Prevalence of Depression and Related Factors among the Bronchiectasis Patients in Central Sri Lanka

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Abstract
Introduction
Bronchiectasis is a common chronic respiratory condition that can lead to severe pulmonary infections and impaired activities of daily living, resulting in premature mortality and chronic morbidity. Co-morbid depression is common in bronchiectasis and is associated with recurrent dyspnea, general fatigue, and loss of functional capacity. The disease contributes to substantial health and economic burden worldwide. There is a gap in the local literature on the prevalence of depression and related factors in patients with chronic respiratory disorders including bronchiectasis. Hence, this study aimed to investigate the prevalence of depression and related factors among patients with bronchiectasis in central Sri Lanka.
Methodology
This cross-sectional, non-experimental study was carried out among 164 stable bronchiectasis patients visiting the respiratory treatment unit-2, National Hospital Kandy, Sri Lanka. The relationship among the risk factors - age, Body Mass Index (BMI), number of exacerbations in the last 12 months, Bronchiectasis severity index (BSI) score > 9, and modified Medical Research Council (mMRC) dyspnea scale score ≥ 3. Depressive symptoms were assessed using Patient Health Questionnaire (PHQ). All the data were collected from May 2018 to May 2021, using a demographic questionnaire, extracted medical records and compatible history. The relationships between these variables were examined using multiple linear regression analysis. Data analysis was carried out using IBM SPSS statistics 23 software.
Results
Of the 164 bronchiectasis cases, 93 (56.7%) were females while the mean age value of this group was 57.3±16.1 years. Out of the total sample, 38 (23.2%) were presented with depression according to the PHQ scale (PHQ-9 ≥ 10). Multiple linear regression analysis showed that the risk factors account for 69.8% of the variance of depression, as measured by the PHQ. Of the predictor variables, BMI, the number of exacerbations in the last 12 months, BSI score > 9, and mMRC dyspnea scale score ≥ 3 made a significant contribution. The number of exacerbations in the last 12 months made the largest unique contribution. BMI was negatively correlated with depressive symptoms and other predictor variables were positively correlated. Thus, the patients with frequent exacerbations in the last 12 months, low BMI, higher baseline dyspnea, and higher bronchiectasis severity were predicted higher depression.
Conclusion
Depression is commonly co-morbid in patients with bronchiectasis. Frequent exacerbations, low BMI, higher baseline dyspnea, and higher bronchiectasis severity were contributing factors. Hence, bronchiectasis patients should be actively screened for depression to improve the treatment outcomes.
Keywords: Bronchiectasis, depression, exacerbations, Sri Lanka

Introduction

Bronchiectasis is a chronic respiratory condition characterized by the abnormal permanent dilation of bronchi resulting in repeated episodes of respiratory tract infections, inflammation and impaired mucociliary clearance [1]. The disease can lead to severe pulmonary infections and impaired activities of daily living, resulting in premature mortality and chronic morbidity [2]. There is an increase in the prevalence of

bronchiectasis worldwide ranging from 67 to 566.1 per 100,000 people [3-6]. Despite the fact that the prevalence and disease burden of bronchiectasis are increasing, there is a vacuum of information in the medical literature of the country [4, 5]. Bronchiectasis causes a considerable financial burden on the healthcare systems, by demanding frequent medical visits and hospitalizations [7]. In Sri Lanka, diseases of the respiratory system excluding diseases of the upper respiratory tract, pneumonia and influenza have been the third leading cause of hospitalization from 2009 up to 2019 except for the year 2017 [8].

Bronchiectasis presents with a variety of symptoms including cough, sputum production, wheezing, shortness of breath, and general fatigue. Chronic sputum production and frequent episodes of chronic infections are common in bronchiectasis patients compared to other respiratory illnesses like chronic obstructive pulmonary disease (COPD) and bronchial asthma [9-11]. Previous evidence from systematic reviews and meta-analysis revealed that patients with chronic respiratory diseases are more prone to be a victim of depression and anxiety imposing a low quality of life and poor medication adherence [12, 13]. The estimated prevalence of depression in patients with bronchiectasis is ranging from 14%-34% [14, 15, 16]. However, limited studies explored depression and its related factors in patients with bronchiectasis in the Asian region. Hence, this non-experimental, cross-sectional study was assessed depression and its related factors among patients with bronchiectasis in central Sri Lanka.

Methodology

This is a cross-sectional, non-experimental study which was carried out among 164 stable bronchiectasis patients visiting the respiratory treatment unit-2, National Hospital Kandy Sri Lanka. An inclusion and exclusion criteria was applied prior to the recruitment of the patients to the study.
Inclusion criteria.
- Patients aged≥ 18 years
- Confirmed bronchiectasis cases by using HRCT and compatible history.

Exclusion criteria
- Patients aged ≤ 18 Years
- Patients with cystic fibrosis
- Patients with secondary traction bronchiectasis.

Patients were closely assessed by the respiratory team headed by the consultant respiratory physician and all the clinical records were extracted. Exacerbations were assessed using the information of the compatible history and medical records.

Bronchiectasis severity index (BSI) was used to assess the disease severity [17]. The BSI consisted of age, body mass index (BMI), Forced Expiratory Volume (FEV1 %) predicted, previous hospitalizations with severe exacerbations in the past 24 months, number of exacerbations in last 12 months, *pseudomonas aeruginosa* colonization, colonization with other organisms, and radio graphical severity ≥ 3lobes involved. Depressive symptoms were assessed using Patient Health Questionnaire (PHQ) [18]. The PHQ contains nine items which are evaluated on a 4-point scale: 0, "not at all"; 1, "several days"; 2, "more than half of the days"; and 3, "nearly every day." by each item. A higher level of score in the PHQ represented severe depressive symptoms.

The study was conducted to answer two research questions:
- What is the prevalence of depression among patients with bronchiectasis in respiratory treatment unit-2, National Hospital Kandy, Sri Lanka?
- What is the relationship between the level of depression and the risk factors such as age, BMI, Number of exacerbations in the last year, BSI score > 9, and mMRC dyspnea scale score ≥ 3, among the patients with bronchiectasis in respiratory treatment unit-2, National Hospital Kandy, Sri Lanka?

Continuous variables were presented as the means ± standard deviations, and categorical variables were presented as the number of cases and percentages. Multiple linear regression analysis was used to assess the relationship between depression and the related factors [19]. In this study, the dependent variable consists of the PHQ score, while the independent variables are the following: Age, BMI, Number of exacerbations in

the last year, BSI score > 9, and mMRC dyspnea scale score ≥ 3. All of these variables were monitored during May 2018 to May 2021. These variables were included in a demographic questionnaire.

Prior to the data analysis, assumptions of the multiple linear regression were assessed [19]. The linearity of variance was confirmed by creating scattered plots for each predictor variable and the response variable. The absence of multicollinearity was confirmed by assessing the Variance Inflation Factors (VIF) and Tolerance statistics. Tolerance statistics were ranged between T = .594 and T = .867 and all VIFs were below 5, ranging between 1.2 and 1.7. To confirm that the observations are independent, the Durbin-Watson test was performed and the value is 1.136 and between +1 and +3 which means that the independence of the observation has been met. The homoscedasticity was confirmed using standardized residual plots. The residuals had constant variance at every point in the linear model. To ensure that the residuals of the model are normally distributed, quantile-quantile plots (Q-Q plots) were created.

Results

Baseline characteristics of the patients.

A total of 164 patients with bronchiectasis were enrolled on this study (Table 1). The mean age was 57.3±16.1 years, and 93 (56.7%) of the participants were female. Out of the total sample, 38 (23.2%) were presented with depression according to the PHQ scale (PHQ-9 ≥ 10) with a mean PHQ score of 7.95±7.17. The mean body mass index value of the sample was 23.1±4.7 kg/m². The number of exacerbations in the last 12 months consisted of a mean value of 1.04±1.4 while 69 (42.1%) of the participants have been hospitalized with a severe exacerbation in the past 24 months. The mean F E V1 was predicted 65.4±20.4%. *Pseudomonas aeruginosa* and other micro-organisms colonization were reported in 14(8.5%) and 8 (4.8%) participants respectively. In this study group, 54 (32.9%), 48 (29.4%), 21 (12.8%), 27 (16.4%), and 14 (8.5%) represented mMRC dyspnea scale scores of 0,1,2,3 and 4 respectively (Table 3). Radiological severity of more than three lobes involved was reported in the HRCT imaging studies of the 68 (41.5%) participants. The mean BSI score was 5.84±5.5 while 83(50.6%) patients had mild bronchiectasis, 51(31.1%) had moderate bronchiectasis and 30 (18.3%) reported severe bronchiectasis. The majority of the participants (94.5%) were not received any form of psychological or psychiatric consultation.

Table 1: Baseline characteristics of the study subjects.

Characteristic			Number (N=164)	Percentage (%)
Age (Mean± SD)			57.3±16.1	
Gender	Male		71	43.3
	Female		93	56.7
Body-mass index, mean (SD), kg/m2			23.1±4.7	
Number of exacerbations in last 12 months (Mean± SD)			1.04±1.4	
Hospitalizations in the last 24 months		Yes	69	42.1
		No	95	57.9
FEV1, %predicted (Mean± SD)			65.4±20.4	
Pseudomonas aeruginosa colonization		Yes	14	8.5
		No	150	91.4
Colonization with other organisms.		Yes	8	4.8
		No	156	95.1
mMRC dyspnoea scale score	0	Only get breathless with strenuous exercise.	54	32.9
	1	Get short of breath when hurrying on the level or walking up a slight hill.	48	29.4
	2	Walk slower than people of the same age on the level because of breathlessness or have to stop for breath when walking at my own pace on the level.	21	12.8
	3	Stop for breath after walking about 100 yards or after a few minutes on the level	27	16.4
	4	Too breathless to leave the house or breathless when dressing.	14	8.5
Radio graphical severity ≥ 3lobes involved		Yes	68	41.5
		No	96	58.5
Bronchiectasis	(Mean± SD)		5.84±5.5	

Severity Index (BSI) Score	0-4	Mild bronchiectasis	83	50.6
	5-8	Moderate bronchiectasis	51	31.1
	9+	Severe bronchiectasis	30	18.3
Consultation with Psychologist/Psychiatrist		Yes	9	5.4
		No	155	94.5
Patient Health Questionnaire score (Mean± SD)			7.95±7.17	

The predictive relationship between the five individual risk factors and depression was examined by the multiple linear regression analysis. Additionally, the level of variance that can be explained by the scores on the PHQ and the best predictor (risk factor) of the depression were examined. The results indicated the risk factors account for 69.8% of the variance of depression, as measured by the PHQ. The overall regression (Table 2) was significant, $F (5, 158) = 73.1$, $p < .001$, Adjusted $R^2 = .698$.

Table 2: Model summary of variance for depression, as measured by the PHQ

R	R^2	Adjusted R^2	F	df1	df2	p value
.836[a]	.698	.689	73.1	5	158	.000[a]

a= Predictors (Constant): Age, BMI, BSI score > 9, mMRC dyspnea scale score ≥ 3, number of exacerbations in the last 12 months.

Of the independent variables, the number of exacerbations in the last 12 months made the largest unique contribution (β = .427), although mMRC dyspnea scale score≥ 3 (β = .210), BMI (β = -.215), and BSI score> 9 also (β = .245) made statistically significant contributions. The patients with frequent exacerbations in the last 12 months tended to have higher depression score than the patients without or less frequent exacerbations. There was a negative correlation between BMI and the depression score of the patients. Participants with low BMI reported higher PHQ score than the patients with an optimal BMI. Patients with high baseline dyspnea in mMRC dyspnea scale (mMRC≥ 3) tended to have higher depression score in PHQ. The patients with higher disease severity (BSI score >9) reported higher PHQ score than the patients with lower disease severity (BSI score<9) as measured by the BSI. There was no statistically significant contribution found between the age of the patients and the depression score in PHQ. Regression weights were summarized in table 3.

Table 3: Summary of analysis for variables predicting depression, as measured by the PHQ.

Model	Unstandardized Coefficients		Standardized Coefficients	t	p
	B	Std. Error	β		
Age	.009	.021	.019	.406	.685
BMI	-.331	.072	-.215	-4.588	.000
BSI score > 9	2.184	.505	.245	4.321	.000
Number of exacerbations in the last 12 months	2.183	.289	.427	7.545	.000
mMRC dyspnoea scale score ≥ 3	3.469	.860	.210	4.032	.000
(Constant)	5.433	2.179		2.494	.014

B = Unstandardized β, Std. Error = standard error of the mean for unstandardized β

Discussion
Bronchiectasis is a chronic lung disease which is associated with abnormal and irreversible dilatation of the bronchi resulting in frequent infections with mild to moderate airway obstructions [1]. Bronchiectasis was considered as an orphan disease during the fast decades [7]. But in recent years the prevalence and disease burden of bronchiectasis were increasing and has no longer been considered as an orphan disease [7]. There is a complex interaction between psychiatric comorbidity and chronic medical conditions including respiratory disorders [20]. Recurrent dyspnea, general fatigue, and loss of functional capacity may lead to depressive symptoms in patients with bronchiectasis [12]. To enhance the health and quality of life of

patients with bronchiectasis, health services needed to adopt a holistic approach including mental health [21]. Hence, the present study provides insights into the prevalence of depression and related factors among a sample of confirmed bronchiectasis cases. This study and its importance were justified by the scarcity of empirical data in the local literature regarding the prevalence of depression and related factors in patients with bronchiectasis in central Sri Lanka.

The previous literature indicated a prevalence of depression among patients with bronchiectasis which ranging from 14% to 34% [15, 16]. In line with them, this study found that 23.2% of the bronchiectasis patients were presented with depressive symptoms.

Multiple studies have shown that, disease severity, dyspnea and the high number of exacerbations as the statistically significant contributing factors to the development of depressive symptoms in patients with bronchiectasis [12, 15, 16].

Elderly patients with chronic diseases including respiratory conditions have an increased risk of developing depression due to the disease outcomes such as pain, disability and social isolation [22, 23]. Hence, we investigated age and its relationship with depressive symptoms of bronchiectasis cases. Nevertheless, there was no statistically significant contribution found between age of the patients and the depression score in PHQ.

There is a scarcity of studies exploring the depression and its relationship with the disease severity in bronchiectasis. Yong et al. 2018 carried out a cross-sectional study between 163 outpatients with bronchiectasis to investigate the association between disease severity and the impact of anxiety and depression on health-related quality of life (HRQoL) in adult outpatients with steady-state bronchiectasis. They discovered that anxiety and depression are common in bronchiectasis and negatively impact on HRQoL, but not related to the severity of the disease as measured by the BSI and FACED (forced expiratory volume in 1 s (FEV1), age, chronic colonization by *Pseudomonas aeruginosa*, radiological extension and dyspnea) score [24]. Contrary to their findings, the current study revealed a significant relationship between disease severity and the rate of depression. The patients with higher disease severity tended to have a higher level of depression. Owing to the multiple linear regression analysis the patients with a disease severity of more than nine in BSI made the second largest unique contribution to the depression score in PHQ.

There is a complex association between dyspnea and depression [25]. Dyspnea may lead to reduced physical functions resulting in psychological symptoms [26]. In the recent study, we use mMRC dyspnea scale to quantify disability attributable to breathlessness and to characterize baseline dyspnea according to the standard guidelines [27]. We found that the patients who reported higher mMRC dyspnea scale scores tended to have a higher depression score in the PHQ.

Most of the previous studies were mainly focused on investigating the relationship between acute exacerbations and depression in patients with COPD and asthma [28-30]. However, recurrent exacerbations can occur in bronchiectasis resulting in deterioration of lung function, progression of the disease, impairment of quality of life, and increased mortality [31]. In the present study, the number of exacerbations in the last 12 months made the largest unique contribution to the depression score in PHQ. Patients with frequent exacerbations are more prone to be a victim of depression than patients with less frequent exacerbations. Recent literature revealed that treatment adherence may be impaired by the presence of depression and anxiety in patients with chronic respiratory diseases such as bronchiectasis [16, 32]. However, the present study was not assessed the treatment adherence of this study group. Considering the fact that treatment adherence is linked to the frequency of exacerbations, identification and treatment of depression are crucial in these groups [15].

BMI is a predictor of mortality in bronchiectasis. Being underweight is associated with increased mortality in bronchiectasis compared to patients with optimal body weight [33]. Moreover, there is a negative relationship between BMI and acute exacerbations [34]. However, the relationship between BMI and depression was minimally addressed in previous studies. In a recent study, Lee et al. 2021 compared the BMI of bronchiectasis patients with and without depression and no significant difference was found [12]. Conversely, we found statistical evidence of a negative relationship between BMI and depression as measured by the PHQ. BMI < 18.5 (underweight) is associated with particularly high rates of depression in bronchiectasis. The World Health Organization describes BMI as an indicator of the nutritional status in

adults [35]. Hence, the patients need to be screened for unintentional weight loss and disease-related malnutrition in routine visits.

Conclusion

Patients with chronic respiratory diseases such as bronchiectasis are more prone to be a victim of depression. A substantial number of patients with bronchiectasis had depressive symptoms and a significant predictive relationship existed between frequent exacerbations low BMI status, higher baseline dyspnea, and higher bronchiectasis severity. These findings suggest that the detection of psychological co-morbidities should be implemented in routine clinical practice in bronchiectasis patients. Further studies should be conducted with a large sample size, demographic variation and widening the selection of risk factors.

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