study participants were physically inactive as shown in **(Table-1).**

Table 1

Sociodemographic, lifestyle, and anthropometric characteristics of study participants attending hospitals of Bahirdar, Ethiopia, 2020 (n=220).

Variable	Category	Study group				
		N (%)	COPD group	Non-COPD group	t-value	p-value
			N (%)	N (%)		
Sex	Male	140(63.6)	70(63.6)	70(63.6)	0.00	1.00
	Female	80(36.4)	40(36.4)	40(36.4)		
Age(years)	µ± SD	63.4±10	63.8±10.9	63±8	0.21	0.823
	40-49	45(20.4)	20(18.2)	25(22.7)		
	50-59	68(30.9)	34(30.9)	34(30.9)	0.13	
	60-69	53(24.1)	23(20.9)	30(27.3)		
	≥70	54(24.5)	33(30)	21(19.1)		
Occupational status	Gov't employee	29(13.2)	28(25.4)	1(0.9)		
	Private employee	69(31.4)	15(13.6)	54(49)	-3.65	0.046
	Merchant	21(9.5)	0	21(19)		
	Farmer	71(35.9)	59(53.6)	11(10)		
	House wife	14(6.3)	8(7.3)	6(5.5)		
	Daily laborer	16(7.3)	0	16(14.5)		
Educational status	Primary	164(74.5)	82(74.5)	82(74.5)	0.00	1.00
	Secondary	12(5.4)	6(5.5)	6(5.4)		
	Collage and above	44(20)	22(20)	22(20)		
Monthly income (ETB)	µ± SD	1426±617	1485±633	1372±606	0.34	0.09
	<1000	105(47.7)	49(44.9)	56(51)		
	1001-2000	40(18.2)	26(23.6)	14(12.7)	0.52	0.06
	>2001	75(34.1)	35(31.8)	40(36.3)		
Marital status	Single	22(10)	8(7.2)	14(12.7)	-4.67	0.01
	Married	128(58.2)	94(85.4)	33(30)		
	Divorced	42(19)	4(3.6)	29(26.4)		
	Widowed	28(12.8)	4(3.6)	24(21.8)		
Religion	Orthodox	190(86.4)	104(94.5)	85(77.3)	0.46	0.69
	Muslim	19(8.6)	3(2.7)	17(15.4)		
	Protestant	9(4.0)	2(1.8)	7(6.3)		
	Catholic	2(0.9)	1(0.9)	1(0.9)		
Residency	Urban	132(60)	44(40)	88(80)	1.34	0.09
	Rural	88(40)	66(60)	22(20)		
BMI(kg/m^2)	µ± SD	24.6±3.2	26.7±3.2	22.6±1.5	-5.32	0.001
Physical activity	In-active	52(23.6)	38(34.5)	14(12.7)	-4.42	0.024
	Active	168(76.4)	72(65.5)	96(87.3)		

µ± SD =mean and standard deviation, ETB=Ethiopian birr

Substance use and clinical characteristics of the study participant

Among the total COPD cases (n=110) 38(34.5%) are non-smokers, 54(49%) were former smokers and 18(16.4%) are current smokers. In the case of alcohol consumption, 58(52.7%) of COPD patients had a history of alcohol consumption. Among the total 110 COPD cases, 60(54.5%) of the study participant chews Khat in their lifetime. Of all, 70% of the study participants had a duration of COPD of greater than two years. About 68.2% of COPD patients had at least one episode of exacerbation as shown in **(Table-2).**

Table 2

Substance use and clinical factor-related characteristics of study participants attending hospitals of Bahirdar, Ethiopia, 2020 (n=220).

Variables		Total N (%)	COPD group	Non-COPD group	t-value	p-value
			N (%)	N (%)		
Smoking	Non-smokers	97(44.1)	38(34.5)	59(53.6)	-7.34	0.001
	Former smokers	70(31.8)	54(49)	16(14.5)		
	Current smokers	53(24.1)	18(16.4)	35(31.8)		
History of Alcohol consumption	Yes	110(50)	58(52.7)	52(47.3)	1.54	0.18
	No	110(50)	52(47.3)	58(52.7)		
History of Khat chewing	Yes	83(37.7)	60(54.5)	23(20.9)	-4.89	0.03
	No	137(62.3)	50(45.5)	87(79.1)		
	No	130(59.1)	32(29.1)	98(89.1)		
Duration of COPD(years)	>2	77(70)	77(70)			
	≤2	33(30)	33(30)			
History of exacerbations	Yes	75(68.2)	75(68.2)			
	No	35(31.8)	35(31.8)			
Oxygen saturation mean		93.19±4.3	89.1±3.7	96.2±2.1	-4.51	0.001
Presence of hypoxemia	Yes	60(27.3)	59(53.6)	1(0.9)	6.43	0.037
	No	160(72.7)	51(46.4)	109(99.1)		
Predicted FEV1 μ± SD		81.6±10.7	73.72±14.71	89.6±9.0	-10.14	0.0001
Severity of COPD	Mild COPD	56(50.9)	56(50.9)			
	Moderate COPD	42(38.2)	42(38.2)			
	Severe COPD	12(10.9)	12(10.9)			

Cognitive status of the study participant

There is a significant mean difference in mean MMSE score among the COPD and non-COPD groups which is 22.15±6.05 and 25.91±2.5 with t-value 4.49 respectively. The total prevalence of cognitive impairment among COPD and control cases after they are adjusted with educational status is 51.8% (95%CI: 41.8-60.9) and 18.2% (95% CI: 14.8-28.2) respectively. Totally 35% (95% CI: 29.1-42.3)) of the study participants had cognitive impairment. Among the cognitively impaired COPD patients, 70.2% of the study participants have mild forms of cognitive impairment as shown in **(Table-3).**

Table 3

Cognitive status of study participants attending hospitals of Bahirdar, Ethiopia, 2020(n=220).

Cognitive status		N (%)	COPD	Non-COPD group	t-value	p-value
			N (%)	N (%)		
MMSE score μ± SD		24.±5	22.15±6.05	25.91±2.5	4.49	0.001
Cognitive impairment	Yes	77(35)	57(51.8)	20(18.2)		
	No	143(65)	53(48.2)	90(81.8)		
Severity of cognitive impairment	Mild	57(74%)	40(70.2)	17(85)	-7.41	0.038
	Moderate	15(19.5%)	12(21)	3(15)		
	Severe	5(6.5%)	5(8.8)	0		

MMSE= Mini mental state examinations

Factors affecting the occurrences of cognitive impairment among COPD.

Binary and multiple logistic regression of Sociodemographic variables

In the present study, age, educational level, occupation, income, and residence were associated with cognitive impairment among COPD patients in binary logistic regression. Of all variables entered into multiple logistic regressions only age and educational level along with the presence and severity of COPD are significantly associated with the occurrences of cognitive impairment. COPD patients aged ≥70 years were 5.8 times [AOR= 5.8, 95% CI (0.25, 27.2), p= 0.01] more risky for cognitive impairment than those ≤50 years. COPD patients who are primary school education and lower have a risk for cognitive impairment 2.3 times (AOR=2.3, 95% CI (1.07-5.5) than that of individuals who attend college and above as shown in **(table-3 and table-4).**

Table 4

Binary and multiple logistic regression of Sociodemographic variables as predictors of cognitive impairment among COPD patients attending hospitals of Bahirdar, Ethiopia, 2020(n=110).

Variables	category	Total N (%)	COPD group (n=110)			
			Cognitive impairment		COR with 95%CI	AOR with 95%CI
			Yes n(%)	No n(%)		
Sex	Male	70(63.6)	32(56.1)	38(71.7)	1	1
	Female	40(36.4)	25(43.9)	15(28.2)	1.98(0.9-4.4)	0.55(0.09-3.2)
Age(Year)	40-49	20(18.2)	6(10.5)	14(26.4)	1	1
	50-59	34(30.9)	14(24.6)	20(37.7)	5.19(0.6-45.2)	0.85(0.03-24.5)
	60-69	23(20.9)	14(24.6)	9(17)	6.5(0.7-60)	4.695(0.14-15.6)
	>=70	33(30)	23(40.3)	10(18.9)	**12.4(2.1-228)**	**5.825(1.15-27.2)**
Education	Primary	82(74.5)	44(77.2)	38(71.7)	**1.673(1.6-4.4)**	**2.3**(1.07-5.5)
	Secondary	6(5.5)	3(5.3)	3(5.7)	0.71(0.1-3.1)	0.49(0.08-7.0)
	Collage and above	22(20)	10(17.5)	12(22.6)	1	1
Occupation	Gov't employ	28(25.4)	18(31.6)	10(18.7)	1	1
	Private employ	15(13.6)	3(5.3)	12(22.6)	0.6(0.17-2)	0.45(0.3-3.1)
	Farmer	59(53.6)	30(52.6)	29(54.7)	**5(1.04-24)**	3.5(0.56-20)
	House wife	8(7.3)	6(10.5)	2(3.8)	0.6(0.56-1.2)	0.09(0.06-2.56)
Income	<1000	49(44.4)	24(42.1)	25(47.1)	**1.15(1.05-1.9)**	0.39(0.08-1.98)
	1001-2000	24(21.8)	16(28)	8(15)	0.37(.12-1.1)	0.74(0.15-3.66)
	>2001	35(31.8)	15(26.3)	20(37.7)	1	1
Marital status	Single	8(7.4)	7(12.3)	1(1.9)	0.4(.02-9)	3.1(0.006-36)
	Married	94(85.4)	44(77.2)	50(94.3)	1	1
	Divorced	4(3.6)	3(5.25)	1(1.9)	**3.4(1.32-33.9)**	0.54(0.025-13)
	Widowed	4(3.6)	3(5.25)	1(1.9)	1.3(0.04-24.5)	2.1(0.572-14)
Religion	Orthodox	104(94.5)	55(96.5)	49(92.4)	0.65(.25-2)	0.75(0.5-3)
	Muslim	3(2.7)	1(1.75)	2(3.8)	0.72(0.27-2.7)	0.92(0.27-2.4)
	Protestant	2(1.8)	0	2(3.8)	1	1
	Catholic	1(1)	1(1.75)	0	0.67(.12-1.1)	0.94(0.15-3.9)
Residence	Urban	44(40)	23(40.3)	21(39.6)	1	1
	Rural	66(60)	34(59.7)	32(60.4)	**1.97(1.45-2)**	0.55(0.093-3.2)
Physical activity	Inactive	38(34.5)	13(22.8)	25(47.2)	1.23(0.32-1.89)	0.43(0.12-1.56)
	Active	72(65.5)	44(77.2)	28(52.8)	1	1

Binary and multiple logistic regressions of substance use and clinical variables

On binary logistic regression cigarette smoking, alcohol consumption, duration of the disease, oxygen saturation, and severity of COPD are associated with cognitive impairment. But on multiple logistic regressions only cigarette smoking, alcohol consumption, oxygen saturation, and severity of COPD were associated with the occurrences of cognitive impairment among COPD. Individuals who consume alcohol have a risk of being cognitively impaired 2.37 times that of non-consumers (AOR= 2.37, 95% CI (1.5-26) p=0.045)). Severe COPD is 3.99 times riskier for cognitive impairment than mild COPD [AOR=3.99 95% CI (1.037-9.0)] as shown in **(table 5).**

Table 5

Binary and multiple logistic regressions of substance use, Anthropometry, and clinical factors as predictors of cognitive impairment among COPD patients attending hospitals of Bahirdar, Ethiopia, 2020 (n=110).

Variables	Category	Total N %	COPD group (n=110)		COR 95% CI	AOR 95% CI
			Cognitive impairment			
			Yes	No		
Cigarette smoking	Never	38(34.5)	13(22.8)	25(47.2)	1	1
	Former	54(49.1)	37(64.9)	17(32)	1.22(0.38-3.9)	0.29(0.04-2.23)
	Current	18(16.4)	7(12.3)	11(20.8)	**1.29(1.10-7.88)**	**1.815(1.12-7.1)**
Alcohol consumption	Yes	58(52.7)	38(66.7)	20(37.7)	**1.3(1.14-13.66)**	**2.37(1.5-26.3)**
	No	52(47.3)	19(33.3)	33(62.3)	1	1
Khat chewing	Yes	60(54.5)	35(61.4)	25(47.2)	0.56(0.26-1.19)	0.34(0.06-1.78)
	No	50(45.5)	22(38.6)	28(52.8)	1	1
Presence of COPD	Yes	110(50)	57(51.8)	53(37.1)	**6.78(1.53-19.7)**	**4.48(1.12-17)**
	No	110(50)	20(48.2)	90(62.9)	1	1
Duration of COPD(years)	<2	33(30)	20(35.1)	13(24.5)	1	1
	>2	77(70)	37(64.9)	40(75.5)	**2.0(1.89-4.7)**	1.55(0.32-20)
History of exacerbation	Yes	75(68.2)	45(78.9)	30(56.6)	**1.35(1.15-5.8)**	**3.3(1.15-15)**
	No	35(31.8)	12(21.1)	23(43.4)	1	1
Presence of hypoxemia	Yes	59(53.6)	33(57.9)	26(49)	**3.14(1.48-8.97)**	**2.13(1.42-4.32)**
	No	51(46.4)	24(42.1)	27(51)	1	1
Severity of COPD	Mild	56(50.9)	23(40.3)	33(62.3)	1	1
	Moderate	42(38.2)	25(43.8)	17(32)	2(0.4-8.6)	0.93(0.016-1.54
	Severe	12(10.9)	9(15.9)	3(5.7)	**4.3(1.0-17.0)**	**3.99(1.37-9.0)**
BMI	Underweight	9(8.2)	4(7.1)	5(9.4)	0.32(0.13-4.1)	0.12(0.05-1.31)
	Normal	70(63.6)	34(59.6)	36(67.9)	1	1
	Overweight	18(16.4)	11(19.3)	7(13.2)	0.98(0.06-1.29)	0.61(0.56-5.1)
	Obese	13(11.8)	8(14)	5(9.4)	1.32(0.45-5)	1.06(0.08-3.14)

Where bold marked ones are significant, BMI=Body mass index, %=percent, N=number

This are statistically significant (p=0.046) and this indicates that there is a statistically significant mean difference in the prevalence of cognitive impairment in different severity of COPD cases as shown in **(table-6).**

Table 6

One-way ANOVA test to identify whether there is a mean difference in cognitive impairment among severity of COPD, Bahirdar, Ethiopia, 2020(n=220).

Cognitive impairment		Sum of Squares	Df	Mean Square	F	Sig.
severity of COPD	Between Groups	1.541	2	.771	3.180	.046
	Within Groups	25.923	107	.242		
	Total	27.464	109			

NB. The dependent variable is the presence of cognitive impairment

Discussion

This is a hospital-based comparative cross-sectional study of cognitive impairment among COPD patients. This is mainly aimed to assess the prevalence of cognitive impairment and identifying the factors responsible for the occurrences of cognitive impairment among COPD patients and also determine whether COPD is an independent determinant for the occurrence of cognitive impairment or not. In the present study, the prevalence of cognitive impairment among COPD patients and controls is 51.8% and 18.2% with a 95%CI (41.8- 60.9) and (14.8-28.2) respectively (Table 3).

In this study higher prevalence of cognitive impairment was found among COPD patients. This

finding is nearly in line with a study done in China and Brazil where a higher prevalence of cognitive impairment was reported among COPD patients (59 % and 60 %) respectively (38, 39). The finding of this study on the prevalence of cognitive impairment is relatively higher than a study done in the USA and Nepal where the prevalence of cognitive impairment among COPD patients is 17.8 % and 36 % respectively (40, 41). This difference in the prevalence of cognitive impairment may be due to differences in socioeconomic status, differences in sample size used, and differences in the educational status of the study participants.

The prevalence of cognitive impairment among healthy controls in the present study is 18.2%. This study is relatively higher than a study done in Italy and Egypt where 14% of healthy controls had cognitive impairment (3, 36). The difference may be due to a difference in the Sociodemographic characteristics and difference in the socioeconomic status of the study participant. The present study indicates that the prevalence of cognitive impairment is significantly higher among COPD groups than healthy controls of the same age and educational status with 4.48 times more risk in COPD groups than healthy controls (AOR=4.48 (2.6-8.9), p <0.001).

The higher prevalence of cognitive impairment among COPD patients may be due to hypoxia in which hypoxia induces neuronal injury and by affecting oxygen-dependent enzymes which involve the synthesis of acetylcholine, a neurotransmitter involved in memory and learning, by the effect of vascular comorbidity including hypertension (42), and due to the neurodegenerative effects of the chemicals present in cigarette smoking which is believed to be the major risk factor in the pathogenesis of COPD (7, 41).

The prevalence of cognitive impairment among COPD patients that are found in this study is relatively smaller than a study done in Canada, and Egypt where 63%, and 72%, were documented (35, 41). The difference may be due to the difference in the instrument used to screen cognitive impairment, the difference in lifestyle factors, and the sample size used in the study. The tool that this study used to screen the presence of cognitive impairment is MMSE and the tool that was used by the study done in Canada, and Egypt were imaging tests and Montegral cognitive assessment tests in addition to the commonly used MMSE.

In this study, the majority (70%) of study participants with cognitive impairment are mild in the severity of the condition. The finding of this study is supported by studies that were done in Egypt, the USA, Canada, Brazil, and China where they conclude that most of the respondents with cognitive impairment had mild forms of cognitive decline (35, 41, 43, 38). The reason behind this is that mild forms of cognitive impairment require 3- 5 years to change into moderate and severe forms of cognitive impairment (17). Concerns should be given for mild cognitive decline conditions because they will be changed into severe forms of cognitive impairment like dementia within three to five years (38, 43).

Among the Sociodemographic factors, being aged (Age≥70) in this study is 5.8 (AOR=5.8, 95% CI (1.15-27.2)) times riskier for cognitive impairment than other lower age groups. This finding is supported by a study done in Iran and New York (26, 44). The mechanisms of age-associated decline in cognitive function may be due to the negative impact of aging on the hippocampus which is a region of the brain involved in the formation and retrieval of memories (42). Hippocampal atrophy was evident on magnetic

resonance imaging (12), with significantly smaller right and left Hippocampal volumes in individuals who are over 65 years of age (45). Moreover, cerebral arterial narrowing/stiffness usually occurred after the age of 65 years old that may decrease blood flow to the brain, which can further impair memory and lead to changes in Cognitive skills (46). Furthermore, the accumulation of amyloid-beta plaques and tau that are linked to brain atrophy and neuronal dysfunction in the brain interferes with neuronal synapses (47). Also, an age-related decline in hormones and proteins (47) that protect and repair brain cells and stimulate neural growth had been documented (7, 45). The educational status of the study participant is also another factor that is significantly associated with the occurrences of cognitive impairment among COPD patients. In this study being primary school and bellow is 2.3(AOR=2.3, 95% CI (1.07-5.5)) times more risk for cognitive impairment than college and above attendees. This finding is supported by a study done in Iran and Newyork (26, 44).

In the present study, it was also observed that individuals with severe forms of COPD have 3.99 (AOR=3.99, 95% CI (1.37-9.0)) times risk for cognitive impairment among mild forms of COPD. This finding is supported by most researches that were done before in Iran, the USA, Egypt, and China (35, 41, 47). The reason behind this is that severe COPD is associated with persistent hypoxemia that results in cognitive dysfunction. In the present study, it was found that individuals who have a history of exacerbations have 3.3(AOR=3.3, 95% CI (1.15-15)) times more risk for cognitive impairment than those individuals who do not have a history of exacerbations. This finding is in concordance with a study done in the USA and China (41, 47). The reason is that individuals who are on exacerbation are in severe forms of COPD and/or they may with comorbidities of COPD (43).

Among the substance used related characteristics individuals who have a history of alcohol consumption are 2.37 (AOR=2.37, 95% CI (1.5-26.3)) times more risk for cognitive impairment than non-consumers. The finding of this study is supported by a study done in China (38). The occurrence of cognitive impairment among alcohol consumers is may be due to the general CNS depressant effects of alcohol. Acute alcohol consumption inhibits NMDA-activated ion currents in the hippocampus (48). In the present study cognitive impairment is 1.8 (AOR=1.815, 95% CI (1.12-7.1)) times higher among current cigarette smokers than never smokers. This finding is supported by a study done in Netherlands (49). The occurrence of cognitive impairment among cigarette smokers is may be due to the neurodegenerative effect of the toxic chemicals present in cigarette smoke (47, 50, 51).

Generally in this study cognitive impairment among COPD patients is highly prevalent particularly from moderate to severe forms of COPD. This may be because moderate to severe forms of COPD are associated with persistent hypoxemia which is believed to be the significant predictor of cognitive impairment. This finding is supported by most researches that wear done before in Iran, Egypt, and China (35, 38, 52).

Limitation of the study

This study fails to do further biochemical and imaging tests which are believed to affect cognitive impairment and that is seen to be the gold standard in the diagnosis of cognitive impairment other than the commonly used mini-mental state examination.

Conclusion

The prevalence of cognitive impairment among CPD patients is 51.8%. Individuals with COPD have a

risk of developing cognitive impairment 4.48 times that of non-COPD individuals. The factors associated with cognitive impairment among COPD clients are age, educational status, cigarette smoking status, and history of alcohol consumption along with the severity of COPD, oxygen saturation, and presence of hypertension.

Recommendation

Concern should be given for cognitive impairment particularly for COPD patients. Researchers should do further longitudinal and large-scale studies.

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