

# Association of comorbid anxiety and depression with chronic obstructive pulmonary disease

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## ABSTRACT

**Background:** Chronic obstructive pulmonary disease (COPD) is a disease with known systemic manifestations including psychiatric comorbidities most commonly being depression and/or anxiety. Studies regarding the association of these psychiatric comorbidities in terms of symptom scores, spirometric variables, and hospitalizations among patients of COPD are lacking, especially in India. **Materials and Methods:** One hundred and twenty-eight patients of COPD attending the Outpatient Department of AIIMS Rishikesh, and fulfilling inclusion criteria were screened by Hospital Anxiety and Depression Scale, and those who scored above the cutoff underwent psychiatric evaluation using the International Classification of Diseases, Tenth Edition Diagnostic Criteria for Research for confirmation of their diagnosis. All patients were then evaluated by physician-administered questionnaire for symptom scores by Modified Medical Research Council Scale (mMRC) for dyspnea, Hindi-validated Clinical COPD Questionnaire (CCQ), and for functional capacity by 6-min walk distance (6MWD) according to the American Thoracic Society Guidelines. All patients also underwent spirometric evaluation, and postbronchodilator forced expiratory volume in 1 s (FEV1), BODE index (body mass index [BMI], postbronchodilator FEV1, mMRC for dyspnea, 6MWD) and a history of hospitalization/exacerbations over the past 1 year was also obtained. Comparison of symptom scores, functional capacity in terms of 6MWD, history of exacerbations or hospitalizations over preceding 1 year and BODE index between patients of COPD with or without anxiety and/or depression was done. **Results:** COPD patients with comorbid anxiety and/or depression had higher dyspnea scores and CCQ scores though the proportion of current smokers, BMI, history of hospitalization over the past 1 year, FEV1, and BODE index was not statistically significant between the two groups. **Conclusions:** Depression is a common comorbidity and leads to higher symptom scores as well as poorer quality of life among COPD patients.

**KEY WORDS:** Anxiety, comorbidity, chronic obstructive pulmonary disease, depression

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## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is one of the most common respiratory ailments affecting the elderly and the 4<sup>th</sup> leading cause of mortality worldwide. With time, the concept of COPD as a disease confined only to the lungs has undergone a radical change, and it is now increasingly recognized as a common preventable

and treatable disease with significant extrapulmonary manifestations. The inflammation in COPD is not only confined to the lungs but rather is believed to have systemic spill-over leading to extrapulmonary effects. The extrapulmonary effects or systemic manifestations include cardiovascular disease, osteoporosis, diabetes, lung cancer, weight loss as well as psychiatric comorbidities.

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There is increasing evidence that depression and anxiety are important comorbidities in COPD and may influence various facets of COPD and may have bidirectional cause and effect relationship.<sup>[1]</sup> There is a paucity of studies regarding both the burden as well as the association of these psychiatric comorbidities in COPD, especially in developing countries where a lack of social support mechanism for the elderly may only aggravate the problem. The present study was planned to assess the association of anxiety and/or depression and COPD in terms of symptom scores, functional capacity, and history of hospitalizations which is a predictor of future exacerbations/hospitalizations and BODE index.

## MATERIALS AND METHODS

All consecutive patients of COPD attending the Outpatient Department of AIIMS Rishikesh, diagnosed by history and clinical examination, were screened for the study from August 2014 to September 2015 by chest X-ray, routine hematological, biochemical investigations, and electrocardiography. Spirometry to record forced expiratory volume in 1 s (FEV1) was performed using turbine-based spirometer confirming to the American Thoracic Society (ATS) and European Respiratory Society guidelines to confirm the diagnosis and stage the patients. Patients >70 years of age and with comorbidities, for example, moderate-to-severe hypertension, diabetes mellitus, ischemic heart disease, chronic liver or renal disease, and any associated significant restrictive lung disease were excluded from the study. Two hundred and fifty patients were screened, and 128 patients consenting for the study were enrolled.

By a detailed questionnaire, baseline parameters were recorded including sociodemographic data, smoking history, any other addictions, and body mass index (BMI). Symptom scores including dyspnea according to Modified Medical Research Council Scale (mMRC) and Clinical COPD Questionnaire (CCQ) – the Hindi language validated tool for health-related quality of life (HRQoL) were also recorded. Scores on CCQ range from 0 to 60 with higher scores suggestive of poorer quality of life. Functional capacity was assessed by 6-min walk distance (6MWD) according to ATS guidelines. History of hospitalization over the past 1 year and BODE index were also evaluated. All patients were then screened by Hospital Anxiety and Depression Scale (HADS). A cutoff score of  $\geq 8$  out of 21 for both depression and anxiety individually was considered. Patients who had more than the cutoff score on HADS were referred for psychiatric evaluation whose diagnosis were then confirmed by a diagnostic interview using the International Classification of Diseases, Tenth Edition Diagnostic Criteria for Research (ICD-10 DCR). The research was approved by the Institute's Ethical Committee.

### Statistics

All statistics were performed using Statistical Package for the Social Sciences 17.0. SPSS 17(IBM). Categorical

variables have been described as frequencies, whereas continuous variables have been tested for normality and are presented as mean and standard deviation. Chi-square test and independent sample *t*-test have been used for statistical analysis. *A priori*, a two-sided level of significance was set at  $P < 0.05$ .

## RESULTS

Of the 128 patients eligible for enrollment in the study, 117 (91.4%) were male with a mean age of 61.04 years. Other clinical variable of the whole sample are mentioned in Table 1.

Table 2 shows the distribution of psychiatric comorbidities in the sample. A total of 40 (31.3%) had depressive disorder and/or anxiety disorders with depression being most common psychiatric comorbidity.

Table 3 shows the comparison of various sociodemographic and clinical variables in the group of COPD patients with and without psychiatric comorbidities. Both the baseline dyspnea scores (by mMRC) and CCQ scores for QoL were significantly more in patients with psychiatric co-morbidity.

Although 6MWD and postbronchodilator FEV1 were

**Table 1: Sociodemographic and clinical variables of the whole sample (n=128)**

Variables	Mean (SD)/n (%)
Age	61.04 (6.618)
Sex, male	117 (91.4)
BMI	19.37 (3.363)
Pack year*	29.61 (21.123)
mMRC	1.84 (0.891)
6MWD (m)	411.44 (73.730)
FEV1 (postbronchodilator)	52.23 (16.392)
BODE index	3.20 (2.005)
HADS total score	10.02 (7.493)
HADS depression score	5.082 (4.22)
HADS anxiety score	4.67 (4.034)
CCQ score	16.02 (6.459)

\*Pack years is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years smoked.  
mMRC: Modified Medical Research Council Scale, FEV1: Forced expiratory volume in 1 s, HADS: Hospital Anxiety Depression Scale, CCQ: Clinical COPD Questionnaire, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, BMI: Body mass index, 6MWD: 6-min walk distance

**Table 2: Different psychiatric comorbidities with chronic obstructive pulmonary disease\***

Psychiatric comorbidities	n (%)
Depressive disorders	29 (22.7)
Anxiety disorders	4 (3.1)
Mixed anxiety and depression	7 (5.5)
None	88 (68.8)

\*Diagnosis was made by a two-stage process, first by screening with HADS and then who were screen positive through clinical interview by a psychiatrist using ICD-10 DCR. HADS: Hospital Anxiety and Depression Scale, ICD-10: International Classification of Diseases, Tenth Edition, DCR: Diagnostic criteria for research

**Table 3: Comparison of various sociodemographic and clinical variables in the group of chronic obstructive pulmonary disease patients with (n=40) and without (n=88) psychiatric comorbidities**

Variables	Mean (SD)/n (%)		t/ $\chi^2$	P
	With psychiatric comorbidity	Without psychiatric comorbidity		
Age	62.58 (4.867)	60.34 (7.193)	2.056	0.042*
Gender				
Male	36 (90)	81 (92)	0.146	0.702
Female	4 (10)	7 (8)		
BMI (kg/m <sup>2</sup> )	18.63 (2.686)	19.70 (3.593)	1.863	0.097
Pack year <sup>a</sup>	32.87 (23.368)	28.13 (19.987)	1.110	0.241
6MWD (m)	397.10 (79.659)	417.95 (70.380)	1.423	0.139
FEV1 <sup>b</sup> (%)	51.60 (16.094)	52.51 (16.610)	0.294	0.772
mMRC				
1	8 (20)	52 (59.1)	19.291	0.002**
2	17 (42.5)	13 (14.8)		
3	14 (35)	22 (25)		
4	1 (2.5)	1 (1.1)		
BODE index				
1	11 (27.5)	36 (40.9)	3.013	0.2
2	19 (47.5)	33 (37.5)		
3	7 (17.5)	16 (18.2)		
4	3 (7.5)	3 (3.4)		
HADS total score	18.30 (6.525)	6.26 (4.131)	10.732	<0.001****
HADS depression	9.25 (4.23)	3.18 (2.31)	10.467	<0.001****
HADS anxiety	8.55 (4.36)	2.84 (2.01)	10.171	<0.001****
CCQ score	20.73 (6.998)	13.89 (4.916)	5.586	<0.001****
Smoking status				
Current smoker	9 (22.5)	21 (23.9)	0.979	0.613
Nonsmoker	0	2 (2.3)		
Ex-smoker	31 (77.5)	65 (73.9)		
Hospitalization over the past 1 year				
Yes	7 (17.5)	11 (12.5)	0.569	0.451
No	33 (82.5)	77 (87.5)		
COPD subgroups according to GOLD classification, 2011				
A (low symptom, low risk)	4 (10.0)	33 (37.5)	27.458	<0.001****
B (high symptom, low risk)	14 (35.0)	7 (8.0)		
C (low symptom, high risk)	4 (10.0)	26 (29.5)		
D (high symptom, high risk)	18 (45.0)	22 (25.0)		
Exacerbations over past 1 year				
Yes	15 (37.5)	27 (30.7)	0.580	0.446
No	25 (62.5)	61 (69.3)		
Spirometric staging (FEV1 postbronchodilator)				
1	2 (5)	6 (6.8)	2.238	0.525
2	21 (52.5)	39 (44.3)		
3	16 (40.0)	35 (39.8)		
4	1 (2.5)	8 (9.1)		

\*\*\*\* $P < 0.001$ , \*\* $P < 0.01$ , \* $P < 0.05$ . Continuous and categorical variables were compared using *t*-test and Chi-square test, respectively. <sup>a</sup>Pack years is calculated by multiplying the number of packs of cigarettes smoked per day by the number of years smoked, <sup>b</sup>FEV1 (1: FEV1 >80%, 2: FEV1 50%-80%, 3: FEV1 30%-50%, 4: FEV1 <30%). mMRC: Modified Medical Research Council Scale, HADS: Hospital Anxiety Depression scale, CCQ: Clinical COPD Questionnaire, FEV1: Forced expiratory volume in 1 s, COPD: Chronic obstructive pulmonary disease, SD: Standard deviation, BMI: Body mass index, 6MWD: 6-min walk distance

lesser in the comorbid group, the difference did not reach statistical significance. There was no significant difference in BMI, the proportion of current smokers, BODE index, and history of hospitalizations/exacerbation between the two groups.

A significant difference in the GOLD classification (based on symptom scores and risk assessment) subcategories between the two groups suggests that a high proportion of patients in the comorbid group belong to the high symptom burden group (80%) irrespective of the risks (low or high), whereas those without comorbidity is underrepresented in the high symptom burden, low-risk group (8%),

whereas almost equally represented among the other subgroups. On the other hand, no significant difference was found between the two groups in terms of spirometric classification and postbronchodilator FEV1.

## DISCUSSION

Anxiety and depression are the most common psychiatric comorbidities associated with COPD. Varying prevalence rates have been reported from various parts of world ranging from 5% to more than 40%<sup>[2-4]</sup> both because of variation in the study participants to various psychological tools having been used for screening. Among these,

HADS has shown to be a reliable and frequently used psychological measurement instrument internationally for COPD patients.<sup>[5]</sup> Although there are few studies regarding the prevalence of anxiety and/or depression among COPD patients in India, there is a paucity of studies regarding the impact of these on COPD where both low awareness levels, as well as financial issues, may worsen the situation.

An Indian study among 100 stable patients of COPD using Hindi language translated Patient Health Questionnaire (PHQ-9) found the cumulative prevalence of depression to be 72% and majority of patients were in spirometric stage 2 or 3 (GOLD guidelines).<sup>[6]</sup> In another Indian study among 126 stable patients of COPD, 33.3% showed moderate-to-severe depressive symptoms, whereas 20.6% patients had major depressive disorder on PHQ-9 Scale. Educational and occupational status, BMI, FEV1, respiratory symptoms, physical impairment, and dyspnea were found to be potential predictors of depression in COPD patients.<sup>[7]</sup> In our study, 31.3% had depression and/or anxiety associated with COPD. Depression was the most common psychiatric comorbidity (22.7%) associated with COPD. As per our study design, all patients were initially screened by HADS, and the diagnosis was then confirmed among screened positive patients by a psychiatrist using ICD 10-DCR. This could account for the lesser prevalence considering our methodology for diagnosis to be comparatively more rigorous.

The association between psychiatric comorbidities and COPD has been evaluated in terms of symptom scores, quality of life, adherence to therapy, risk of hospitalizations, readmissions, mortality, outcomes in rehabilitation, smoking rates, and cognitive decline in different studies. Studies have also evaluated link between medication adherence and adherence to rehabilitation and presence of psychiatric comorbidities.<sup>[8]</sup> Moreover, variable scales and variable patient groups have been used in studies world over. Studies in developing countries evaluating the impact of psychiatric comorbidities are far and few.

In a study conducted in China, 701 COPD patients entering pulmonary rehabilitation were assessed using HADS, and it concluded that symptoms of anxiety and/or depression are associated with impaired HRQoL as measured by St. George Respiratory Questionnaire (SGRQ).<sup>[3]</sup> Another study among 307 stable COPD reported that symptom scores in terms of COPD assessment test scores (that also evaluates HRQoL) had modest correlation with HADS scores though the study did not find differences in the proportions of patients with clinically relevant symptoms of anxiety and/or depression between GOLD Groups A to D.<sup>[9]</sup> Another prospective cohort study among 376 hospitalized patients of COPD concluded by multivariate analyses that depression affects symptoms, activities, and impacts HRQoL as measured by SGRQ at the index hospitalization and 1-year later, even after controlling for confounders (such as chronicity and severity of COPD, comorbidities, and behavioral, psychosocial, and socioeconomic variables). Depression

was also significantly associated with mortality, longer index and total hospital stay, and persistent smoking at 6 months.<sup>[10]</sup> Some of the differences might have been due to the different sample (hospitalized patients vs. patients enrolled for rehabilitation vs. outpatients) or the tools used for evaluation of HRQoL.

A study among 337 clinically stable COPD patients using SGRQ for assessing HRQoL and HADS concluded by multivariate analyses that anxiety, depression, or both conditions were associated with poor HRQoL for all SGRQ domains.<sup>[11]</sup> The INSPIRE-II study enrolled 162 patients and evaluated them using multiple psychosocial test battery including Brief Fatigue Inventory, SGRQ, Shortness of Breath Questionnaire, State-Trait Anxiety Inventory, and Beck Depression Inventory (BDI). It concluded after covariate adjustment that higher anxiety and depression levels were associated with greater levels of fatigue, shortness of breath, and frequency of COPD symptoms<sup>[12]</sup> similar to conclusions from our study. Studies evaluating HRQoL using CCQ have also found association with anxiety/depression.<sup>[13]</sup> Our study also showed similar results and found patients with psychiatric comorbidities had poorer HRQoL evaluated by CCQ as well as higher symptom scores, both of which are possibly interlinked. Moreover, we also found a large proportion of patients with psychiatric comorbidity to be in GOLD Group B and D (high symptom burden group) as was found in one study<sup>[14]</sup> though others found either uniform distribution of this comorbidity in all GOLD Subgroups 9 or overrepresentation in Group D3. A few studies have even reported a totally contradictory result and found no association between anxiety and/or depression and deterioration of QoL<sup>[15]</sup> or activity-related dyspnea.<sup>[16]</sup>

Possible association between symptoms of depression and current smoking in COPD patients has been demonstrated in few studies.<sup>[10,17,18]</sup> Although we found an association with QoL in our study, no significant difference in terms of current smokers was seen between the two groups [Table 3]. Possible reasons for the latter discrepancy might be due to cultural difference, longitudinal versus cross-sectional study design and inclusion versus exclusion of comorbid medical disorders in the sample, and generally lower rate of psychiatric comorbidity compared to the above studies.

Studies evaluating the association between depression and functional capacity in terms of 6MWD and spirometric variables (FEV1) also throw up conflicting results. In a multicentric cross-sectional study, clinically significant depression was associated with worse quality of life, reduced exercise capacity, greater dyspnea, and a higher score in the BODE index.<sup>[19]</sup> Other studies have reported no association between emotional status and exercise tolerance including 6MWD.<sup>[20-22]</sup> While some studies have reported no association between GOLD staging of COPD and depression,<sup>[23]</sup> others have found significant correlation between scores on BDI and FEV1, general health perception, vitality, general mental health, and physical



function but no correlation between 6 MWT and emotional status, and quality of life.<sup>[22]</sup> A large study done in China reported COPD severity (assessed by ADO index [age, dyspnea, and airflow obstruction]) was significantly correlated with anxiety and depression, physical strength, daily living activities, and social activities (evaluated through an indigenously designed comprehensive scale).<sup>[24]</sup>

A study from India concluded that as spirometric severity of COPD increases, score on PHQ-9 (that evaluate severity of depressive symptoms) also increases.<sup>[6]</sup> Our study shows no significant association between the two and possible reason could be lesser patients of very severe COPD in our enrolled population.

Association between psychiatric comorbidities and hospitalizations, their frequency, mortality, and overall prognosis in terms of indices such as BODE has been an area of active research, and conflicting results have been reported. Few studies have reported association of depression not only with increased symptom burden but also with longer hospitalization stays,<sup>[17]</sup> significantly higher risk of exacerbations, costs,<sup>[25]</sup> readmissions,<sup>[26-27]</sup> poorer prognosis,<sup>[28]</sup> and higher risk of death.<sup>[9]</sup> In a review, in which 22 cohort studies were included, sixteen of the studies showed that depression was associated with increased mortality and more COPD exacerbations.<sup>[28]</sup> A review of English-language peer-reviewed longitudinal and retrospective studies concluded that though some acceptable evidence suggested that psychological distress confers greater risk for exacerbations, more specifically symptom-based exacerbations or those treated in the patient's own environment, Most studies showed an absence of a positive association, especially with exacerbations leading to hospitalization.<sup>[29]</sup> Similarly, the absence of association between depression and rehospitalization was reported by other studies.<sup>[30]</sup> Although our study demonstrated higher hospitalizations in COPD patients with comorbidity than those without [Table 3], did not reach level of statistical significance. Overall prognosis in terms of BODE index also was not statistically significant between the two groups, unlike other studies.<sup>[24,31]</sup>

## CONCLUSIONS

World-over studies have evaluated widely both the prevalence as well as the impact of depressive and anxiety disorders on the course of COPD. However, the studies from developing countries have been few and mostly focusing on the prevalence of these disorders rather than their impact. Our study has tried to evaluate the association of these disorders with various facets of COPD in terms of symptom scores, quality of life, history of hospitalizations, functional capacity in terms of 6MWD, and overall prognosis in terms of BODE index.

COPD patients with anxiety and/or depressive disorder comorbidities have more symptoms pertaining to dyspnea

and poorer quality of life compared to COPD patients without these comorbidities in spite of having similar spirometric variables. In our busy clinical practice screening for depression and/or anxiety, especially in those COPD patients with higher symptom scores and poorer quality of life should atleast be performed.

Our study also has its own limitations in terms of small sample size and inclusion of only stable patients of COPD. Moreover, being a hospital-based study, the prevalence reported here might be higher compared to that in a community-based sample. In addition, our study also has an edge over other studies that not only used HADS as screening tool; diagnosis in screening positive patients was also confirmed by a diagnostic psychiatric interview using ICD 10-DCR increasing the diagnostic accuracy of psychiatric comorbidities.

The presence of depression and/or anxiety leads to poorer quality of life and higher symptom scores. Screening for psychiatric comorbidities should be performed in all COPD patients, especially with higher symptom scores and poorer quality of life.

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## Conflicts of interest

There are no conflicts of interest.

## REFERENCES

1. Atlantis E, Fahey P, Cochrane B, Smith S. Bidirectional associations between clinically relevant depression or anxiety and COPD: A systematic review and meta-analysis. *Chest* 2013;144:766-77.
2. Fumagalli G, Fabiani F, Forte S, Napolitano M, Marinelli P, Palange P, *et al.* INDACO project: A pilot study on incidence of comorbidities in COPD patients referred to pneumology units. *Multidiscip Respir Med* 2013;8:28.
3. Janssen DJ, Spruit MA, Leue C, Gijzen C, Hameleers H, Schols JM, *et al.* Symptoms of anxiety and depression in COPD patients entering pulmonary rehabilitation. *Chron Respir Dis* 2010;7:147-57.
4. Lou P, Zhu Y, Chen P, Zhang P, Yu J, Zhang N, *et al.* Prevalence and correlations with depression, anxiety, and other features in outpatients with chronic obstructive pulmonary disease in China: A cross-sectional case control study. *BMC Pulm Med* 2012;12:53.
5. Maurer J, Rebbapragada V, Borson S, Goldstein R, Kunik ME, Johannes AM, *et al.* Anxiety and depression in COPD: Current understanding, unanswered questions, and research needs. *Chest* 2008;134:435-56S.
6. De S. Prevalence of depression in Stable Chronic Obstructive Pulmonary Disease. *Indian J Chest Dis Allied Sci* 2011;53:35-9.
7. 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.
8. Khmour MR, Hawwa AF, Kidney JC, Smyth BM, McElnay JC. Potential risk factors for medication non-adherence in patients with chronic obstructive pulmonary disease (COPD). *Eur J Clin Pharmacol* 2012;68:1365-73.

9. Hilmarsen CW, Wilke S, Engan H, Spruit MA, Rodenburg J, Janssen DJ, *et al.* Impact of symptoms of anxiety and depression on COPD assessment test scores. *Eur Respir J* 2014;43:898-900.
10. 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.
11. Balcells E, Gea J, Ferrer J, Serra I, Orozco-Levi M, de Batlle J, *et al.* Factors affecting the relationship between psychological status and quality of life in COPD patients. *Health Qual Life Outcomes* 2010;8:108.
12. Doyle T, Palmer S, Johnson J, Babyak MA, Smith P, Mabe S, *et al.* Association of anxiety and depression with pulmonary-specific symptoms in chronic obstructive pulmonary disease. *Int J Psychiatry Med* 2013;45:189-202.
13. Henoeh I, Strang S, Löfdahl CG, Ekberg-Jansson A. Health-related quality of life in a nationwide cohort of patients with COPD related to other characteristics. *Eur Clin Respir J* 2016;3:31459.
14. Lee YS, Park S, Oh YM, Lee SD, Park SW, Kim YS, *et al.* Chronic obstructive pulmonary disease assessment test can predict depression: A prospective multi-center study. *J Korean Med Sci* 2013;28:1048-54.
15. Liang L, Lin Y, Yang T, Zhang H, Li J, Wang C, *et al.* Determinants of health-related quality of life worsening in patients with chronic obstructive pulmonary disease at one year. *Chin Med J (Engl)* 2014;127:4-10.
16. Sanchez O, Caumont-Prim A, Gillet-Juvin K, Callens E, Graba S, Essalhi M, *et al.* Activity-related dyspnea is not modified by psychological status in people with COPD, interstitial lung disease or obesity. *Respir Physiol Neurobiol* 2012;182:18-25.
17. Gudmundsson G, Gislason T, Janson C, Lindberg E, Suppli Ulrik C, Brøndum E, *et al.* Depression, anxiety and health status after hospitalisation for COPD: A multicentre study in the Nordic countries. *Respir Med* 2006;100:87-93.
18. Chavannes NH, Huibers MJ, Schermer TR, Hendriks A, Van Weel C, Wouters EF, *et al.* Associations of depressive symptoms with gender, body mass index and dyspnea in primary care COPD patients. *Fam Pract* 2005;22:604-7.
19. Martinez Rivera C, Costan Galicia J, Alcázar Navarrete B, Garcia-Polo C, Ruiz Iturriaga LA, Herrejón A, *et al.* Factors associated with depression in COPD: A Multicenter study. *Lung* 2016;194:335-43.
20. Borak J, Chodosowska E, Matuszewski A, Zielinski J. Emotional status does not alter exercise tolerance in patients with chronic obstructive pulmonary disease. *Eur Respir J* 1998;12:370-3.
21. Light RW, Merrill EJ, Despars JA, Gordon GH, Mutalipassi LR. Prevalence of depression and anxiety in patients with COPD. Relationship to functional capacity. *Chest* 1985;87:35-8.
22. Ulubay G, Sariç Ulaşlı S, Akinci B, Görek A, Akçay S. Assessment of relation among emotional status, pulmonary function test, exercise performance, and quality of life in patients with COPD. *Tuberk Toraks* 2009;57:169-76.
23. Kim KU, Park HK, Jung HY, Ahn JJ, Moon E, Kim YS, *et al.* Association of depression with disease severity in patients with chronic obstructive pulmonary disease. *Lung* 2014;192:243-9.
24. Zhang L, Lou P, Zhu Y, Chen P, Zhang P, Yu J, *et al.* Impact of risk factors, activities and psychological disorders on the health of patients with chronic obstructive pulmonary disease in China: A cross-sectional study. *BMC Public Health* 2013;13:627.
25. Dalal AA, Shah M, Lunacsek O, Hanania NA. Clinical and economic burden of depression/anxiety in chronic obstructive pulmonary disease patients within a managed care population. *COPD* 2011;8:293-9.
26. Coventry PA, Gemmel I, Todd CJ. Psychosocial risk factors for hospital readmission in COPD patients on early discharge services: A cohort study. *BMC Pulm Med* 2011;11:49.
27. Iyer AS, Bhatt SP, Garner JJ, Wells JM, Trevor JL, Patel NM, *et al.* Depression is Associated with Readmission for Acute Exacerbation of Chronic Obstructive Pulmonary Disease. *Ann Am Thorac Soc* 2016;13:197-203.
28. Salte K, Titlestad I, Halling A. Depression is associated with poor prognosis in patients with chronic obstructive pulmonary disease - A systematic review. *Dan Med J* 2015;62:A5137.
29. Laurin C, Moullec G, Bacon SL, Lavoie KL. The impact of psychological distress on exacerbation rates in COPD. *Ther Adv Respir Dis* 2011;5:3-18.
30. Gudmundsson G, Gislason T, Janson C, Lindberg E, Hallin R, Ulrik CS, *et al.* Risk factors for rehospitalisation in COPD: Role of health status, anxiety and depression. *Eur Respir J* 2005;26:414-9.
31. An L, Lin YX, Yang T, Zhang H, Jiao X, Zhang S, *et al.* Predictive validity of BODE index for anxious and depressive symptoms in patients with chronic obstructive pulmonary disease. *Chin Med J (Engl)* 2010;123:1845-51.