



Depression and anxiety and their related factors in non-cystic fibrosis stable bronchiectasis

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Abstract

Introduction: Bronchiectasis, as a chronic lung disease, may be associated with depression and anxiety disorders and thus decreased quality of life.

Objectives: The aim of this study was to clarify the relationship of depression and anxiety with non-cystic fibrosis bronchiectasis.

Patients and Methods: A total of 62 patients with non-cystic fibrosis bronchiectasis referred to Referral University hospitals in Qazvin, Iran, were enrolled in this case-control study. The participants' depression and anxiety levels were measured using Beck Depression Inventory and Kettle's anxiety questionnaire, respectively. The control group was selected from healthy individuals with similar demographic characteristics to the patients.

Results: Depression and anxiety were observed in 40.4% and 43.6% of patients respectively. The corresponding values were 32.8% and 32.2% in the control group. Mild anxiety had a significant relationship with bronchiectasis, since bronchiectasis increased the risk of mild anxiety by almost three times. This relationship remained significant after adjustments for gender and age ($P=0.013$). No significant relationships were found between bronchiectasis and the prevalence of depression. Cough severity and sputum volume had a significant correlation with anxiety in patients with bronchiectasis ($R=0.374$, $P=0.007$ and $R=0.325$, $P=0.022$ respectively). Additionally, cough severity had a significant correlation with depression ($R=0.298$, $P=0.037$). Depression and anxiety were not associated with demographic characteristics, pulmonary function test, 6-minute walk test, colonization of airways with *Pseudomonas aeruginosa* and CT scan findings.

Conclusion: Prevalence of anxiety and depression is high in stable non-cystic fibrosis bronchiectasis. The severity of cough and daily sputum volume are most related factors; therefore treatment of these symptoms is very important for management of psychological aspect of the disease.

Introduction

The incidence of chronic respiratory diseases is growing worldwide (1,2). Bronchiectasis refers to the abnormal and irreversible expansion of airways characterized by chronic airway inflammation (3). As a chronic lung disease, bronchiectasis may be associated with depression and anxiety disorders and thus decreased quality of life. Therefore, timely diagnosis of depression and anxiety disorders may be necessary for the support and general management of patients with bronchiectasis (4). Due to chronic psychological stress and social pain, frequent hospital admissions and dependence on medical and nursing staff, daily life activities can be difficult in patients with chronic lung diseases (5). Depression and anxiety decrease individuals' social function and quality of life and accelerate disease (6). The diagnosis of depression and/or anxiety is, hence, critical in patients with

Key point

As a chronic lung disease, bronchiectasis may be associated with depression and anxiety disorders. Prevalence of anxiety and depression is high in stable non-cystic fibrosis bronchiectasis. Severity of cough and daily sputum volume are most related factors, thereby treatment of these symptoms is very important for management of psychological aspect of the disease.

chronic pulmonary disease. Although a close correlation between anxiety and depression is widely accepted, few studies have investigated their simultaneous effects on patients with bronchiectasis (7).

Objectives

This study aimed to find two aims; First of all finding the prevalence of anxiety and depression among bronchiectasis patients

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and the second aim is exploring clinical and paraclinical factors related to the anxiety and depression in these patients.

Patients and Methods

Study design

In this cross-sectional study we evaluated adult patients (>18 years old) with diffuse non-cystic fibrosis bronchiectasis (≥ 2 lobes involvement) that had been diagnosed in our center from October 2015 to October 2017 (Velayat hospital, Qazvin, Iran). They were evaluated in stable phase (free from acute exacerbation for at least 4 weeks prior to the start of the study). Patients with bronchiectasis caused by tuberculosis or those simultaneously suffering from any other chronic diseases were excluded. The control group was preferably selected from the patient's own healthy companions. These people were not suffering from particular underlying conditions. The patients referred to the hospital in the fasting state in the morning, and were investigated by a trained team. Demographic questionnaires were filled out for both groups. All study participants were asked to complete the Beck Depression Inventory (BDI), and Kettle's anxiety scale (KAS). The BDI is a multiple-choice self-reporting scale that included 21 questions. The BDI is used as a tool to assess both the presence and the seriousness of depression. Every question had a four-point scale of answers regarding the intensity of depression symptoms (0–3), with a total score range of 0–63. The participants were classified as normal (0–9), mild (10–18), moderate (19–29) and severe (30–63) depression. Kettle's anxiety scale is a 40-item questionnaire designed by Kettle in 1962. Anxiety levels of the two groups were also categorized as normal, mild, moderate, severe, and very severe on the basis of KAS (8,9). Validity and reliability of these questionnaires were previously confirmed in the Iranian population (10).

In the case group, the following factors were evaluated; 6-minute walk test (6MWT), number of exacerbations in last year, body mass index (BMI), dyspnea with Medical Research Council (MRC) scale, cough with Leicester Cough Questionnaire (LCQ), sputum volume, spirometry, sputum microbiology and CT scan. Their correlation with BDI and KAS was investigated. Height and weight were measured with the approximation of 0.5 cm and 500 g, and BMI was calculated. BMI < 18.5 kg/m² was considered as the malnutrition criteria (11). Level of dyspnea was calculated based on MRC's dyspnea scale. This five-level scale evaluates the level of dyspnea on daily activities of the individual (12). Level 1 represents the lowest severity of dyspnea and Level 5 is the worst severity of dyspnea. For evaluating the severity of cough, Leicester Cough Questionnaire (LCQ) was employed (13). Patients were asked to collect the sputum for 24 h and report its volume by phone. Exacerbation frequencies leading to the hospitalization of patients in the past year were recorded based on the reports of the individual. Pulmonary

function test was performed (Jaeger Ltd Hoechberg, Germany) in accordance with American Thoracic Society (ATS) standards in two steps before and after receiving 200 µg of salbutamol inhaler (14). FEV₁, FVC, $\frac{FEV_1}{FVC}$ and values were defined based on absolute number as well as percentage. The patients were also divided into two groups of nonreversible (NR) and reversible (R) in terms of reversibility in FEV₁. An increase of above 12% and 200 cc in FEV₁ was considered as a reversibility standard. High-resolution computed tomography was used to determine extent of pulmonary involvement. The extent of pulmonary involvement was evaluated by an expert radiologist based on the Bhalla score (15). Each lung lobe was scored as 0 (no bronchiectasis), 1 (cylindrical bronchiectasis in a single lung segment), 2 (cylindrical bronchiectasis in more than one lung segment), or 3 (cystic bronchiectasis). The maximum score was 18 points. According to the standards of the distance traveled per 6 minutes the 6MWT was performed in a 30-m hall, the arterial oxygen saturation (Sat_aO₂) and oxygen variations were calculated and recorded. Drop $\geq 4\%$ in Sat_aO₂ after test, recorded as significant variation (16). For bacteriological studies, the morning sputum was collected after oral washing. Bacteriological smear and culture was performed in a normal environment. According to the bacteria isolated from sputum smear and cultures, the patients were divided into three groups of patients with *Pseudomonas aeruginosa*, patients with non-*Pseudomonas aeruginosa*, and patients with negative culture.

Ethical issues

The research followed the tenets of the Declaration of Helsinki. The institutional ethical committee at Qazvin University of Medical Sciences approved all study protocols. Accordingly, written informed consent was taken from all participants before any intervention. This study was extracted from M.D thesis of Azadeh Esmaeilian at this university (Thesis #639).

Data analysis

SPSS 16.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analyses and P values less than 0.05 were considered significant. For categorical variables, group comparisons were performed using Pearson's chi-square or Fisher's exact test. In order to compare groups of patients, the analysis of variance (ANOVA) and Kruskal-Wallis test were used for normally and non-normally distributed data, respectively. For comparisons between the two groups, student's *t* test and Mann-Whitney U test were used for normally and non-normally distributed data, respectively. Pearson's correlation assessed the association between anxiety and depression with bronchiectasis. To evaluate the risk factors for depression and anxiety, multivariate logistic regression analysis was performed incorporating all factors with $P < 0.05$ in bivariate analysis. Correlation test used for finding relationship between clinical,

paraclinical and demographic data with depression and anxiety in the bronchiectasis patients.

Results

This study surveyed 62 patients with bronchiectasis (mean age: 44.1 ± 15.8 years) and 61 controls (mean age: 35.0 ± 9.71 years). Table 1 shows baseline characteristics of participants. The subjects in the control group are males, more educated, with lower age. The prevalence of males in the case and control groups was 38.7% and 59%, respectively. Depression and anxiety were observed in 40.4% and 43.6% of the patients, respectively. The corresponding values were 32.8% and 32.2% in the control group. The prevalence of mild anxiety is higher in the case group than control (20.0 versus 6.8%) however ANOVA test shows this difference is not significant. No significant differences were observed in the incidence of depression between the case and control groups ($P = 0.437$.) We could not find any significant relationships between these parameters after adjustments for gender, age, smoking habit, and education (Table 2). Table 3 shows correlation between anxiety and depression with characteristics of bronchiectasis patients. There is a negative correlation between LCQ with anxiety in these patients ($r = -0.0326$, $P = 0.007$) and with depression ($r = -0.298$, $P = 0.036$). In addition, we found a positive correlation between sputum volume and anxiety ($r = 0.323$, $P = 0.022$)

Discussion

Based on our knowledge, limited studies have evaluated the relationship of bronchiectasis with depression

and anxiety. According to our findings prevalence of anxiety and depression is high in non-cystic fibrosis bronchiectasis. Totally, depression and anxiety had a high prevalence and were recorded in 40.4% and 43.6% of the patients, respectively. In this study, depression was more prevalent in the case group compared to the control group, however the difference was not significant ($P = 0.437$). Likewise, no significant relationships were detected between the prevalence of depression and age, smoking, and gender, of patients. Only a small number of patients suffered from severe depression and anxiety. This study has shown that the most important factors involved in anxiety and depression in patients with stable non-cystic fibrosis bronchiectasis are the clinical symptoms. The volume of the sputum and the severity of cough were more effective on anxiety and depression than extension of lung involvement in CT scan and the severity of airway obstruction.

Previous studies have reported different frequencies for depression and anxiety in patients with bronchiectasis (10%–55%) (17–20). Moreno et al reported depression in 34% and trait and state anxiety in 55% of non-cystic fibrosis bronchiectasis cases (17). However, in another study Oliveira et al reported depression symptoms in 12.68% and anxiety symptoms in 18% of bronchiectasis cases (20). None of them compare the patients with normal population. Bahali et al evaluated psychological symptoms in children and adolescents with non-cystic fibrosis bronchiectasis and compare it with healthy subjects. He reported no significant difference between patient and control groups for mean depression and trait anxiety scores (21). Therefore, the relationship between diseases and depression might actually be affected by the high prevalence of depression in the Iranian community.

However, Oliveira et al have reported a relationship between age, gender, frequent of exacerbation and depression/anxiety but we found no significant relationships between anxiety and depression in patients with bronchiectasis with these factors (20). Additionally, Niksarlioglu et al reported depression score was related to family situation, and admission to an emergency department within the last year and anxiety score was related to female gender, and admission to an emergency department within the last year (19). Moreno et al concluded that colonization with *Pseudomonas* was associated with trait and state anxiety and indicated that women comparatively presented a higher depression level (17). Likewise, Oliveira et al found significant relationships between depression and both ability to exercise and dyspnea (20). The same author also presented evidence of a direct link between aging and increased depression and anxiety. Moreover, anxiety increased the number of attacks. However, based on the results of our study in stable non-cystic fibrosis bronchiectasis only severity of cough has a significant correlation with anxiety and depression, while sputum volume has a significant correlation with

Table 1. Baseline characteristics of participants

Parameter	Case	Control	P value
	N = 62	N = 61	
Age (y)	44 ± 15.8	35.0 ± 9.71	<0.001
Male, n (%)	24 (38.7)	36 (59.0)	0.049
BMI (kg/m ²) (mean ± SD)	25.3 ± 6.6	26.1 ± 4.8	0.54
FEV1 _{pre} (mean ± SD)	57.8 ± 23.3%		
FEV1/FVC _{pre} (%)	66.8 ± 12%		
CT score	3.29 ± 1.4		
6MWD (m)	446 ± 94		
Education n(%)			<0.001
Illiterate	0 (0.0)	4 (6.4)	
Primary school	4 (6.6)	14 (22.6)	
Middle school	5 (8.2)	9 (14.5)	
High school	21 (34.4)	13 (21)	
University degree	31 (50.8)	22 (35.5)	
Anxiety			0.21
Yes, n (%)	27 (43.6)	19 (32.2)	
No, n (%)	35 (56.4)	42 (67.8)	
Depression			0.437
Yes, n (%)	25 (40.1)	20 (32.8)	
No, n (%)	37 (59.6)	41 (67.2)	

Table 2. Relationship between depression and anxiety with bronchiectasis

		Depression	P value	Anxiety	P value
Unadjusted model	Normal	1		1	
	Mild	0.7 (0.15-3.55)	0.70	3.54 (1.03-12.2)	0.045
	Moderate	1.08 (0.32-3.24)	0.97	0.72 (0.22-2.35)	0.58
	Sever	1.48 (0.47-4.70)	0.51	1.93 (0.50-7.46)	0.33
	Very Sever			1.29 (0.17-9.68)	0.80
Model 1	Normal	1		1	
	Mild	1.15 (0.22-5.97)	0.86	5.96 (1.45-24.5)	0.013
	Moderate	1.22 (9.36-4.11)	0.75	0.91 (0.24-3.50)	0.89
	Sever	1.58 (0.47-5.31)	0.45	3.82 (0.90-16.3)	0.07
	Very Sever			1.31 (0.11-15.02)	0.83
Model 2	Normal	1	0.91	1	
	Mild	0.89 (0.12-6.38)	0.61	4.52 (0.61-33.6)	0.14
	Moderate	0.67 (0.15-3.04)	0.93	0.19 (0.03-1.32)	0.09
	Sever	0.93 (0.21-4.09)	0.98	2.75 (0.56-13.3)	0.21
	Very Sever			0.98 (0.70-13.8)	0.99

Model 1: Age and gender adjusted.

Model 2: adjusted by gender, age, smoking and education.

anxiety. In our study anxiety/depression was not related to level of education.

The findings of spirometry, extension of pulmonary involvement in CT scan, exercise capacity, as well as microbial colonization are the most important factors in evaluation of patients with non-cystic fibrosis bronchiectasis. We did not find any correlation between these parameters and prevalence of anxiety/depression in our patients. In chronic obstructive pulmonary disease, FEV1 and FVC are considered to be the risk factors for depression (22). However Boussoffara et al reported the prevalence of depression and anxiety to be correlated with

FEV1 in bronchiectasis (18), since other investigators like our results reported that pulmonary function tests do not affect the risk of depression/anxiety in adults with bronchiectasis (17,19,20).

In our study, we detected that sputum volume and severity of cough were independent risk factors for anxiety. We also found that severity of cough was a risk factor for depression. Cough and sputum are common symptoms in bronchiectasis cases, particularly during exacerbations. These symptoms led to feeling of embarrassment and sickness. Oliveira et al determined that the amount of sputum was associated with depression (20) while Moreno et al indicated that anxiety was associated with the daily amount of sputum and presence of bacterial colonization in the sputum (17). However, Niksarlioglu et al did not find any relationship between the amount of sputum and depression and anxiety (19).

Conclusion

This study confirms that patients with bronchiectasis often encounter psychological disorders. The high prevalence of anxiety and depression among patients with bronchiectasis in this study necessitates serious attention to the mental health of such patients. Health care providers caring for these patients should routinely screen for anxiety and depression. Since anxiety and depression are not related to the extension of the disease, hence it is necessary to evaluate all patients in this regard. Treatment of cough and phlegm is one of the main steps in treating depression and anxiety in these patients.

Limitations of the study

Small sample size was the main limitation of this study. The major strength of this study, in comparison to similar studies, is recruiting a control group.

Table 3. Correlation between anxiety and depression with characteristics of bronchiectasis patients

		Depression		Anxiety	
		R	P value	R	P value
Demographic	Age	0.083	0.501	-0.164	0.081
	BMI, kg/m ²	-0.056	0.692	-0.056	0.688
Clinical data	Sputum volume	0.193	0.19	0.323	0.022
	MRC	-0.008	0.93	0.044	0.74
	LCQ	-0.298	0.036	-0.374	0.007
	Exacerbation	0.016	0.931	0.033	0.853
Para clinic data	FEV1/FVC	0.046	0.74	0.240	0.08
	FVC	0.096	0.50	0.208	0.130
	Reversibility	0.212	0.16	-0.008	0.958
	Microbiology	-0.136	0.40	-0.296	0.063
	CT	-0.303	0.08	-0.248	0.95
	6MWD	-0.153	0.280	0.104	0.459
	Sat _a O ₂ at rest	-0.073	0.60	0.182	0.193

LCQ: Leicester cough questionnaire, BMI: body mass Index, MRC: medical research council, 6MWD: 6 minute walk distance.

Authors' contribution

RS and MZ were the principal investigators of the study and contributed to conception of the work. All authors contributed to design of the work and acquisition of data, drafting the work and revising it. All authors have approved the final version submitted for publication and take responsibility for the statements made in the published article.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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References

- Chalmers JD, Sethi S. Raising awareness of bronchiectasis in primary care: overview of diagnosis and management strategies in adults. *NPJ Prim Care Respir Med*. 2017;27:18. doi: 10.1038/s41533-017-0019-9.
- Bell SC, Elborn JS, Byrnes CA. Bronchiectasis: treatment decisions for pulmonary exacerbations and their prevention. *Respirology*. 2018;23(11):1006-22. doi: 10.1111/resp.13398
- Flume PA, Chalmers JD, Olivier KN. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. *The Lancet*. 2018;392(10150):880-90. doi: 10.1016/S0140-6736(18)31767-7
- Gao YH, Guan WJ, Zhu YN, Chen RC, Zhang GJ. Anxiety and depression in adult outpatients with bronchiectasis: Associations with disease severity and health-related quality of life. *Clin Respir J*. 2018;12(4):1485-1494. doi: 10.1111/crj.12695.
- Aras YG, Tunc A, Gungen BD, Gungen AC, Aydemir Y, Demiyurek BE. The effects of depression, anxiety and sleep disturbances on cognitive impairment in patients with chronic obstructive pulmonary disease. *Cogn Neurodyn*. 2017;11(6):565-71. doi: 10.1007/s11571-017-9449-x
- Dueñas-Espín I, Demeyer H, Gimeno-Santos E, Polkey MI, Hopkinson NS, Rabinovich RA, et al. Depression symptoms reduce physical activity in COPD patients: a prospective multicenter study. *Int J Chron Obstruct Pulmon Dis*. 2016;11:1287. doi: 10.2147/COPD.S101459
- McDonnell MJ, Aliberti S, Goeminne PC, Restrepo MI, Finch S, Pesci A, et al. Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicenter cohort study. *Lancet Respir Med*. 2016 Dec;4(12):969-979. doi: 10.1016/S2213-2600(16)30320-4.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry*. 1961;4(6):561-71. doi: 10.1001/archpsyc.1961.01710120031004
- Beck AT, Steer RA, Ball R, Ranieri WF. Comparison of Beck Depression Inventories-IA and-II in psychiatric outpatients. *J Pers Assess*. 1996;67(3):588-97. doi:10.1207/s15327752jpa6703_13
- Ghassemzadeh H, Mojtabei R, Karamghadiri N, Ebrahimkhani N. Psychometric properties of a Persian-language version of the Beck Depression Inventory--Second edition: BDI-II-PERSIAN. *Depress Anxiety*. 2005;21(4):185-92. doi: 10.1002/da.20070.
- Who EC. Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. *Lancet (London, England)*. 2004;363(9403):157. doi:10.1016/S0140-6736(03)15268-3
- Long term domiciliary oxygen therapy in chronic hypoxic cor pulmonale complicating chronic bronchitis and emphysema. Report of the Medical Research Council Working Party. *Lancet*. 1981 Mar 28;1(8222):681-6. PMID: 6110912.
- Birring S, Prudon B, Carr A, Singh S, Morgan M, Pavord I. Development of a symptom specific health status measure for patients with chronic cough: Leicester Cough Questionnaire (LCQ). *Thorax*. 2003;58(4):339-43. doi: 10.1136/thorax.58.4.339
- Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. *Eur Respir J*. 2005;26(2):319-38. doi:10.1183/09031936.05.00034805
- Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman B, McCauley D, et al. Cystic fibrosis: scoring system with thin-section CT. *Radiology*. 1991;179(3):783-8. doi: 10.1148/radiology.179.3.2027992
- Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, et al. *Eur Respir Soc*; 2014.
- Moreno RMG, Vasconcelos GF, Cisneros C, Gómez-Punter RM, Calvo GS, Ancochea J. Presence of anxiety and depression in patients with bronchiectasis unrelated to cystic fibrosis. *Arch Bronconeumol*. 2013;49(10):415-20. doi: 10.1016/j.arbres.2013.01.012
- Boussoffara L, Boudawara N, Gharsallaoui Z, Sakka M, Knani J. Troubles anxiodépressifs et dilatation des bronches. *Rev Mal Respir*. 2014;31(3):230-6. doi: 10.1016/j.rmr.2013.04.028
- Niksarlioglu EYÖ, Özkan G, Günlüoğlu G, Uysal MA, Gül S, Kilic L, et al. Factors related to depression and anxiety in adults with bronchiectasis. *Neuropsychiatr Dis Treat*. 2016;12:3005. doi: 10.2147/NDT.S121147
- Olveira C, Olveira G, Gaspar I, Dorado A, Cruz I, Soriguer F, et al. Depression and anxiety symptoms in bronchiectasis: associations with health-related quality of life. *Qual Life Res*. 2013;22(3):597-605. doi: 10.1007/s11136-012-0188-5
- Bahali K, Gedik AH, Bilgic A, Cakir E, Kahraman FU, Osmanoglu NK, et al. The relationship between psychological symptoms, lung function and quality of life in children and adolescents with non-cystic fibrosis bronchiectasis. *Gen Hosp Psychiatr*. 2014;36(5):528-32. doi: 10.1016/j.genhosppsych.2014.05.019
- Rivera CM, Galicia JC, Navarrete BA, Garcia-Polo C, Iturriaga LAR, Herrejón A, et al. Factors associated with depression in COPD: a multicenter study. *Lung*. 2016;194(3):335-43. doi: 10.1007/s00408-016-9862-7