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Fatigue as a symptom in COPD and its correlation with pulmonary function, exercise tolerance and health related quality of life in a tertiary care hospital of North India

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Abstract
Aim: To determine the relationship between fatigue and pulmonary function, exercise tolerance, depression, and quality of life in patients with COPD.
Methods: This descriptive cross-sectional study was conducted among 123 patients at MMIMSR, Mullana. Spirometric measures of pulmonary function were carried out in each patient. The Multidimensional Fatigue Inventory was used to measure five subscales of fatigue: general, physical and mental fatigue, reduction in activity, and reduction in motivation. The St. George Respiratory Questionnaire, used to measure quality of life, has three subscale dimensions i.e. symptom, activity and impact as well as an overall or total quality of life score.
Results: Mean age was 63.8±2.18, mean FEV_1 was 1.18±0.58 and FEV_1 % predicted was 37.8±18.8. General fatigue significantly correlated with FEV_1, percent predicted ($r = -0.32$, $p < 0.05$), exercise tolerance ($r = -0.55$, $p < 0.05$), and overall quality of life ($r = 0.75$, $p < 0.01$).
Conclusions: This data shows a relationship between dimensions of fatigue and pulmonary function, exercise tolerance, and quality of life in COPD. Therefore, fatigue is an important symptom requiring evaluation and management in patients with COPD.

Keywords: COPD, quality of life, fatigue, FEV_1 % predicted

Introduction
According to the Global Initiative for Chronic Obstructive Lung Disease group (GOLD) guideline, COPD is a disease state characterized by airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases [1]. COPD is characterized by cough, sputum production and breathlessness associated with airflow obstruction. Smoking and occupational exposure to irritants such as dust and fumes are the major causes of COPD, approximately 85 to 90% of all cases being attributed to smoking. The incidence of respiratory symptoms and smoking may indicate that its prevalence will rise in the future. However, accurate estimates of prevalence, incidence and mortality are lacking from many countries [2]. Chronic obstructive pulmonary disease progresses over many decades and tends to present in advanced stages, thus most treated patients are middle aged or elderly. Chronic obstructive pulmonary disease is the fourth leading cause of death worldwide resulting in more than 2.7 million deaths in 2000 [3]. There is growing evidence that shows that relying only on mortality and lung function measures for assessing effectiveness of treatments could be misleading in conditions like COPD that have notable non-respiratory systemic manifestations [4, 5]. As such, Health Related Quality of Life (HRQL) measures has achieved widespread acceptance because it provides a holistic assessment of the impact of the disease and benefits of treatments. Among these quality of life measures, the St Georges Respiratory Questionnaire (SGRQ) has been shown to be valid and specific for COPD [6, 7]. Activity tolerance and ability to carry out activities of daily living are considered components of quality of life. Fatigue in non-pulmonary populations has been associated with reduced physical activity and decreased self-care abilities [8]. Furthermore, fatigue, along with dyspnea, is a primary symptom limiting exercise tolerance in patients with COPD [9]. The evaluation of fatigue in relationship to activities and exercise tolerance in COPD patients is infrequently reported in research and in clinical settings. Quality of life (QoL) evaluation is relatively new in South East Asian region. Little data has been reported on the relationship between various dimensions of fatigue and quality of life in COPD patients [10, 11].
The primary purpose of this study, therefore, was to determine broad similarities in the relationship between fatigue and pulmonary function, exercise tolerance, and quality of life in adult patients with COPD.

Materials and Methods
Study design and population
A descriptive cross-sectional study was conducted among 123 patients with clinical symptoms of moderate to severe chronic obstructive pulmonary disease who were attending outpatient respiratory clinics at tertiary care hospital.

Informed consent & Ethical approval
Written informed consent was obtained from each participant. The study protocol was approved by the institutional ethical committee.

Procedure
1. Pulmonary function tests (FEV_1 and FEV_1percent predicted) were carried out according to American Thoracic Society Guidelines [12].
2. Subjective fatigue was measured with the multidimensional fatigue index 20 (MFI-20)

questionnaire [13]. This 20-item questionnaire provides scores for each of five fatigue dimensions (sample items): general fatigue (I feel tired), physical fatigue (physically, I feel only able to do a little), reduced activity (I think I do very little in a day), reduced motivation (I dread having to do things), and mental fatigue (it takes a lot of effort to concentrate on things).

3. Exercise performance was evaluated by a 6minute walking test [14] which was performed in hospital corridor 100 meters long. Patients were asked to walk as far as possible in 6minutes.
4. HRQL: Quality of life was assessed using the St. George respiratory questionnaire (SGRQ), a 53-item disease-specific questionnaire that provides an overall measure for quality of life with subscale scores in three areas: symptoms, activity, and impact of disease on daily life. The SGRQ is self-administered by each patient. The symptom subscale elicits information as regards cough, sputum, wheeze, and dyspnea, but not fatigue. To calculate the total and subscale scores, each item has a unique empirically derived "weight." from zero to 100. Weighted scores are summed for each dimension. Subscale and total quality of life scores of summed weights are divided by the maximum possible weight for each dimension. Each score is expressed as a percentage of the maximal possible score.

Statistical Analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages, means and standard deviations were calculated. The statistical test applied for the analysis was Pearson correlation test. The confidence interval and p-value were set at 95% and ≤ 0.05 respectively.

Results

Table 1: Among all 123 patients, 84 male and 39 female with moderate to severe COPD were enrolled in the study. Mean age was 63.8±2.18, mean FEV_1 was 1.18±0.58 and FEV1 % predicted was 37.8±18.8Table 2: Significant negative relationships were found between FEV_1, percent predicted, general and physical dimensions of fatigue. No significant relationship was shown between FEV1, percent predicted, and the other subscales of fatigue. Activity tolerance showed significantly strong negative relationships with three subscale dimensions of fatigue i.e. general, physical and reduced activity. Table 3: Scores for overall quality of life and the impact dimension of quality of life showed significant moderate-to-strong correlations with all five dimensions of fatigue. Symptom and activity quality of life dimensions demonstrated also significant moderate-to-strong correlations with three dimensions of fatigue i.e. general, physical, and reduced activity.

Discussion

To date, dyspnea is considered the primary activity limiting symptom in COPD. Thus, in routine clinical evaluation and in studies of respiratory impairment, dyspnea is the symptom primarily and often singularly evaluated. Data from the present study show that fatigue is associated with the presence of other respiratory symptoms, reduction in motivation to carry out activities, reduction in activity and exercise tolerance, altered functional impact and overall impairment in quality of life in patients with COPD.

Table 1: Demographic and pulmonary functions characteristics

Variables	N= 123 (Mean±SD)
Gender (M/F)	84/39
Age	63.8±2.18
FEV_1	1.18±0.58
FEV, % predicted	37.8±18.8

Table 2: Correlations between Fatigue dimensions and Pulmonary Function, Exercise Tolerance

Fatigue Dimension	FEV1,% Predicted	Exercise tolerance
General	- 0.321*	-0.554*
Physical	- 0.433**	- 0.531*
Reduced activity	- 0.394*	-0.547*
Reduced motivation	-0.265	- 0.041
Mental	- 0.021	-0.407

*p < 0.0.5.**p < 0.01.

Table 3: Correlations between Fatigue and Health Related Quality of Life dimensions

Fatigue Dimension	HRQL Dimension		
	Symptom	Activity	Impact
General	0.565**	0.603**	0.681**
Physical	0.524**	0.664**	0.525**
Reduced activity	0.307*	0.401**	0.421**
Reduced motivation	0.223	0.293	0.468**
Mental	0.224	0.341	0.363**

*p < 0.0.5.**p < 0.01.

Physical subscales of MFI-20 correlated with measures of physical functioning, including lung function and activity limitation, whereas the cognitive components of fatigue showed no relationship to physical subscales. We found that greater impairment in pulmonary function was associated with greater perception of general and physical dimensions of fatigue. FEV_1 measured as the percent of predicted value, showed relationship with general fatigue, physical fatigue, and reduction in activity. Physical dimensions of fatigue correlated well with subjective and objective measures of activity performance, the activity component of quality of life, and the activity tolerance. Lack of significant correlation between the more cognitive components of fatigue measured, reduced motivation and mental fatigue, and exercise tolerance and pulmonary function is not considered an unusual finding. In contrast, it shows distinct differences between dimensions of fatigue and their effects on specific patient outcomes. Considerable evidence demonstrates a reduction in activity and exercise tolerance in patients with advancing COPD, very often reported in relationship to the sensation of dyspnea [15]. Fatigue is generally not measured and reported in COPD populations. Our findings indicate a strong association between fatigue and COPD. If evaluated, knowledge of patient fatigue in COPD may provide important clinical information. Fatigue can be improved by self-management education, pulmonary rehabilitation, nutritional support and mind body intervention. Hence, importance should be given to identify this symptom and promote rehabilitation among the patients of COPD. In addition to the associations with pulmonary function and activity tolerance, we demonstrate positive correlations between general and physical dimensions of fatigue and the

presence of respiratory symptoms, or the symptom dimension of quality of life. Symptoms included in the SGRQ were dyspnea, cough, sputum production, and wheeze. The perception of fatigue may be a precursor of or may coexist with [16] and may occur in response to [17] other symptoms experienced by patients with COPD. It has been shown previously that 45% of a sample of patients with COPD, asthma, and pulmonary hypertension could not distinguish between dyspnea and fatigue [15]. In the present study high levels of fatigue reported and its association with functional patient outcomes, the evaluation of fatigue in the clinical setting and strategies in coping and the management of fatigue require consideration. Data from one controlled study [18] have shown improvement in fatigue following a 12-week home rehabilitation program in patients with severe COPD.

Limitations

Present study has not measured the functional alterations which are common in patients with moderately severe and severe COPD, like decreased weight and muscle mass, hypoxemia, decreased strength and endurance, and decreased cognition which may be related to the sensation of fatigue [19, 20]. Respiratory tract infection, also a frequent occurrence in COPD patients, may contribute to subjective fatigue [21]. Association of exacerbation with fatigue was not evaluated in our study. Since previous investigations have shown that dyspnea is strongly related to quality of life in COPD patients, studies comparing dyspnea and fatigue as predictors of quality of life should be carried out.

Conclusion

Data from the present study was analysed for relationship between fatigue and the outcome measures. Our study concluded that increased fatigue is associated with an increase in the severity of pulmonary impairment, reduction in exercise tolerance, and impairment in quality of life in patients with moderate-to-severe COPD. Strategies to prevent subjective fatigue, to ameliorate fatigue intensity and distress responses, and to improve fatigue limited activity tolerance, functional state, and quality of life in COPD patients require development and evaluation.

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