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ORIGINAL ARTICLE

Gender Differences: Does It Affect Clinical, Radiological and Microbiological Features in Adult Non-Cystic Fibrosis Bronchiectasis?

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ABSTRACT

Objective: This study aimed to investigate the gender effect on the clinic, radiological, and microbiological features in adult non-cystic fibrosis bronchiectasis.

Material and Methods: This was a cross-sectional study of 217 patients with adult non-CF BR. Patients with a confirmed diagnosis of bronchiectasis with high resolution computed tomography were investigated. Patients were clinically stable in the previous four weeks enrolled in the study. Symptoms, pulmonary function tests, radiological findings, microbiological results, and bronchiectasis severity index (BSI) were recorded.

Results: The mean age of patients was 49.7±15.3 years (range 18-82). Fourty-one percent patients had smoking history. BR patients had a history of pneumonia sequel (47.9%), post-tuberculosis (33.6%) and idiopathic (15.7%). Patients divided into gender groups: females in group I, n=122 (56.2%)) and males in group II, n=95 (43.8%). There were differences in cough (84.4% vs 71.6%, p=0.029), smoking history (19.7% vs 75.9 %,p=0.001), chronic obstructive pulmonary disease (4.1% vs 37.9%, p=0.001), diabetes mellitus (21.3% vs 9.5%, p=0.025), depression history (36.1% vs 10.6%, p=0.001), panic disorders (10.7% vs 3.2%, p=0.039), long term oxygen usage (6.6% vs 17.9%,p=0.017). Forty-two percent of male BR patients had post-tuberculosis history, fifty-six female had post-pneumonia history, also. FEV1 and FVC value were higher in man (1.5±0.7 vs 1.9±0.9,p= 0.001; 1.9±0.7 vs 2.7±1.0, p=0.0001 respectively). And also, FEV1/FVC ratio was lower in male (73.8±12.3 vs 67.8±15.3, p=0.01). There was no difference between gender and age, dyspnea, heamoptysis, BSI category, radiologic severity using Reiff's score, microbiological features and bilevel positive airway pressure usage.

Conclusion: We concluded that gender differences in non-CFBR might be clinically important in our study population. It is important to consider the gender differences might be effect symptoms, comorbidity, and pulmonary function test results in non-CF BR patients.

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INTRODUCTION

Previous studies reported that chronic respiratory disease such as asthma, chronic obstructive pulmonary disease (COPD), lung cancer might represent somewhat difference in clinical picture between female and male patients [1,2]. Gender-related differences are described in some studies, especially in cystic fibrosis (CF) patients [3,4].

Bronchiectasis (BR) is characterized by anatomic

distortion of the bronchi, with chronic cough, chronic sputum production, and recurrent respiratory infections [5]. According to US data, the estimated prevalence of bronchiectasis is 53 cases per 100,000 adults [2]. The prevalence increases with age and is higher in females. To our knowledge, there is no study considering gender difference in adult non-cystic fibrosis BR in Turkey. We aimed to investigate the gender effect on clinical, radiological findings and microbiological results on adult non-CF BR patients.

MATERIALS and METHODS

This cross-sectional study was conducted between 1 January 2017 and 31 December 2018 in adult non-cystic fibrosis BR patients in a Yedikule Chest Disease and Thoracic Surgery Training and Research Hospital. In all cases, BR was diagnosed by high-resolution computed tomography (HRCT) of the chest. Exclusion criteria were age <18 and >90 years, interstitial lung disease, lung cancer, active tuberculosis, non-tuberculosis mycobacterial disease, malignancy. Demographic parameters, respiratory symptoms, duration of illness, comorbidities, pulmonary function tests, HRCT findings, complete blood count, and sputum culture results in a stable period were all recorded. Sputum samples were considered acceptable if they contain less than ten squamous cells and more than 25 leukocytes per low-power microscopic field [6]. The study was reviewed and approved by the Local Ethics Committee (Approval no: 2019/1814).

The radiological severity of HRCT abnormalities was scored by using the modified Reiff's score (range 1-18), which evaluates the number of lobes involved (the lingula was considered as a separate lobe, tubular BR = 1, varicose BR = 2 and cystic BR = 3 points) [7]. The Bronchiectasis Severity Index (BSI) was applied to determine disease severity. The ranges of scores for the mild, moderate, and severe bronchiectasis according to BSI, were defined as 0-4, 5-8, and ≥9 points, respectively [8].

Statistical analyses were carried out using the SPSS package version 20. The variables were investigated using analytic methods (Kolmogorov-Simirnov/Shapiro–Wilk test) to determine whether or not they are normally distributed. Continuous variables were presented as the mean ± standard deviation (SD), or median (minimum-maximum), when there were a non-normal distribution and categorical variables were presented as proportions.

RESULTS

A total of 217 non-cystic fibrosis BR patients were enrolled in the study. Their mean age was 49.7±15.3 years (range 18-82), and 122 (56.2%) were women. Demographic parameters of the all study group was shown in Table 1. Most common causes of BR were pneumonia sequel (104; 47.9%), post-tuberculosis (73; 33.6%) and idiopathic (34; 15.7%). One hundred and six (48.8%) of BR patients had comorbidities: hypertension (22.6%), depression (24.9%), COPD (18.9%), asthma (17.5%) and diabetes (16.1%). The most common symptoms were dyspnea and cough in all study group. Twenty-five patients (11.5%) used long-term oxygen treatment, 39 patients (18%) used nebulization, and 8 (3.7%) patients used non-invasive mechanical ventilation at home.

Patients divided in to two groups according to gender: group I were females, n=122 (56.2%) and group II were male, n=95 (43.8%). The percentage of the smokers was lower in the female BR group (19.7% vs 75.9%, p=0.001, respectively) and the same occurred with smoking packs-year (21.1±17.2 vs 30.6±22.5, p=0.015, respectively). There was a statistically significant difference in cough (84.4% vs 71.6%, p=0.029), COPD (4.1% vs 37.9%, p=0.001), diabetes mellitus (21.3% vs 9.5%, p=0.025), depression history (36.1% vs 10.6%, p=0.001), panic disorders (10.7% vs 3.2%, p=0.039), using long term oxygen treatment (LTOT) (6.6% vs 17.9%, p=0.017). But, there was no significant difference between gender and age, dyspnea, haemoptysis, BPAP and nebulizator usage at home (Table 2).

Table 1: Demographic parameters of study group

Parameters	Results, Total number= 217
Age, years	49.7±15.3 (range 18-82)
Female/Male	122 (56.2)/95 (43.8)
Active smoker	61 (28.1)
Ex-smoker	29 (13.4)
Smoking packs-year	27.5±22.7
BMI	26.1±5.0 (12.5- 41.5)
Etiology	
Post tuberculosis	73 (33.6)
Pneumonia sequel	104 (47.9)
Idiopathic	34 (15.7)
Comorbidities	106 (48.8)
Hypertension	49 (22.6)
Coronary artery disease	14 (6.5)
Diabetes mellitus	35 (16.1)
COPD	41 (18.9)
Asthma	38 (17.5)
Depression	54 (24.9)
Panic disorders	16 (7.4)
Symptoms	
Dyspnea	175 (80.6)
Cough	171 (78.8)
Haemoptysis	57 (26.3)
Sputum	120 (55.3)
FEV1	1.7±0.8 (0.42- 4.95)
FVC	2.2±0.9 (0.46-5.65)
FEV1/FVC	71.2 ±14.0 (31.7-98.4)
Reiff s score	5.1±2.9 (1-18)
BSI	5.33±4.10 (1-18)
Sputum culture positivity	46 (40)
Nebulizator	39 (18)
LTOT	25 (11.5)
BPAP	8 (3.7)

Data presented as n (%) or mean±SD. BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FEV1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, BSI: Bronchiectasis severity index, LTOT: Long term oxygen treatment, BPAP: Bi-level positive airway pressure.

Table 2: Factors associated with gender differences in adult BR patients.

Parameters	Female Group n=122, (56.2%)	Male Group n=95, (43.8%)	P value
Age, years	48.5±15.8	51.3±14.6	0.171
Smoking history	24(19.7)	63(75.9)	0.001
BMI	25.9±5.2	26.3±4.7	0.556
COPD	5(4.1)	36 (37.9)	0.001
Asthma	25 (20.5)	13 (13.7)	0.212
Diabetes mellitus	26(21.3)	9 (9.5)	0.025
Hypertension	31 (25.4)	18 (18.9)	0.326
Coronary artery disease	7 (5.7)	7 (7.4)	0.782
Depression history	44(36.1)	10(10.6)	0.001
Panic disorders	13(10.7)	3(3.2)	0.039
Post tuberculosis	33 (27)	40 (42.1)	0.021
Post pneumonia	69 (56.6)	35 (36.8)	0.004
Idiopathic	19 (15.6)	15 (15.8)	1.000
Cough	103 (84.4)	68 (71.6)	0.029
Dyspnea	97 (79.5)	78 (82.1)	0.730
Haemoptysis	36 (29.5)	21 (21.1)	0.277
Sputum,	66 (54.1)	54 (56.8)	0.783
FEV1,L	1.5±0.7	1.9±0.9	0.001
FVC,L	1.9±0.7	2.7±1.0	0.001
FEV1/FVC	73.8±12.3	67.8 ±15.3	0.01
FEV1 % predicted	63.1±22.8	57.7±27.3	0.087
FVC % predicted	67.8±21.6	63.7±23.3	0.179
Reiff's score	5.3±3.0	4.8±2.8	0.258
BSI	4.96±3.8	5.76±4.4	0.171
Sputum culture positivity	28 (47.5)	18 (32.1)	0.128
Nebulization	17 (13.9)	22 (23.2)	0.108
LTOT	8 (6.6)	17(17.9)	0.017
BPAP	3 (2.5)	5 (5.3)	0.302

Data presents as n (%) and mean±SD. BMI: Body mass index, COPD: Chronic obstructive pulmonary disease, FEV1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, BSI: Bronchiectasis severity index, LTOT: Long term oxygen treatment, BPAP: Bi-level positive airway pressure.

Pulmonary function tests were available for all patients. The mean forced expiratory volume in 1 second (FEV1) was 1.7±0.8 L (range 0.42-4.95), forced vital capacity (FVC) was 2.2±0.9 L (range 0.46-5.65), and FEV1/FVC was 71.2±14 (range 31.7-98.4) results were shown in the table 1. FEV1 and FVC value were higher in man (1.5±0.7 vs. 1.9±0.9, p= 0.001; 1.9±0.7 vs. 2.7±1.0, p=0.0001 respectively). But the FEV1/FVC ratio was higher in female (73.8±12.3 vs. 67.8 ±15.3, p=0.01).

Evaluation of radiological findings by Reiff's score revealed that the mean score was 5.1±2.9 (range 1-18). The BSI score that applied to detect disease severity was 5.31±4.1 (range 1-18). This score reflected that our study group had moderate bronchiectasis. But, there was no difference between gender and radiologic severity using Reiff's score and the severity of patients according to the BSI scores (Table 2).
A sputum sample was obtained from 115 (53%) patients, 102 (47%) could not give sputum in a stable period. Sixty-nine patients (60%) had negative sputum culture results. The most frequently isolated microorganisms was Pseudomonas aeruginosa (n=21, 45.7%) and Haemophilus influenza (n=11, 23.9%) in a stable period of BR patients.

DISCUSSION

The results of this study indicate that clinical and functional differences were detected between female and male patients with adult non-cystic fibrosis BR patients. Male BR patients had a high frequency of COPD that related to high smoking exposure and post-tuberculosis sequel, which is known as one of the important reason for BR. And also, FEV1/FVC ratio was higher in female BR group; FEV1 and FVC value was higher in male BR patients than female BR group. In female BR group, the cough was a more predominant symptom. Post-pneumonia sequel frequency, diabetes, depression history, panic disorders were more frequent in female BR patients. Gender was not effected microbiological features of adult non-cystic fibrosis BR patients.
Weycker et al. investigated prevalence and incidence of non-cystic fibrosis BR among US adults and reported that mean age of persons with BR was 68 years, and prevalence was higher among women than men in all age groups [9]. European Respiratory Society guidelines for the management of adult bronchiectasis reported that prevalence of BR increases with age and female gender [10]. A study from Korea showed that the mean age of adult BR patients was 60 years, and 64% of BR patients were female [11]. In this study population, non-cystic fibrosis BR patient was younger than these study groups, and similarly, most of the patients were female. But there was no difference between age and gender in this study group.
Previous studies reported that bronchial hyperresponsiveness was frequently detected in female BR [12,13]. And also, previous studies showed that female hormonal influences could be effect laryngeal hypersensitivity, hypersensitivity of airway afferent fibers via the modulation of nerve excitability and laryngeal dysfunction with paradoxical vocal cord movement. [14-16]. In this study population, the cough was a predominant symptom in female BR patients. This result might be explained by bronchial hyperresponsiveness, hormonal, and physiological differences in female patients. Likewise, because of the morphological differences in lung structure between sexes; the female has smaller diameter airways, lower lung volumes and the fewer total number of alveoli and these differences probably effect pulmonary function tests (FEV1 and FVC % predicted value) of a female with BR patients [17].
In this study, 48.8% of BR patients had comorbidities. The most common comorbidities were diabetes, COPD, asthma, hypertension, coronary artery disease, depression, and panic disorders. But, there was no difference in comorbidities between two groups except diabetes. In Satman's study's from Turkey, diabetes was more common in women than men (17.2% vs. 16%, p=0.008) [18]. Conversely, Roglic et al. reported that globally, diabetes prevalence is similar in men and female, but it is slightly higher in men <60 years old [19]. This study found that the rate of diabetes was higher in female BR than men BR patients (21% vs 9.5%, respectively) like another Turkish study [20].
The most important risk factor for developing COPD is smoking. In a study group, the rate of smoking history was higher in male BR patients. It's not surprising that the diagnosis of COPD was significantly higher in male BR patients and those with low FEV1/FVC ratio. The observed gender differences among pulmonary function test suggest that female gender was associated with lower FEV1 and FVC value, but there were no differences between gender and FEV1 % predicted, FVC % predicted value. According to Stewart study, presence of BR in COPD has been associated with higher airflow obstruction, but they did not evaluate gender differences in COPD and

BR with COPD patients [21]. Some studies reported that pulmonary structural and morphological differences, reproductive hormones, biomarkers such as interleukin 6, vascular endothelial growth factor, and genetic polymorphism were pulmonary effect function tests results [22-24]. But this study did not plan to explain the reason for gender differences on BR clinics.

In recent studies, the prevalence of depression and anxiety was high in adult non-cystic fibrosis bronchiectasis [25,26]. We previously published data about depression/anxiety in adult non-cystic fibrosis BR patients that female group had more anxiety score than male BR patients [26]. But, depression and anxiety were high in a female group that may be related to female BR patients had more symptomatic like cough and lower pulmonary function tests results or vice versa.

Chronic sputum production is a major symptom of BR patients. The sputum production rate was 55.3% for all study groups, and sputum culture positivity was detected in 40% in BR patients. In Angrill study, more than 60% of BR patients colonized with Haemophilus influenza (26%) and Pseudomonas spp (26%) in stable clinical period [27]. In our study population, the most common isolated microorganisms were Pseudomonas aeroginosa (45.7%) and Haemophilus influenza (23.9%) in a stable situation. A recent study that investigated gender differences in bronchiectasis reported sex-related differences in anatomical structure, pulmonary function, and microbiome composition might affect early pulmonary infection in female [28]. As female sex hormones effect airway cilia function, microbial colonization may be influenced by gender [28,29]. But, in this study, no microbiological features difference was detected between female and male BR patients. In previous studies, radiological and clinical severity was determined using Reiff's score and BSI in BR patients [30,31]. In this study, although Reiff's scores (determine the radiological severity) and BSI (which using radiologic, clinical and microbiological features which is a strong predictor with morbidity and mortality) were similar between two groups; but, there were statistically difference in cough symptom, etiology of BR, some comorbidities, FEV1, FVC, pulmonary function tests, LTOT usage in female and male adult non-cystic fibrosis BR patients. In this study group, 37.9% of male patients had COPD, and this might help to elucidate the difference LTOT usage between sexes in adult non-cystic fibrosis BR patients.

Several limitations of this study should be mentioned. This was a cross-sectional study. Hence, it did not provide details related to the causative mechanisms of the relationship between gender and clinical features of BR patients. This was a single center study, so, study population did not represent a population-based sample, and it is uncertain whether these findings apply to the general population. Study results will be consistent with the results of prospective studies.

In conclusion, it is important to consider the gender differences might be effect symptoms, comorbidity, and pulmonary function test results in adult non-CF BR patients.

CONFLICT of INTEREST

The author declares that she has no conflict of interest regarding this study.

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