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Depression, Anxiety and Stress among COPD Patients: A Comparative Cross Sectional Study

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ABSTRACT

Background: Chronic Obstructive Pulmonary Disease (COPD) is associated with depression, anxiety and stress, which are the commonest disorders resulting in significant morbidity and mortality. There is paucity of information regarding the association between depression, anxiety, and stress and chronic obstructive pulmonary disease in the present setup. This comparative cross-sectional study was designed to determine the magnitude of Depression, Anxiety and Stress and associated factors among COPD patients.

Methods: Sixty five COPD patients and equal number of age and sex matched healthy individuals were included in the study. The study was conducted at Jimma University Specialized Hospital JUSH), from March 01 to April 30/2016. Spirometric assessment was done to evaluate severity of COPD. Depression, anxiety and stress scale (DASS 21) was used for the assessment of severity of depression, anxiety and stress. Chi-square test, independent t-test, Fisher's exact test, one way ANOVA and linear regression were carried out to determine the association between independent and outcome variables and variables with $p < 0.05$ were considered as significant.

Results: Statistically significant difference between COPD patient and healthy controls was recorded on the prevalence of depression, anxiety and stress (47.7%, 49.2 %, and 56.9% respectively, $p < 0.001$). Depression score was significantly associated with severity of COPD ($p < 0.01$). Duration of hospital admission was a common positive predictor for depression, anxiety and stress scores ($\beta = 0.156$, 0.144 and 0.123 respectively, $p < 0.001$), while FEV1 was a negative predictor of depression ($\beta = -4.209$) and stress score ($\beta = -3.003$), $p < 0.001$. Higher educational level was a negative predictor of depression ($\beta = -7.100$) and anxiety scores ($\beta = -5.15$, $p < 0.05$). Income was a negative predictor of stress score ($\beta = -0.002$, $p < 0.05$). Cigarette smoking was a positive predictor of both depression ($\beta = 13.39$, $p < 0.01$) and anxiety scores ($\beta = 6.75$, $p < 0.05$), while khat chewing was positive predictor of only depression score ($\beta = 5.28$, $p < 0.05$).

Conclusion: The present study showed that the prevalence of depression, anxiety and stress among COPD patients were significantly high. Educational status, duration of admission, FEV1, current khat chewing and cigarette smoking were predictors of depression score. At the same time educational status, cigarette smoking, history and duration of admission were predictors of anxiety score. The severity of depression, anxiety and stress was correlated with the severity of COPD. Therefore, appropriate intervention should be given by the concerned body to treat DAS among COPD patients.

Keywords: Depression; Anxiety; Stress; Chronic obstructive pulmonary disease; Comparative study

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Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; DAS: Depression, Anxiety and Stress; FEV1: Forced Expiratory Volume in 1 Second; FVC: Forced Vital Capacity

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease characterized by persistence air flow limitation that is usually progressive and associated with an enhanced chronic inflammatory response in the air ways and the lungs to noxious particles or gases [1]. It is responsible for higher range of morbidity and mortality; the fourth leading cause of death worldwide with a substantial economic burden [2,3]. It is predicted that in 2030, COPD will be the third leading cause of death in the world [2,4]. A COPD diagnosis is confirmed by a simple Spirometery test and it is based on the documentation of a post bronchodilator FEV1/FVC< 70% [5]. Patients with COPD suffered from dyspnea, deteriorating exercise performance, restricted mobility, social isolation and decrease in peripheral muscle strength [6,7]. Main risk factors for COPD are tobacco smoking, indoor and outdoor air pollution, occupational dusts and chemicals vapors, irritants, and fumes [8].

Mental health-related disorders specifically, mood disorders such as depression and anxiety disorders, phobia and panic disorders are common among patients with COPD. Among these mental illnesses anxiety and depression are the two most common comorbidities of COPD [9]. Hypoxia, smoking, inflammation, severity of symptoms and quality of life in COPD patients are assumed to be the cause of depression anxiety and stress. Among these, severity of symptoms and reported quality of life were strongest predictors of depression among patients with COPD [10]. Mental health problems specifically anxiety was found to be high among substance (chat, alcohol and cigarette) users [11]. Khat (Catha edulis) is a flowering evergreen shrub which contains two alkaloids, cathinone and cathine, which act as stimulants. Symptoms of anxiety and depression were more frequent in female patients and those with no education [12].

These mental illnesses have significant impact on patients, their families, society, and the course of the disease [13]. Generally the estimate prevalence of depression and anxiety in COPD was comparable to or higher than prevalence rates in other advanced diseases such as cancer, AIDS, heart disease, and renal disease [14]. Depression and anxiety are experienced by more than one third of COPD patients [15]. These disorders associated with COPD respond well to appropriate pharmacologic and non-pharmacologic therapy, but only a small proportion of COPD patients with these disorders receive effective treatment. Untreated and under-recognized depression, anxiety and stress symptoms in patients with COPD have deleterious effects on physical functioning and on social interaction, increasing fatigue and healthcare utilization and decreases cigarette smoking-cessation efforts [6,16]. Therefore identifying depression, anxiety and stress, and developing appropriate treatment strategies as early as possible are critical to improve the quality of life of COPD patients and decrease the growing public health impact of COPD. The main aim of the present study was to determine the magnitude of DAS and associated factors among patients with COPD.

RESEARCH METHODOLOGY

A comparative cross sectional study was conducted among 65 COPD patients and the same number of age and sex matched healthy individuals at Jimma University Specialized Hospital, South West Ethiopia from March 01 to April 30/2016. Patients who had been diagnosed for COPD and for controls relatively healthy individuals were included in the study. COPD Patients with other diseases like pulmonary tuberculosis, diabetes mellitus, hypertension and congestive heart failure were excluded from the study. For controls attendants of critically ill patients were excluded.

Pulmonary function test

In order to determine severity of COPD, a post bronchodilator pulmonary function test was performed using spirometer (digital spirometer: 67085). Global Initiative for Chronic Obstructive Lung Disease (GOLD) was followed. GOLD criteria help us classify severity of air flow limitation in COPD patients with ratio of FEV1/FVC<0.7, into four stages; Mild (FEV1 > 80% predicted), Moderate [50<FEV1<80% predicted), Severe [30<FEV1<50% predicted) and very severe (FEV1< 30% predicted) [1].

Assessment of depression, anxiety and stress

Depression, anxiety and stress were assessed by an adopted Lovibond's short version of the Depression Anxiety Stress Scale (DASS). This Scale 21 (DASS 21) had been validated as a reliable self-administered psychological instrument consisting of 21 items in the three domains (Depression Anxiety Stress Scale) [17]. Each domain comprises seven items assessing three dimensions of mental health symptoms: depression, anxiety and stress. Respondents were asked to indicate the presence of these symptom (s) over the last one week on a 4-point Likert scale scoring from 0 to 3. (0: did not apply at all over the last week, 1: applied to some degree, or some of the time; 2: applied a considerable degree, or a good part of time; 3: applied very much or most of the time). The results were summed up and categorized as "normal", "mild", "moderate", "severe" and "extremely severe", according to the DASS manual.

Statistical analysis

The data were checked for completeness and entered in to Epi-Data version 3.1 and were exported to SPSS Version 20 for Windows. Continuous variables were expressed as mean and standard deviation. Categorical variables were expressed as frequencies and percent. Independent sample t-test and one way ANOVA test were used to assess the statistical significance of the mean difference between two and more than two groups

respectively. Chi-Square (X^2) and Fisher's exact test were used to compare the COPD and healthy groups. Preliminary assessment was done and it has showed that there were no violation of assumption of normality, linearity and homoscedasticity. Simple and multiple linear regression analysis were performed to identify significant predictors of depression, anxiety and stress after controlling for other independent variables. First, variables were entered in to the simple linear regression model. The variables found to be significantly associated with the dependent variables were entered into multiple linear regression with enter method. The assumptions in multiple linear regression (linearity, normality and multicollinearity) were checked. A significance level of $p<0.05$ was used in all tests.

Ethical approval

Ethical approval for the study was given by institutional review board of College of Health Science, Jimma University. Written informed consent was obtained from all study participants and confidentiality was kept.

Operational definitions

Substance use: Use of at least one of the substances (alcohol, khat, cigarettes,) in an individual's life time to alter mood or behavior.

Current user: A person who consumed any substance at least once in the past 30 days.

Life time use: Referred to as use of any of the substances at least once in an individual's life time.

DAS scale

Depression: Mild= Score Of 10-13, Moderate = 14-20, Severe = 21-27, Extremely

Severe =28+.

Anxiety: Mild=Score of 8-9, Moderate = 10-14, Severe = 15-19, Extremely Severe=20+.

Stress: Mild=Score Of 15-18, Moderate=19-25, Severe=26-35, Extremely Severe=34+.

RESULTS

Socio-demographic characteristics of respondents

The study was conducted on 130 respondents (65 COPD patients and 65 age and sex matched healthy controls). Thirty eight (58.5%) patients were males with the same sex distribution for relativelq1r y healthy groups. The mean ages of COPD patients and healthy groups were 55.48 (SD ± 10.32) and 54.74 (SD ± 10.09) respectively. There was no significant difference between COPD group and the control groups in terms of socio-demographic characteristics. The mean FEV1 and FEV1% predicted of COPD patients was 1.73 (SD ± 0.72) and 61.3% (SD ± 22.63) respectively (Table 1). There was no significant difference between COPD and healthy groups with respect to substance use except that of life time cigarette smoking, which was high among COPD patients ($p<0.01$). The life time prevalence of cigarette smoking habit among COPD and non COPD groups were 18 (27.7%) and 6 (9.2%) respectively. The current prevalence of khat chewing, alcohol use and cigarette smoking among COPD patients was 14 (21.5%), 10 (15.4%) and 5 (7.7%) respectively.

Table 1: Frequency distribution of sociodemographic and clinical characteristics of COPD patients and healthy group at JUSH, Jimma, Ethiopia, April 2016.

Variables		Study groups (n=130)				X^2/t	p-value
		COPD group (n=65)		Controls group (n=65)			
		N	%	N	%	-	-
Sex	Male	38	58.5	38	58.5	0	1
	Female	27	41.5	27	41.50%	-	-
Age[*]		55.48	10.322	54.74	10.095	-0.412 t	0.681
Religion	Muslim	31	47.70%	21	32.30%	5.5[**]	0.197
	Orthodox	26	40.00%	30	46.20%	-	-
	Protestant	6	2%	12	18.5	-	-
	Catholic	1	1.50%	2	3.1	-	-

	Others#	1	1.50%	0	0	-	-
Ethnicity	Oromo	38	58.50%	34	52.3	-	-
	Amhara	10	15.40%	15	15.40%	6.5**	0.362
	Tigrie	6	9.20%	3	4.6	-	-
	Kefa	5	7.70%	2	3.1	-	-
	Gurage	2	3.10%	5	7.7	-	-
	Kulo	2	3.10%	5	7.7	-	-
	Others#	2	3.10%	1	1.5	-	-
Educational status	No education	25	38.50%	21	32.30%	1.94**	0.584
	Primary school	24	36.90%	23	35.40%	-	-
	Secondary school	7	10.80%	6	9.20%	-	-
	Collage and above	9	13.80%	15	23.10%		
Marital Status	Married	52	80.00%	54	83.10%	1.07**	0.876
	Widowed	6	9.20%	7	10.80%	-	-
	Single	4	6.20%	2	3.10%	-	-
	Divorced	3	4.60%	2	3.10%	-	-
Occupation	Governmental employee	14	21.50%	26	40.00%	3.85**	0.57
	Farmer	16	24.60%	11	16.90%	-	-
	House wife	16	24.60%	7	10.80%	-	-
	Private employee	7	10.80%	6	9.20%	-	-
	Merchant	8	12.30%	13	20.00%	-	-
	Daily laborer	4	6.20%	2	3.10%	-	-
Residence	Urban	37	56.90%	42	56.90%	0.808	0.236
	Rural	28	43.10%	23	43.10%	-	-
Duration of COPD*		8.28	6.64	-	-	-	-
History of admission	Yes	46	70.8	-	-	-	-
	No	19	29.2	-	-	-	-
Duration of admission*		21.9	19.45	-	-	-	-
History of O$_2$ therapy	Yes	38	58.5	-	-	-	-
	No	27	41.5	-	-	-	-

FEV1[*]	1.73	0.72	-	-	-	-
FEV1% predicted[*]	61.3	22.63%	-	-	-	-

N=number [*] Continuous variables which are expressed in mean and SD, [**] fishers exact test, [#] Adventist, [##] Seltie, t, t-test

Prevalence of depression, anxiety and stress symptoms among COPD patients

The prevalence of depression, anxiety and stress among COPD patients was 47.7%, 49.2% and 56.9% respectively, which was higher than that of healthy groups with prevalence of 15.4%, 18.5% and 23.1% respectively. COPD patients were 5, 4.3 and 4.4 times more likely to develop depression, anxiety and stress respectively than that of controls (Table 2). A highly statistical significant difference between COPD and healthy groups was observed (p=0.001) regarding depression score, anxiety score, stress score, severity of depression, anxiety and severity of stress (Table 3).

Table 2: Occurrence and frequency of DAS symptoms in last one week among COPD and healthy groups at JUSH, Jimma, Ethiopia, April 2016.

Outcome	Population (n=130)		RR	95% CI	p-value
	COPD group (n=65)	Healthy group (n=65)			
	N (%)	N (%)			
Depression	31 (47.7%)	10 (15.4%)	5.015	2.184-11.514	<0.001
Anxiety	32 (49.2%)	12 (18.5%)	4.283	1.938-9.466	<0.001
Stress	37 (56.9%)	15 (23.1%)	4.405	2.065-9.396	<0.001

Table 1: Frequency distribution of sociodemographic and clinical characteristics of COPD patients and healthy group at JUSH, Jimma, Ethiopia, April 2016.

Outcome variables	Study groups (n=130)		p-value	X^2/t
	COPD group (n=65)	Healthy group (n=65)		
	N (%)	N (%)		
Depression score#	11.71 (8.73%)	5.38 (6.041%)	<0.001[*]	-4.801t
Anxiety score#	9.32 (7.100%)	3.88 (3.773%)	<0.001[*]	-5.400 t
Stress score#	17.72 (8.938 %)	9.54 (8.203 %)	<0.001[*]	-5.439 t
Level of depression				
Normal	34 (52%)	55 (84.6%)	<0.01[**]	15.99
Mild	10 (15.4%)	4 (6.2%)	-	-
Moderate	10 (15.4%)	4 (6.2%)	-	-
Severe	7 (10.8%)	1 (1.5%)	-	-
Very severe	4 (6.2%)	1 (1.5%)	-	-

		Level of anxiety		
Normal	33 (50.8%)	53 (81.5%)	<0.001**	17.44
Mild	8 (12.3%)	6 (9.2%)	-	-
Moderate	11 (16.9%)	5 (7.7%)	-	-
Severe	5 (7.7%)	1 (1.5%)	-	-
Very severe	8 (12.3%)	0 (0.0%)	-	-
		Level of stress		
Normal	28 (43.1%)	50 (76.9%)	<0.001**	18
Mild	10 (15.4%)	4 (6.2%)	-	-
Moderate	14 (21.5%)	7 (10.8%)	-	-
Severe	8 (12.3%)	4 (6.2%)	-	-
Very severe	5 (7.7%)	0 (0.0%)	-	-

N=number * Continuous variables which are expressed in mean and SD, ** fishers exact test, # Adventist, ## Seltie, t, t-test

Association between DAS and severity of COPD

Severity of COPD was assessed by performing Spirometric measurement of FEV1% predicted to classify it in to four groups according to GOLD, 2015. A one way ANOVA was conducted to evaluate the impact of severity of COPD on DAS score. The COPD group was divided in to four groups; Groups 1, 2, 3, 4 representing mild, moderate, severe and very severe COPD respectively. The result showed that there was a significant difference in depression score for the levels of COPD groups (F=4.3, p=0.008). Post-hoc showed that the mean depression score for each group was statistically significant from each other,

G1 (Mean =8.43 ± SD=6.89) was statistically different from G4 (M=19.22 ± SD=9.18). G1 was statistically different from G3 (M=14.15 ± SD=8.5). Also G2 (M=10.32 ± SD=6.88) was statistically different from G4. As indicated by the depression mean score, severe form of COPD results in an increase in depression score. Patients with severe and very severe COPD had more depressive symptoms than other groups (p<0.01). There was highly significant relationship between severity of depression and stress, with severity of COPD (p<0.001, p<0.05 respectively) (Table 4).

Table 4: Comparison between cases with different COPD severity as regards DAS at JUSH, Jimma, Ethiopia, April 2016 (n=65).

Outcomes	Mild COPD	Moderate COPD	Severe COPD	Very Severe COPD	P	X^2/F
	Mean + SD	Mean + SD	Mean + SD	Mean + SD		
Depression score	8.43 (6.889)	10.32 (6.889)	14.15 (8.503)	19.22 (9.189)	<0.01*a	4.13F
Anxiety score	7.90 (6.526)	8.45 (6.646)	11.07 (8.470)	12.22 (7.172)	0.331*	1.16F
Stress score	15.33 (8.132)	17.41 (9.733)	18.23 (8.833)	23.33 (7.550)	0.163*	1.76F
		Level of depression				
Normal	16 (76.2%)	13 (59.1%)	4 (30.8%)	1 (11.1%)	<0.001***	10.42
Mild	2 (9.5%)	3 (13.6%)	2 (15.4%)	3 (33.3%)	-	-
Moderate	1 (4.8%)	4 (18.2%)	4 (30.8%)	1 (11.1%)	-	-

Severe	1 (4.8%)	1 (4.5%)	2 (15.4%)	3 (33.3%)	-	-
Very severe	1 (4.8%)	1 (4.5%)	1 (7.7%)	1 (11.1%)	-	-
Level of anxiety						
Normal	14 (66.7%)	11 (50.0%)	6 (46.2%)	2 (22.2%)	0.109[***]	2.564
Mild	1 (4.8%)	3 (13.6%)	2 (15.4%)	2 (22.2%)	-	-
Moderate	2 (9.5%)	5 (22.7%)	1 (7.7%)	3 (33.3%)	-	-
Severe	2 (9.5%)	1 (4.5%)	2 (15.4%)	0 (0.0%)	-	-
Very severe	2 (9.5%)	2 (9.1%)	2 (15.4%)	2 (22.2%)	-	-
Level of stress						
Normal	11 (52.4%)	10 (45.5%)	5 (38.5%)	2 (22.2%)	<0.05[***]	5.681
Mild	5 (23.8%)	4 (18.2%)	1 (7.7%)	0 (0.0%)	-	-
Moderate	3 (14.3%)	5 (22.7%)	3 (23.1%)	3 (33.3%)	-	-
Severe	1 (4.8%)	0 (0.0%)	4 (30.8%)	3 (33.3%)	-	-
Very severe	1 (4.8%)	3 (13.6%)	0 (0.0%)	1 (11.1%)	-	-
Depression status						
Yes	5 (23.8%)	9 (40.9%)	4 (30.8%)	8 (88.9%)	<0.01[**]	13.65
No	16 (76.2%)	13 (59.1%)	9 (69.2%)	1 (11.1%)	-	-
Anxiety status						
Yes	7 (33.3%)	11 (50.0%)	7 (53.8%)	7 (77.8%)	0.167[**]	5.06
No	14 (66.7%)	11 (50.0%)	6 (46.2%)	2 (22.2%)	-	-
Stress status						
Yes	10 (47.6%)	12 (54.5%)	8 (61.5%)	7 (77.8%)	0.501[**]	2.431
No	11 (52.4%)	10 (45.5%)	5 (38.5%)	2 (22.2%)	-	-

[*]ANOVA ([a] Gr1 Vs Gr4, Gr2 Vs Gr4, Gr3 v Gr1 by Post Hoc test); [**] Chi-Square test; [***] Fisher's exact test; F=F-test value.

Predictors of depression, anxiety and stress among COPD patients

A simple linear regression analysis revealed that depression score had a significant association with educational status, monthly income, duration of admission, history of oxygen therapy, FEV1, current khat chewing and cigarette smoking. Similarly these variables except substance use had showed significant association with anxiety and stress scores. Residence was significantly associated with only stress score. Age, sex, marital status, duration of COPD and alcohol use didn't show a significant association with any of the outcome variables (Table 5).

Table 5: A simple linear regression model showing predictors of DAS among COPD patients at JUSH, Jimma, Ethiopia, April 2016 (n=65).

Variables	Depression score	Anxiety score	Stress score

	β	Sig	95% CI	β	sig	95% CI	β	Sig	95% CI
Age	0.034	0.75	(-0.179,-0.246)	0.141	0.102	(-0.029, 0.31)	0.047	0.109	(-0.171, 0.27)
Sex Female	0.034	0.114	(-0.86, 7.81)	0.09	0.47	(-2.30, 4.86)	0.199	0.112	(-0.863, 8.02)
Educational status									
No education	4.245	0.056	(-0.110,8.600)	4.6	0.01	(1.54,8.066)	6.17	0.006	(1.81,-10.489)
Secondary	-7.037	0.043	(-13.849,-0.23)	-4.685	0.099	(-10.28,0.914)	-5.61	0.117	(-12.677,1.45)
College & above	-7.012	0.024	(-13.077,-0.95)	-5.147	0.043	(-10.12,-0.18)	-8.19	0.01	- (14.32,-2.07)
Marital status									
Single	-3.418	0.453	(-12.45,-5.62)	2.32	0.531	(-5.038,9.677)	-1.31	0.78	(-10.59,7.989)
Divorced	5.199	0.318	(-5.117,15.515)	3.505	0.408	(-4.902,11.92)	3.785	0.478	(-6.815,14.38)
Widowed	6.198	0.098	(-1.176,13.572)	3.684	0.229	(-2.374, 9.74)	4.71	0.221	(-2.911,12.330
Monthly income	-0.002	0.029	(-0.003,-0.001)	-0.001	0.107	(-0.002,0.602)	-0.01	0.014	(-0.03,0.005)
Residence Rural	2.145	0.331	(2.225, 6.518)	2.068	0.248	(-1.478,5.612)	4.88	0.028	(0.54,9.212)
Duration of COPD	-0.063	0.707	(-0.393,0.268)	0.029	0.829	(-0.24,0.298)	-0.14	-0.422	(-0.473,0.201)
History of admission									
Yes	4.198	0.078	(0.481,8.877)	6.48	0.001	(2.94,10.023)	5.186	0.032	(0.454,9.919)
Duration of admission	0.187	0.007	(0.054,0.315)	0.159	0.005	(0.052-0.265)	0.136	0.022	(0.020,0.35)
History of O$_2$ therapy									
Yes	6.34	0.003	(2.213,10.472)	4.164	0.019	(0.72,7.607)	6.178	0.005	(1.92,10.434)
FEV1	4.901	0.001	(2.091,7.711)	3.923	0.001	(1.632,6.215)	3.722	0.016	(0.72,6.72)
Khat chew Yes	5.289	0.044	(0.151,10.428)	3.95	0.064	(-0.24,8.156)	1.081	0.692	(-4.34,6.5)
Alcohol drink Yes	5.3.09	0.077	(-0.588,11.207)	1.273	0.606	(-3.63,6.178)	3.4	0.272	(-2.729,9.529)
Cigarette smoke									
Yes	14.62	0	(7.302,21.931)	8.1	0.013	(1.764,14.43)	8.1	0.051	(-0.028,16.22)

Male, primary education, married, urban and "no" for history of admission, history of O$_2$ therapy chat chewing, alcohol intake and cigarette smoking were used as reference category.

Multiple linear regression analysis was employed to determine the best linear combinations of those variables which were significant in simple linear regression model. These combinations of variables significantly predicted depression score (secondary education, college and above, duration of hospital admission, FEV1, current khat chewing and cigarette smoking). Of these variables, educational level of college and above, duration of admission and current cigarette smoking were significant predictor of anxiety score. In addition no education and history of hospital admission were predictors of anxiety score. Illiteracy, low monthly income, long duration of hospital admission and low FEV1 were predictors of stress score. Patients with secondary level of education had a mean depression score of 5.43 (β =-8.447, 95 %CI [-14.83, -2.06] p<0.01). For a one day increase in duration of hospital admission, depression score was increased by 0.156 (β = 0.156, CI [0.033, 0.279], p<0.01). A one unit increase in FEV1 has resulted in a decrease in depression score by 4.209 (β = -4.029, CI [-8.001,-0.417], p<0.05). Khat chewing has resulted in an increase in depression score by 5.28 (β = 5.28, CI [1.51, 10.42],

p<0.05). Similarly cigarette smoking has resulted in an increase in depression score by 13.39 (β =13.39, CI [5.87, 20.96], p<0.01) as compared to non-smokers. Illiteracy resulted in an increase in anxiety score by 4.58 (β =4.58, CI [0.399, 8.766], p<0.05) whereas college and above level of education decreased depression score by 5.15 (β =-5.15, CI [-9.95,-0.358], p <0.05). For a one day increase in duration of admission, anxiety score was increased by 0.144 (β =0.144, CI [0.042, 0.247], p<0.01).

Similarly being cigarette smoker resulted in an increase in anxiety score by 6.75 (β =6.75, CI [0.56, 12.94], p<0.05) as compared to the nonsmokers. Illiteracy resulted in an increase in stress score by 5 (β =5.003, CI [0.7, 9.316], p<0.05). Stress score was decreased by 0.002 (β =-0.002, CI [-0.003, -0.001], p<0.005) for a one unit increase in monthly income. Similarly for a unit increase in FEV1, stress score was decreased by 3 (β =-3.003, CI [-5.92, -0.085], P<0.05) (Table 6).

Table 6: Multivariable linear regression model showing predictors of depression, anxiety and stress among COPD patients at JUSH, Jimma, Ethiopia, April 2016 (n=65).

Variables	Depression score		Anxiety score		Stress score	
	β	95% CI	β	95% CI	B	95% CI
No education	NI	-	4.58*	0.399, 8.766	5.003*	0.7,9.316
Secondary	-8.447**	-14.83, -2.06	NI	-	NI	-
College & above	-7.100*	-12.99, -1.39	-5.15*	-9.95,-0.358	-5.85	-11.94, 0.24
Monthly income	-0.001	-0.002, 0.001	NI	-	-0.002*	-0.003, -0.001
Residence Rural	NI	-	NI	-	4.647	-0.099,8.192
History of admission						
Yes	NI	-	6.052*	0.52, 10.83	0.74	-5.7, 7.18
Duration of admission	0.156**	0.033, 0.279	0.144**	0.042, 0.247	0.123*	0.010, 0.236
History of O$_2$ therapy						
Yes	4.456	-1.96, 10.87,	3.199	-2.166, 8.57	5.041	-0.547, 10.629
FEV1	-4.209*	-8.001,-0.417	-0.043	-0.131, 0.045	-3.003*	-5.92, -0.085
Khat chewing Yes	5.28*	1.51, 10.42	NI		NI	-
Cigarette smoke yes	13.39**	5.87, 20.96	6.755*	0.56, 12.94	NI	-
Adjusted R2	0.296	-	0.233		0.167	-

*Significant (p< 0.05), **Highly significant (p<0.01). The reference groups were primary education, urban and "no" for history of admission, history of O$_2$ therapy, khat chewing and cigarette smoking), NI: not included in the final model. NB: Negative values of β show that the corresponding factors are the negative predictors of depression, anxiety or stress.

DISCUSSION

The current investigation depicted that COPD patients suffer from the disease itself and associated common mental disorders like depression, anxiety and stress. This study has provided data about the association of depression, anxiety and stress with chronic obstructive pulmonary disease in comparison with age and sex matched controls. The prevalence of depression, anxiety and stress among 65 COPD patients was 47.7%, 49.2% and 56.9% respectively. It was higher than that of the controls with the prevalence of 15.4%, 18.5% and 23.1% for depression, anxiety and stress respectively. The depression score of the present finding coincides with the study done in Egypt [18,19].

The study was also more or less in line with another study done in china [20]. The slight difference may be due to sociocultural, economic and lifestyle difference. Another study conducted in Turkey also agrees with the present study which showed that the prevalence of depression and anxiety among COPD patient group was 41.7 % and 46.7% respectively [21]. In the present study COPD patients were 5, 4.3 and 4.4 times more likely to develop depression, anxiety and stress respectively than that of healthy group. This finding was in line with a study done in Egypt in 2015 which showed that the prevalence of depressive and anxiety symptoms were significantly higher (3.5 times more risk) among COPD patients than that of the controls [22]. This agrees with a study done in Italy [23]. In the current study, a

highly significant difference between COPD and healthy groups regarding DAS scores and severities of was recorded. This finding was consistent with a studies in Egypt and Korea [18,19]. The possible difference for the observed difference could be due to the presence of COPD induced dyspnea and exercise limitation that lead to low self-esteem, social isolation and dependence on caregivers, which makes daily activities effortful and stressful, and increased the risk of depression and anxiety in patients with COPD. Anxiety and stress scores were higher in those individuals who were illiterate than those who are educated secondary and above. This result was in line with a study in Ethiopia [24]. This might be due to the difference in reasoning ability and cope up mechanisms when they face different problems.

In the present study, a unit increment in FEV1 had decreased depression score by 4.2, which is in line with a studies done in Egypt, Korea, Turkey and Japan [18,19,25,26]. Similarly a unit increment in FEV1 had decreased stress score by 3 unites. The possible reason is that the decrease in FEV1 is associated with worsening of airway obstruction that results in breathlessness, dyspnea and hypoxia which in turn result in occurrence and worsening of depression, anxiety and stress. Anxiety score of patients with history of admission was 6 units higher than those of patients who hadn't history of admission. This finding is supported by other studies in Ethiopia and China [24,27,28].

The duration of hospital admission was also a significant positive predictor of depression, anxiety and stress scores. A one day increase in duration of admission had increased depression, anxiety and stress scores by 0.156, 0.144 and 0.123 units respectively. This finding is more or less in line with a study done in Ethiopia and other countries [24,27,28]. A study in Norway also showed that hospitalization was the cause of stress [29]. This might be due to different environmental factors in the hospital that contributed to increased levels of stress, such as the death of a patient who they had shared a room with. In addition it might be due to fear of re-admission and other psychological problems; they assume themselves that they are severely diseased and have short life span which all results in fear, stress and anxiety. On the other hand, in a study in Korea, the history of admission to the emergency room was not correlated with depression or anxiety [19]. This difference may be due to the difference in the room (ward versus emergency room) and duration of admission. As the duration of admission increased, there will be more risk of facing different problems including economic costs which in turn result in stressful life.

The present study shows that patients with severe and very severe COPD had more depressive symptoms than other groups, which is in agreement with a study in Egypt [18]. In the current study, highly significant increase in severity of depression and stress was observed with an increase in severity of COPD. Another study agreed with result of this study which showed that increased severity and frequency of depressive symptoms were correlated with increased disease severity [30]. Moreover the finding of this study is in agreement with a study [31] which described that patients with severe COPD had a significantly higher depression and anxiety scores than mild and moderate groups. The main reason behind is that as severity of COPD

increase there will be an increase in severity of dyspnea, hypoxia, level of inflammatory markers, exercise limitation and dependency on care givers that lead to fear, terror and hopelessness thereby initiating a vicious circle that perpetuates stress, anxiety and depression.

Depression score of current khat chewer patients was 5.28 higher than those who didn't chew. This coincides with a study of depression on the general population of Jimma [32]. This might be due to the effect of khat. Even though depression symptoms disappear during khat chewing they will re-occur following cessation of khat chewing because khat contains psychoactive chemicals cathinone and cathin that have amphetamine like action in the brain that activate the release of monoaminergic neurotransmitters such as dopamine in the limbic system [33], resulting in relief of depression and feeling of happiness but after cessation of khat, there will be a decrease in release of monoaminergic neurotransmitters due to disruption of stimulation, finally it will leads to depression.

Current smoking status was also found to be a strong positive predictor of depression score. This result was in line with a study which states that smoking had significantly increased the risk of major depression [34] and current smokers were more likely to be depressed than former or never smokers [35]. Other studies on COPD patients [19,36] also agrees with this study, and shows that there was a significant association between current smoking and depression. It was shown that smoking and depression have a bidirectional interactions, depressed individuals are more likely to smoke. Conversely, smokers are more likely to be depressed [37]. This might be due to nicotine in cigarette which stimulates monoamine-releasing neurons via activation of pre-synaptic nicotinic acetylcholine receptors (nAChRs). Activation of these nAChR subtypes lead to influx of Na+ and Ca^{2+} into neurons, which produces neuronal membrane depolarization and neurotransmitter release [38]. Majorly nicotine increase level of dopamine in the mesolimbic system, particularly in the nucleus accumbens. In addition certain tobacco constituents, but not nicotine, have been proposed as inhibitors of the monoamine oxidase (MAO) enzyme and consequently result in an increased level of monoamines like serotonin, norepinephrine and dopamine which are important for pleasure and happiness [39]. But up on withdrawal the stimulation effect will decrease and the level of neurotransmitters will be low; then there will be development of symptoms of depression. In the current study, current cigarette smoking was also a significant predictor of anxiety score. This might be due to free radicals, another highly concentrated component of cigarette smoke, that stimulate production of cell mediated immune cytokines such as interferon-gamma (IFN-γ). These pro-inflammatory cytokines can influence serotonin metabolism, by activating indoleamine 2, 3-dioxygenase to oxidize it and results deficit of both tryptophan and serotonin, which has been associated with increased depressive and anxiety symptoms [40].

LIMITATION OF THE STUDY

The tool used for assessing DAS was used for screening rather than diagnosing of the problem. In addition, the small sample size allowed detecting only relatively strong associations.

CONCLUSION

This study showed that the prevalence of depression, anxiety and stress among COPD patients were significantly higher than those of the controls. Educational status of the participants, duration of admission, the level of FEV1, current khat chewing and cigarette smoking were predictors of depression score. At the same time educational status, history of admission, duration of admission and cigarette smoking were predictors of anxiety score. Stress score was also shown to be predicted by educational status, monthly income, duration of admission and FEV1. Severity of depression and stress were correlated with severity of COPD. Age, sex, marital status, occupation, and duration of COPD illness did not correlate with depression, anxiety and stress scores. Life time chat chewing, cigarette smoking and alcohol intake didn't have any significant association with depression, anxiety and stress scores.

COMPETING INTERESTS

None of the authors have any conflicts of interest to declare.

AUTHORS' CONTRIBUTIONS

YA design the study, performed data analysis and drafted the manuscript. AM involved with designing the study, data analysis, reviewed the manuscript. ST participated with data analysis, designing the study and reviewed the manuscript. All authors read and approved the final manuscript.

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