# Original Article

# The Pattern of Psychiatric Morbidity in Chronic Obstructive Pulmonary Disease: A Cross-Sectional, Case–Control Study from a Tertiary Care Hospital in Kashmir, North India

Shabir Ahmad Dar, Bilal Ahmad Bhat, Naveed Nazir Shah[1], Syed Bushra Imtiyaz

Departments of Psychiatry and [1]Chest Medicine, Government Medical College, Srinagar, Jammu and Kashmir, India

**ABSTRACT**

**Introduction:** Psychiatric morbidity has an increased prevalence in chronic obstructive pulmonary disease (COPD). Patients overall psychosocial status plays an important role in the development of depression which, when major, is said to occur in 19%–42% of cases of COPD. We aimed to study patterns of psychosocial issues in patients with COPD. **Materials and Methods:** This study was conducted over a period of 6 months in an Outpatient Department of Government Chest Disease Hospital Srinagar. A total of 100 COPD patients and 100 sex- and age-matched controls were included in this study and compared. The diagnosis of COPD was assessed by spirometry. Patterns of psychiatric morbidities were assessed using the Mini-International Neuropsychiatric Interview. **Results:** The frequency of psychiatric comorbidities was significantly higher ($P < 0.001$) in COPD patients (47%) as compared to controls (12%). The highest frequency of psychiatric morbidities in COPD patients was major depressive episode in 28% in comparison to 9% of controls. Other morbidities include panic disorder, dysthymia, generalized anxiety disorder, and suicidality. **Conclusion:** The frequency of psychiatric morbidities is increased in COPD patients as compared to controls. We recommend that all patients with COPD should be screened for psychiatric morbidity as there is enough scope for psychiatric services to be made available to these patients.

**KEYWORDS:** *Chronic obstructive pulmonary disease, depression, panic disorder, suicidality*

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive, partially reversible, preventable, and treatable lung disease characterized by long-term breathing problems which typically worsens over time. The main symptoms include shortness of breath and cough with sputum production.[1,2] Acute exacerbations and frequent comorbidities contribute to the overall severity in individual patients eventually everyday activities, such as walking or getting dressed, become difficult.[3]

The prevalence of COPD among Indian males is 5% and 3.2% in females. It usually affects over 35 years of age.[4] Smoking is the most common cause of COPD with factors such as air pollution and genetics playing a minor role.[5] Long-term exposures to the irritants start an inflammatory response in the lungs resulting in narrowing of the small airways and breakdown of lung tissue.[6]

The diagnosis of COPD is based on poor airflow as measured by lung function tests in contrast to asthma, where airflow reduction does not improve much with the use of a bronchodilator.[7,8] COPD is diagnosed on

**Address for correspondence:** Dr. Shabir Ahmad Dar, Department of Psychiatry, Government Psychiatric Diseases Hospital Srinagar, G4, Residential Quarters, Srinagar - 190 001, Jammu and Kashmir, India.
E-mail: shabir1055@gmail.com

the basis of symptoms, pulmonary function tests and the finding of a post-bronchodilator forced expiratory volume in 1 (FEV1)/forced vital capacity (FVC) <70%. Chronic inflammation of the small bronchoalveolar tree leads to progressive destruction of the lungs leading to physical disability. This often leads to psychiatric comorbidities such as depression and anxiety disorders and poor quality of life in such patients.[9,10]

Chronic inflammation followed by hypoxemia leads to disruption in noradrenergic and dopaminergic synthesis, release, and replenishment that may lead to symptomatology seen in depressive disorders.[11] Anxiety and depressive symptoms are common in patients affected by COPD, even when their disease is mild in terms of FEV1 and respiratory symptoms. The etiology between COPD and depression seems to be complex and bidirectional.[12]

The prevalence of depression varies widely in different populations, which could be attributed to different ethnicity, different cultural backgrounds, and heterogeneous demography of the study populations and different screening tools.

We undertook this study to estimate the prevalence of psychiatric morbidity in patients with a diagnosis of COPD presenting to the outpatients department at the postgraduate department of chest disease Srinagar, Jammu and Kashmir. To the best of our knowledge, this is the first study to look into the psychological issues in patients of COPD from the lone tertiary care hospital in Kashmir Valley.

## MATERIALS AND METHODS

Postgraduate department of chest diseases provides tertiary medical care to the whole of Kashmir region along with some adjoining areas of Jammu and Ladakh, the population of about 6 million. One hundred consecutive consenting patients diagnosed with COPD were included in the study. The study was approved by the Institutional Ethical Committee of Government Medical College Srinagar. The diagnosis of COPD was made by consultant pulmonologist using clinical, biochemical, radiological, and pulmonary function tests. It was a hospital-based, cross-sectional, case–control study conducted from October 2015 to March 2016.

An equal number of age- and gender-matched normal healthy volunteers unrelated to patients were randomly assigned and were taken in the comparison group. Patients with uncontrolled chronic physical illnesses such as hypertension, hypothyroidism, and diabetes mellitus were excluded from the study. Those not consenting, on corticosteroids or oral contraceptives, or having an acute exacerbation of COPD were excluded from the study.

Detailed history, physical examination, and relevant investigations were done by the resident psychiatrist before screening for any psychiatric diagnosis.

An informed written consent was taken from participants and was briefed about the study before participation. All of the cases were interviewed for sociodemographic parameters such as age, gender, and socioeconomic level. Smoking history was taken as number of pack-years smoked in both groups. Both the cases and comparison group were evaluated to investigate the psychiatric morbidity using Diagnostic and Statistical Manual for Mental Disorders, Fourth Edition (DSM-IV) criteria by means of Mini-International Neuropsychiatric Interview (M.I.N.I.) is a short structured diagnostic interview, developed jointly by psychiatrists and clinicians in the United States and Europe, for DSM-IV and ICD-10 psychiatric disorders. administered by qualified psychiatrist. The choice of MINI as an instrument was based on its high levels of reliability and validity, which have been reported in several studies.[13]

The MINI is a structured interview tool, designed to evaluate the presence of psychiatric disorders according to Axis I, of the DSM-IV.

### Statistical analysis

During 6-month study, a total of 100 patients with COPD and 100 ages and sex-matched controls were enrolled as per our inclusion and exclusion criteria. The sociodemographic and clinical variables of patients and controls were tabulated in an excel sheet and results were statistically analyzed. Data were analyzed using the SPSS version 20.0. $P < 0.05$ was taken as statistically significant.

## RESULTS

An equal number of cases and controls were recruited for the study. Mean age of patients was 56.24 years (ranges between 42–72 years) in comparison to controls 54.78 years. Majority of cases and controls were from rural background belonging to middle socioeconomic class. A significant difference was found with regards to cigarette smoke exposure [Table 1]. About 73% of case group were smokers as compared to only 10% in the

| Table 1: Smoking history of study population | | | | |
|---|---|---|---|---|
| **Smoking history** | **Group** | | $\chi^2$ | **Significant-value** |
| | **Patient group (*n*=100)** | **Control group (*n*=100)** | | |
| Yes | 73 | 10 | 81.74 | 0.001 |
| No | 27 | 90 | | |
| Pack years (mean±SD) | 14.29±9.22 | 5.88±1.28 | 9.02 (*t*) | |

SD: Standard deviation

control group. The mean pack-years of smoking were significantly higher in cases (14.29 ± 9.22) as compared to (5.88 ± 1.28) in control group.

The average FEV1 in our cases was 37.64% ± 12.62% as compared to 89.10% ± 1.64% in controls. The mean FEV1/FVC ratio in our cases was 54.85% ± 10.32% as compared to 97.20% ± 1.88% in controls.

47% of patients in COPD group were having a morbid psychiatric illness as compared to only 12% of healthy voluntary controls in the comparison group [Table 2].

The frequency of psychiatric morbidity was highest for major depressive episode with a prevalence of 28% followed by panic disorder in both the cases and the control group [Table 3]. The frequency of psychiatric morbidity in COPD patients increased with the severity of the illness.

## DISCUSSION

COPD is characterized by progressive obstruction to airflow due to pulmonary inflammatory reactions to noxious particles.[14] COPD is not only the leading cause of morbidity and mortality worldwide but also associated with considerable social and economic burden as well as significant impairments in occupational capacity and quality of life.[15] Patients with diagnosis COPD, especially with advanced conditions, usually suffer from differing degrees of depression, in response to unfavorable health status, an increased degree of immobility and dependence on others, and to a worsening quality of life. The overall impact of the psychosocial status of patients plays an important role in the development of depression which, when major, is said to occur in 19%–42% of cases.[16,17]

Depression is a highly prevalent comorbidity in patients with COPD and its other associated negative aspects in the course of the disease. It contributes significantly to the social and economic burden of patients. Other studies also indicate that there is a high prevalence of anxiety and depression in patients with COPD (44.1%).[18] The reason for the higher prevalence of depression in patients with COPD seems to be the biological factors like increased levels of 5-hydroxyindoleacetic acid as reported by Sekiduka-Kumano *et al*.[19]

It has been seen that increased plasma 5-hydroxyindoleacetic acid levels are associated with poor lung function, hypoxia, and hypercapnia. Poor lung function is closely correlated with a poor Health-related quality of life and may result in depression. In COPD patients, it has been shown that hypoxia and/or hypercapnia induces oxidative stress and results in an increase of reactive oxygen species throughout the whole body including the lungs, brain, and muscles.[20-22]

The other possible factors responsible for the increased prevalence of psychiatric comorbidities in COPD patients could be psychological factors such as low self-esteem and low self-worth resulting from suffering a chronic medical illness. Social factors such as social isolation and low productivity may also contribute to this increased prevalence.

In our study, 73% of cases were smokers compared to 10% in controls ($P < 0.001$). In a study in Northern Sweden by Lindberg *et al*., the prevalence of COPD among men who were smokers was 89%.[23] The mean pack years in cases was 14.29 ± 9.22 while in controls, it was 5.88 ± 1.28 ($P = 0.001$). These findings of ours are consistent with smoking being a risk factor in pathophysiology of COPD. It has been seen that smoking enhances the chances and intensity of COPD, makes routine activities effortful and full of stress, therefore increases the risk of depression in patients with COPD.[24]

Smoking and depression are linked in bidirectional manner. Individuals with depression are more likely to smoke, have a higher risk to commence smoking and find smoking cessation more difficult. Conversely, smokers are more likely to be depressed, which could be caused by the activation of nicotinic acetylcholine receptors, or direct inflammatory effects of smoking.[25]

In our study, cases had psychiatric comorbidity of 47% as compared to 12% in controls ($P = 0.005$). This was in unison with Sharma *et al*., where the prevalence of psychiatric comorbidity in cases was found to be around 44.8%.[26] The most frequent psychiatric comorbidity in our studied patients was major depressive episode with a frequency of 28%. Our study results are concordant with Negi *et al*. where depression was seen in 33.3% of patients.[27] The prevalence of depressive symptoms in COPD patients varies considerably. Mikkelsen *et al*.[28] found an incidence ranging from 6% to 57%, and Van Ede *et al*.[29] from 6% to 42%, whereas recent studies have found a range of 42%–57%.[30,31] In a review of three studies, Solano *et al*.[32] had observed the prevalence of depression ranged from 37% to 71% of COPD patients and the cumulative prevalence rate of depression in our study is comparable with their results.

Little is known about the prevalence of depression in patients with COPD in India. A study done in Indian COPD patients has shown the cumulative prevalence of depression in 72% of patients.[33] However, studies from other countries reported the prevalence of depression in patients with COPD varying from 6% to 56%.[34-36] The variation in the prevalence of depression in COPD can be partly attributed to the use of different measures for depression.

### Table 2: Presence of psychiatric morbidity

| Psychiatric disorders | Groups | | Total (%) |
|---|---|---|---|
| | COPD (%) group | Control (%) group | |
| Present | 47 | 12 | 100 |
| Absent | 53 | 88 | 100 |
| Total | 100 | 100 | 200 |

COPD: Chronic obstructive pulmonary disease

### Table 3: Prevalence of different psychiatric morbidities

| Psychiatry morbidity | Groups (*n*=100 in each group) | | χ² | Significant value |
|---|---|---|---|---|
| | Patient group (%) | Control group (%) | | |
| Major depressive episode | 28 | 9 | 1.18 | 0.00 |
| Panic disorder | 9 | 3 | | |
| Dysthymia | 4 | 0 | | |
| Generalized anxiety disorder | 2 | 0 | | |
| Adjustment with depressive features | 1 | 0 | | |
| Obsessive compulsive disorder | 1 | 0 | | |
| Suicidality | 2 | 0 | | |
| No diagnosis | 53 | 88 | | |

Studies from other countries such as Japan and Turkey reported the prevalence of depression in patients with COPD ranging from 40.5% to 46.7%.[37,38] Maurer *et al.* also found a prevalence of depression in COPD patients to vary from 10% to 42%.[39] The risk of depression in COPD patients is high in comparison to healthy individuals. The presence of under-recognized subclinical depression in patients with COPD is a major concern, as they are at the risk of developing major depression and may increase the burden of physical disability.[40]

Several factors can be attributed for developing depression in patients with COPD. Severe shortness of breath, progressive and irreversible condition and associated hypoxia may be responsible for organic causes of depression in severe COPD. In addition, advanced age, low socioeconomic condition, and the chronic nature of the disease may result in social isolation and leads to more depressive feelings.[41] In patients with COPD even after adjusting the severity, depression is responsible for fatigue, shortness of breath and disability.[39]

Panic disorder was the second-common diagnosis with a frequency of 9% in cases and only 3% of controls. Karajgi *et al.*,[42] in their study using the Structured Clinical Interview for DSM-III-R, found a prevalence rate of 8% for panic disorder which is 5.3 times as

high as in the general population and the results are concordant with our results.[43] Moore and Zebb[44] on the other hand have however found an even higher rate of panic disorder (32%) using self-report measures of panic disorder symptoms based on DSM-IV criteria for panic disorder. Porzelius *et al.*[45] found that 37% of patients experienced a panic attack in the previous 3 weeks. Not only is anxiety highly common among COPD patients but the reverse is also true. The lifetime prevalence of the respiratory disease is higher in people with panic disorder (47%) than with other psychiatric diagnoses.[46]

Dysthymia, generalized anxiety disorder, and suicidality were the other morbid diagnosis. The prevalence of generalized anxiety disorder among patients with COPD ranges from 10% to 15.8% when using standard diagnostic procedures[47-49] compared with lifetime rates of 3.6% to 5.1% in the general public.[50,51] It has been reported that the severity of depression in patients with COPD is closely associated with suicidal ideation.[52,53]

Therefore, it would be worthwhile to rank COPD patients in terms of current suicide risk. Taken together, the data suggest that a depressive status and the severity of COPD may be related to increased plasma 5-HIAA level in depressed COPD patients.

### Limitations

It was a hospital-based study, and its results cannot be generalized for the community. The number of subjects enrolled in our study was not estimated by any statistical tool. The study was conducted in a single center.

## Conclusion

In view of high psychiatric morbidity associated with COPD, there is enough scope for psychiatric services to be made available to these patients. In additions, personal involved in the treatment of these patients should be trained for early detection of psychiatric symptoms for better treatment outcome.

### Acknowledgement

### Conflicts of interest

There are no conflicts of interest.

### References

1. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: NHLBI/WHO Global Initiative for Chronic Obstructive Lung Disease (GOLD) Workshop summary. American journal of respiratory and critical

care medicine. 2001;163:1256-76.

2. Pauwels RA, Buist AS, Calverley PM, Jenkins CR, Hurd SS; GOLD Scientific Committee, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO global initiative for chronic obstructive lung disease (GOLD) workshop summary. Am J Respir Crit Care Med 2001;163:1256-76.

3. Ullah R, Ashraf S. Chronic obstructive lung disease: A rising problem for the world. Pak J Chest Med 2018;23:130-3.

4. Jindal SK. COPD: The unrecognized epidemic in India. J Assoc Physicians India 2012;60 Suppl: 14-6.

5. Zubair T, Sardar MA. Adequacy of inhaler technique in the patients of copd and asthma. KJMS 2015;8:221.

6. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, *et al.* Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2007;176:532-55.

7. Nathell L, Nathell M, Malmberg P, Larsson K. COPD diagnosis related to different guidelines and spirometry techniques. Respir Res 2007;8:89.

8. Chronic Obstructive Pulmonary Disease (COPD)- World Health Organization. Available from: http://www.who.int/news-room/fact-sheets/detail/chronic-obstructive-pulmonary-disease-(copd). [Last accessed on 2018 Jun 06].

9. Murray CJ, Lopez AD. Alternative projections of mortality and disability by cause 1990-2020: Global burden of disease study. Lancet 1997;349:1498-504.

10. Jennings JH, Digiovine B, Obeid D, Frank C. The association between depressive symptoms and acute exacerbations of COPD. Lung 2009;187:128-35.

11. Norwood R. Prevalence and impact of depression in chronic obstructive pulmonary disease patients. Curr Opin Pulm Med 2006;12:113-7.

12. Laviolette L, Laveneziana P; ERS Research Seminar Faculty. Dyspnoea: A multidimensional and multidisciplinary approach. Eur Respir J 2014;43:1750-62.

13. Sheehan DV, Lecrubier Y, Sheehan KH, Amorim P, Janavs J, Weiller E, *et al.* The mini-international neuropsychiatric interview (M.I.N.I.): The development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. J Clin Psychiatry 1998;59 Suppl 20:22-33.

14. Pauwels RA, Rabe KF. Burden and clinical features of chronic obstructive pulmonary disease (COPD). Lancet 2004;364:613-20.

15. Bentsen SB, Rokne B, Wahl AK. Comparison of health-related quality of life between patients with chronic obstructive pulmonary disease and the general population. Scand J Caring Sci 2013;27:905-12.

16. Barnes PJ, Celli BR. Systemic manifestations and comorbidities of COPD. Eur Respir J 2009;33:1165-85.

17. Fabbri LM, Luppi F, Beghé B, Rabe KF. Complex chronic comorbidities of COPD. Eur Respir J 2008;31:204-12.

18. Ng TP, Niti M, Tan WC, Cao Z, Ong KC, Eng P, *et al.* Depressive symptoms and chronic obstructive pulmonary disease: Effect on mortality, hospital readmission, symptom burden, functional status, and quality of life. Arch Intern Med 2007;167:60-7.

19. Sekiduka-Kumano T, Kawayama T, Ito K, Shoji Y, Matsunaga K, Okamoto M, *et al.* Positive association between the plasma levels of 5-hydroxyindoleacetic acid and the severity of depression in patients with chronic obstructive pulmonary disease. BMC Psychiatry 2013;13:159.

20. Mannino DM. COPD: Epidemiology, prevalence, morbidity and

mortality, and disease heterogeneity. Chest 2002;121:121S-6S.

21. Schneider C, Jick SS, Bothner U, Meier CR. COPD and the risk of depression. Chest 2010;137:341-7.

22. Xu W, Collet JP, Shapiro S, Lin Y, Yang T, Platt RW, *et al.* Independent effect of depression and anxiety on chronic obstructive pulmonary disease exacerbations and hospitalizations. Am J Respir Crit Care Med 2008;178:913-20.

23. Lindberg A, Bjerg A, Rönmark E, Larsson LG, Lundbäck B. Prevalence and underdiagnosis of COPD by disease severity and the attributable fraction of smoking report from the obstructive lung disease in Northern Sweden studies. Respir Med 2006;100:264-72.

24. Goodwin RD, Lavoie KL, Lemeshow AR, Jenkins E, Brown ES, Fedoronko DA, *et al.* Depression, anxiety, and COPD: The unexamined role of nicotine dependence. Nicotine Tob Res 2012;14:176-83.

25. Sinden NJ, Stockley RA. Systemic inflammation and comorbidity in COPD: A result of 'overspill' of inflammatory mediators from the lungs? Review of the evidence. Thora×2010;65:930-6.

26. Sharma BB, Singh S, Sharma VK, Choudhary M, Singh V, Lane S, *et al.* Psychiatric morbidity in chronic respiratory disorders in an Indian service using GMHAT/PC. Gen Hosp Psychiatry 2013;35:39-44.

27. Negi H, Sarkar M, Raval AD, Pandey K, Das P. Presence of depression and its risk factors in patients with chronic obstructive pulmonary disease. Indian J Med Res 2014;139:402-8.

28. Mikkelsen RL, Middelboe T, Pisinger C, Stage KB. Anxiety and depression in patients with chronic obstructive pulmonary disease (COPD). A review. Nord J Psychiatry 2004;58:65-70.

29. van Ede L, Yzermans CJ, Brouwer HJ. Prevalence of depression in patients with chronic obstructive pulmonary disease: A systematic review. Thora×1999;54:688-92.

30. Dowson C, Laing R, Barraclough R, Town I, Mulder R, Norris K, *et al.* The use of the hospital anxiety and depression scale (HADS) in patients with chronic obstructive pulmonary disease: A pilot study. N Z Med J 2001;114:447-9.

31. Lacasse Y, Rousseau L, Maltais F. Prevalence of depressive symptoms and depression in patients with severe oxygen-dependent chronic obstructive pulmonary disease. J Cardiopulm Rehabil 2001;21:80-6.

32. Solano JP, Gomes B, Higginson IJ. A comparison of symptom prevalence in far advanced cancer, AIDS, heart disease, chronic obstructive pulmonary disease and renal disease. J Pain Symptom Manage 2006;31:58-69.

33. Jones PW. Quality of life measurement for patients with diseases of the airways. Thora×1991;46:676-82.

34. Fan VS, Ramsey SD, Giardino ND, Make BJ, Emery CF, Diaz PT, *et al.* Sex, depression, and risk of hospitalization and mortality in chronic obstructive pulmonary disease. Arch Intern Med 2007;167:2345-53.

35. Garrod R, Marshall J, Barley E, Jones PW. Predictors of success and failure in pulmonary rehabilitation. Eur Respir J 2006;27:788-94.

36. Cinciripini PM, Wetter DW, Fouladi RT, Blalock JA, Carter BL, Cinciripini LG, *et al.* The effects of depressed mood on smoking cessation: Mediation by postcessation self-efficacy. J Consult Clin Psychol 2003;71:292-301.

37. Hayashi Y, Senjyu H, Iguchi A, Iwai S, Kanada R, Honda S, *et al.* Prevalence of depressive symptoms in Japanese male patients with chronic obstructive pulmonary disease. Psychiatry Clin Neurosci 2011;65:82-8.

38. Tetikkurt C, Ozdemir I, Tetikkurt S, Yılmaz N, Ertan T, Bayar N, *et al.* Anxiety and depression in COPD patients and correlation with

sputum and BAL cytology. Multidiscip Respir Med 2011;6:226-31.

39. Maurer J, Rebbapragada V, Borson S, Goldstein R, Kunik ME, Yohannes AM, *et al.* Anxiety and depression in COPD: Current understanding, unanswered questions, and research needs. Chest 2008;134:43S-56S.

40. Yohannes AM, Baldwin RC, Connolly MJ. Prevalence of sub-threshold depression in elderly patients with chronic obstructive pulmonary disease. Int J Geriatr Psychiatry 2003;18:412-6.

41. van den Bemt L, Schermer T, Bor H, Smink R, van Weel-Baumgarten E, Lucassen P, *et al.* The risk for depression comorbidity in patients with COPD. Chest 2009;135:108-14.

42. Karajgi B, Rifkin A, Doddi S, Kolli R. The prevalence of anxiety disorders in patients with chronic obstructive pulmonary disease. Am J Psychiatry 1990;147:200-1.

43. Robins LN, Helzer JE, Weissman MM, Orvaschel H, Gruenberg E, Burke JD Jr., *et al.* Lifetime prevalence of specific psychiatric disorders in three sites. Arch Gen Psychiatry 1984;41:949-58.

44. Moore MC, Zebb BJ. The catastrophic misinterpretation of physiological distress. Behav Res Ther 1999;37:1105-18.

45. Porzelius J, Vest M, Nochomovitz M. Respiratory function, cognitions, and panic in chronic obstructive pulmonary patients. Behav Res Ther 1992;30:75-7.

46. Zandbergen J, Bright M, Pols H, Fernandez I, de Loof C, Griez EJ, *et al.* Higher lifetime prevalence of respiratory diseases in panic disorder? Am J Psychiatry 1991;148:1583-5.

47. Yellowlees PM, Alpers JH, Bowden JJ, Bryant GD, Ruffin RE. Psychiatric morbidity in patients with chronic airflow obstruction. Med J Aust 1987;146:305-7.

48. Aghanwa HS, Erhabor GE. Specific psychiatric morbidity among patients with chronic obstructive pulmonary disease in a Nigerian general hospital. J Psychosom Res 2001;50:179-83.

49. Aydin IO, Uluşahin A. Depression, anxiety comorbidity, and disability in tuberculosis and chronic obstructive pulmonary disease patients: Applicability of GHQ-12. Gen Hosp Psychiatry 2001;23:77-83.

50. Kellner R, Samet J, Pathak D. Dyspnea, anxiety, and depression in chronic respiratory impairment. Gen Hosp Psychiatry 1992;14:20-8.

51. Wittchen HU, Zhao S, Kessler RC, Eaton WW. DSM-III-R generalized anxiety disorder in the national comorbidity survey. Arch Gen Psychiatry 1994;51:355-64.

52. Goodwin RD. Is COPD associated with suicide behavior? J Psychiatr Res 2011;45:1269-71.

53. Lacasse Y, Beaudoin L, Rousseau L, Maltais F. Randomized trial of paroxetine in end-stage COPD. Monaldi Arch Chest Dis 2004;61:140-7.