Allergy Asthma Immunol Res. 2023 Jan;15(1):83-93
https://doi.org/10.4168/aair.2023.15.1.83
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Original Article

Impacts of Asthma in Patients With Bronchiectasis: Findings From the KMBARC Registry

Seong Mi Moon,[1†] **Hayoung Choi**,[2,3†] **Hyung Koo Kang**,[4] **Sei Won Lee**,[5] **Yun Su Sim**,[2] **Hye Yun Park**,[6] **Yong-Soo Kwon**,[7] **Sang-Heon Kim**,[8] **Yeon-Mok Oh**,[5] **Hyun Lee**[8*]

[1]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Changwon Hospital, Sungkyunkwan University School of Medicine, Changwon, Korea
[2]Division of Pulmonary, Allergy, and Critical Care Medicine, Department of Internal Medicine, Hallym University Kangnam Sacred Heart Hospital, Hallym University College of Medicine, Seoul, Korea
[3]Division of Molecular and Clinical Medicine, University of Dundee, Ninewells Hospital and Medical School, Dundee, United Kingdom
[4]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Ilsan Paik Hospital, Inje University College of Medicine, Goyang, Korea
[5]Department of Pulmonary and Critical Care Medicine, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea
[6]Division of Pulmonary and Critical Care Medicine, Department of Medicine, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea
[7]Department of Internal Medicine, Chonnam National University Hospital, Chonnam National University Medical School, Gwangju, Korea
[8]Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

Received: Apr 19, 2022
Revised: Jul 20, 2022
Accepted: Aug 9, 2022
Published online: Oct 26, 2022

Correspondence to
Hyun Lee, MD, PhD
Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, 222-1 Wangsimni-ro, Seongdong-gu, Seoul 04763, Korea.
Tel: +82-2-2290-8350
Fax: +82-2-2292-1477
Email: namuhanayeyo@hanyang.ac.kr

†Seong Mi Moon and Hayoung Choi contributed equally to this work.

ORCID iDs
Seong Mi Moon
https://orcid.org/0000-0003-3566-4221
Hayoung Choi
https://orcid.org/0000-0003-4812-0653
Hyung Koo Kang
https://orcid.org/0000-0001-9671-0944
Sei Won Lee
https://orcid.org/0000-0003-4814-6730

ABSTRACT

Purpose: Although the coexistence of asthma and bronchiectasis is common, the impacts of asthma on bronchiectastic patients (BE) have not been well evaluated because this issue using bronchiectasis cohorts has been investigated in only a few studies.
Methods: In the present study, 598 patients who were prospectively enrolled in the Korean bronchiectasis registry were evaluated. The clinical characteristics between BE with asthma and those without asthma were compared.
Results: Asthma was found in 22.4% of BE. BE with asthma had a higher body mass index (BMI) ($P = 0.020$), more dyspnea ($P < 0.001$), larger sputum volume ($P = 0.015$), and lower forced expiratory volume in 1 second (FEV1) ($P < 0.001$) than those without asthma. BE with asthma had a higher rate of previous pneumonia ($P = 0.017$) or measles ($P = 0.037$) than those without asthma. Regarding treatment, BE with asthma used inhaled corticosteroids, long-acting muscarinic antagonists, and leukotriene receptor antagonists more frequently than those without asthma. Although intergroup differences were not observed in disease severity of bronchiectasis ($P = 0.230$ for Bronchiectasis Severity Index and $P = 0.089$ for FACED), the Bronchiectasis Health Questionnaire (BHQ) scores indicating the quality of life, were significantly lower in BE with asthma than in those without asthma (61.6 vs. 64.8, $P < 0.001$). In a multivariable model adjusting for age, sex, body mass index, forced expiratory volume in 1 second %predicted, sputum volume, modified Medical Research Council dyspnea scale ≥ 2, and the number of involved lobes, asthma was associated with lower BHQ scores (β-coefficient = −2.579, $P = 0.014$).

Yun Su Sim
https://orcid.org/0000-0002-3746-4947
Hye Yun Park
https://orcid.org/0000-0002-5937-9671
Yong-Soo Kwon
https://orcid.org/0000-0001-5121-4488
Sang-Heon Kim
https://orcid.org/0000-0001-8398-4444
Yeon-Mok Oh
https://orcid.org/0000-0003-0116-4683
Hyun Lee
https://orcid.org/0000-0002-1269-0913

Disclosures
There are no financial or other issues that might lead to a conflict of interest.

Conclusions: BE with asthma have more respiratory symptoms, worse lung function, and poorer quality of life than those without asthma. A better understanding of the impacts of asthma in BE will guide appropriate management in this population.

Keywords: Asthma; bronchiectasis; quality of life; symptom exacerbations

INTRODUCTION

Non-cystic fibrosis bronchiectasis (hereafter referred to as bronchiectasis) is a chronic airway disease characterized by recurrent respiratory symptoms, such as cough, copious production of sputum, dyspnea, and recurrent or persistent infection.[1,2] The prognosis of bronchiectasis is worse when it is accompanied by comorbidities.[3] Furthermore, in prior studies, bronchiectasis-related comorbidities have been shown to be important determinants of disease severity, quality of life, exacerbations, and long-term prognosis, including mortality in bronchiectatic patients (BE).[3-5]

Overlap between bronchiectasis and chronic airway diseases, including asthma and chronic obstructive pulmonary disease (COPD), are common in BE.[6] The prevalence of overlap was reported as 3%–29% for asthma and 14%–37% for COPD in BE.[4,6-11] These conditions are significantly associated with an increased disease burden of bronchiectasis in terms of exacerbations and mortality.[5,12] Thus, adequate management of comorbid airway diseases may be critical for improving treatment outcomes in BE.

Comorbid asthma has been suggested to further worsen the relevant exacerbation risk and mortality in BE.[5,13,14] However, the impacts of asthma on the clinical characteristics of bronchiectasis have not been well elucidated except for exacerbations and mortality and most previous study results were derived from studies using asthma registries.[15-17] Thus, limited information exists on the differences in demographics, pulmonary functions, and quality of life in BE with comorbid asthma.

Due to the high prevalence of asthma in BE and the impacts of asthma on the poorer prognosis of bronchiectasis,[6,18] studies in which impacts of asthma on many aspects in BE are important. Accordingly, in the present study, the impacts of asthma on clinical characteristics including demographics, disease severity, treatment, quality of life, and acute exacerbation (AE) in BE were evaluated using a prospective multicenter bronchiectasis registry in Korea.

MATERIALS AND METHODS

Study design and participants

The present study included patients enrolled in the Korean Multicenter Bronchiectasis Audit and Research Collaboration (KMBARC) registry between August 2018 and December 2019.[10,19] The study population consisted of adult patients (≥ 18 years of age) with stable bronchiectasis confirmed with chest computed tomography. Exclusion criteria were as follows: patients with bronchiectasis due to cystic fibrosis, traction bronchiectasis associated with interstitial lung disease; patients actively being treated for infectious disease including pneumonia, pulmonary tuberculosis, or non-tuberculous mycobacterial pulmonary disease; or pregnant patients. The detailed registry protocol was previously described.[19]

https://doi.org/10.4168/aair.2023.15.1.83

Definition

At the time of registry enrollment, patients had stable bronchiectasis. The presence of asthma was determined using a questionnaire regarding comorbidities: "Does the patient have a self-reported or physician diagnosis of asthma?"

Regarding radiologic findings, cystic bronchiectasis was defined as when at least one lobe was involved due to cystic bronchiectasis. Modified Reiff score was used to assess radiological severity.[20] Pre-bronchodilator spirometry with or without post-bronchodilator spirometry was performed; positive bronchodilator response was defined as an increase of ≥ 12% and ≥ 200 mL in forced expiratory volume in 1 second (FEV_1) compared with pre-bronchodilator results.[21] The bronchiectasis severity was evaluated using Bronchiectasis Severity Index (BSI) score[1] and FACED score,[22] and quality of life was assessed using the validated Korean version of Bronchiectasis Health Questionnaire (BHQ),[23,24] Any AEs were defined as one or more exacerbations of respiratory symptoms.[25] In the present study, severe AE was defined as requiring hospitalization or visiting the emergency room.[26]

Statistical analyses

Continuous data are presented as median with interquartile range (IQR) and were compared using the Mann-Whitney U test. Categorical data are presented as numbers (%) and were compared using Pearson's χ^2 test or Fisher's exact test, as appropriate. *P* values < 0.05 in two-sided tests were considered to indicate statistical significance. To explore the effect of asthma on quality of life (BHQ scores) and the presence of any AEs in the previous year, both univariable and multivariable analyses were performed. Regarding variables for multivariable analyses, demographics and other variables that are significantly different between patients with and without asthma were selected. For BHQ scores analyses, multivariable linear regression analyses were performed; demographics (age, sex, and body mass index (BMI) were adjusted in Model 1; and in Model 2, sputum volume, modified Medical Research Council (mMRC) dyspnea scale ≥ 2, number of involved lobes, and $FEV_{1\%}$predicted were further adjusted in addition to the variables included in Model 1. In the multivariable logistic analyses for AE in the previous year, demographics (age, sex, and BMI) were adjusted in Model 1; in Model 2, sputum volume, mMRC dyspnea scale ≥ 2, number of involved lobes, $FEV_{1\%}$predicted, and BHQ scores were further adjusted in addition to the variables included in Model 1. Data were analyzed by using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, USA) and Stata (Release 16; StataCorp LP, College Station, TX, USA). Graphs were compiled using GraphPad Prism version 9.0.2 (GraphPad Software, San Diego, CA, USA).

Ethical statement

This study protocol was approved by the Institutional Review Board of all institutions participating in the KMBARC registry, including Hallym University Kangnam Sacred Heart Hospital (application No, 2018-07-16), and written informed consent was obtained from all patients.

RESULTS

Patient characteristics

In the present study, 598 BE were analyzed and divided into 2 groups into BE with asthma (n = 134, 22.4%) and those without asthma (n = 464, 77.6%). The characteristics of the patients are shown in **Table 1**. Among the 598 patients, 334 (55.9%) were female and the median age of all patients was 65.6 years (IQR, 59.8–71.5 years). BE with asthma had higher BMI (23.8 vs.

https://doi.org/10.4168/aair.2023.15.1.83

Allergy, Asthma & Immunology Research AAIR

Table 1. Baseline characteristics

Characteristics	BE with asthma (n = 134, 22.4%)	BE without asthma (n = 464, 77.6%)	*P* value
Age (yr; n = 598)	67 (61–73)	65 (60–71)	0.146
Sex (female; n = 598)	82 (61.2)	252 (54.3)	0.157
BMI (kg/m^2; n = 562)	23.8 (21.0–25.7)	22.8 (20.5–25.2)	0.020
Smoking history (n = 598)			0.151
Never-smoker	94 (70.1)	293 (63.1)	
Current- or ex-smoker	40 (29.9)	171 (36.9)	
Sputum volume (mL; n = 581)	20 (10–30)	10 (5–30)	0.015
mMRC dyspnea scale (n = 598)			0.001
< 2	91 (67.9)	377 (81.2)	
≥ 2	43 (32.1)	87 (18.8)	
Comorbidities			
History of pneumonia (n = 597)	67 (50.4)	180 (38.8)	0.017
History of measles (n = 550)	34 (31.5)	97 (21.9)	0.037
History of pulmonary tuberculosis (n = 597)	39 (29.3)	159 (34.3)	0.286
NTM-PD (n = 597)	15 (11.3)	47 (10.2)	0.702
COPD (n = 598)	65 (48.5)	161 (37.4)	0.005
Cardiovascular diseases (n = 598)	49 (36.6)	129 (27.8)	0.054
Chronic kidney disease (n = 588)	3 (2.3)	9 (2.0)	0.737
Diabetes mellitus (n = 597)	15 (11.2)	58 (12.5)	0.678
Osteoporosis (n = 597)	21 (15.7)	49 (10.6)	0.127
Depression (n = 596)	7 (5.2)	17 (3.7)	0.423
Rheumatoid arthritis (n = 597)	7 (5.3)	30 (6.5)	0.612
Gastrointestinal reflux disease (n = 597)	23 (17.3)	66 (14.2)	0.381

Values are presented as numbers (percentages) or medians (interquartile ranges).
BE, bronchiectatic patients; BMI, body mass index; mMRC, modified Medical Research Council; NTM-PD, non-tuberculous mycobacterial pulmonary disease; COPD, chronic obstructive pulmonary disease.

22.8 kg/m^2, $P = 0.020$) and larger sputum volume (20 vs. 10 mL, $P = 0.015$) than those without asthma. More BE with asthma had mMRC dyspnea scale ≥ 2 than those without asthma (32.1% vs. 18.8%, $P = 0.001$). BE with asthma were diagnosed with bronchiectasis earlier than those without asthma ($P < 0.001$). Previous respiratory infections, including pneumonia ($P = 0.017$) or measles ($P = 0.037$) and concurrent COPD ($P = 0.005$), were also more frequent in BE with asthma than in those without asthma.

Fig. 1 shows the comparison of respiratory medications between the 2 groups. BE with asthma used inhalers, including inhaled corticosteroid (ICS) (11.3% vs. 1.9%, $P < 0.001$), ICS/long-acting beta agonist (LABA) (47.4% vs. 7.4%, $P < 0.001$), and long-acting muscarinic antagonist (LAMA) (20.3% vs. 11.5%, $P = 0.009$) as well as oral medications such as leukotriene receptor antagonists (19.5% vs. 5.2%, $P < 0.001$), more frequently than those without asthma.

Comparison of laboratory, radiographic, microbiologic, and pulmonary function test results in BE with and without asthma

Table 2 shows the comparison of laboratory, radiographic, pulmonary function, and microbiologic results between the 2 groups. BE with asthma tended to show higher eosinophil count (149.6/μL vs. 74.4/μL, $P = 0.111$) than those without asthma, albeit without statistical significance. Regarding radiological findings, BE without asthma had more involved lobes ($P = 0.025$), including more frequent involvement in the left upper lobe upper division ($P = 0.008$) and lingular division ($P < 0.001$) compared with those with asthma. However, the modified Reiff score did not differ between the 2 groups with a median score of 5 (IQR, 3–9; $P = 0.406$). BE with asthma had significantly lower $FEV_{1\%}$predicted ($P = 0.003$) and FEV_1/forced vital capacity ratio ($P < 0.001$) than those without asthma. Intergroup differences in *Pseudomonas* isolation were not observed ($P = 0.324$).

https://doi.org/10.4168/aair.2023.15.1.83

Allergy, Asthma & Immunology Research AAIR

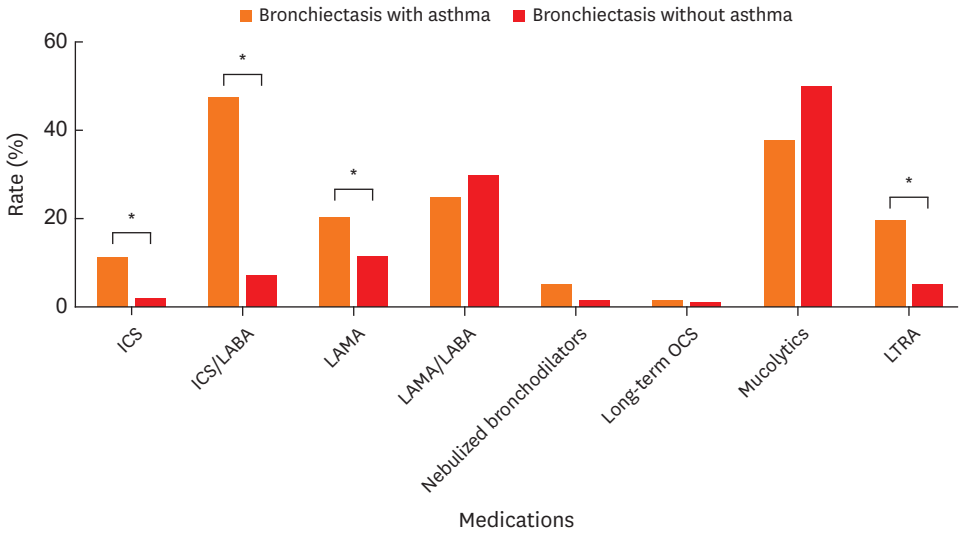

Fig. 1. Comparison of treatment based on the presence or absence of asthma.
ICS, inhaled corticosteroid; LABA, long-acting beta-agonist; LAMA, long-acting muscarinnic antagonist; OCS, oral corticosteroid; LTRA, leukotriene receptor antagonist.
*$P < 0.05$.

Table 2. Laboratory, radiographic, pulmonary function test, and microbiological results

Variables	BE with asthma (n = 134, 22.4%)	BE without asthma (n = 464, 77.6%)	*P* value
Laboratory findings			
WBC (/μL; n = 387)	7,300 (5,900–9,200)	6,800 (5,600–8,600)	0.299
Eosinophil, count (/μL; n = 59)	149.6 (74.5–264.3)	74.4 (19.2–161.5)	0.111
Eosinophil ≥ 300/μL (n = 59)	3 (25.0)	3 (6.4)	0.092
Hemoglobin (g/dL; n = 383)	13.4 (12.1–14.3)	13.1 (12.2–14.1)	0.528
Platelet (/μL; n = 383)	250 (192–288)	248 (209–300)	0.617
ESR (n = 156)	30 (12–51)	26 (14–48)	0.745
CRP (n = 313)	0.90 (0.11–2.58)	0.39 (0.15–1.42)	0.082
Total IgE (n = 119)	77.8 (29.6–233.0)	53.8 (14.2–160.1)	0.249
Radiologic findings (n = 582)			
Cystic bronchiectasis in any lobes	63 (47.0)	208 (44.8)	0.826
No. of involved lobes	3 (2–4)	3 (2–5)	0.025
Involved lobe			
RUL	55 (42.3)	192 (42.5)	0.972
RML	76 (58.5)	285 (63.1)	0.342
RLL	81 (62.3)	265 (58.6)	0.451
LUL upper division	35 (26.9)	179 (39.6)	0.008
LUL lingular division	46 (35.4)	265 (58.6)	< 0.001
LLL	99 (76.2)	338 (74.8)	0.749
Modified Reiff score	5 (3–9)	5 (3–9)	0.406
Pulmonary function tests (n = 532)			
FEV_1 (L)	1.40 (1.04–1.83)	1.66 (1.30–2.07)	< 0.001
FEV_1 %predicted	56.7 (46.3–71.3)	64.1 (50.2–78.7)	0.003
FVC (L)	2.31 (1.92–2.81)	2.52 (2.01–3.10)	0.018
FVC %predicted	72.1 (61.1–80.1)	73.1 (62.9–84.5)	0.378
FEV_1/FVC	60.5 (50.2–70.2)	67.3 (57.9–75.0)	< 0.001
FEV_1/FVC < 0.7	92 (74.8)	232 (56.7)	< 0.001
Positive bronchodilator response (n = 464)	7 (6.3)	11 (3.1)	0.157
Microbiological findings			
Pseudomonas aeruginosa colonization (n = 372)	23 (33.3)	83 (27.4)	0.324

Values are presented as numbers (percentages) or medians (interquartile ranges).
BE, bronchiectatic patients; WBC, white blood cell; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; Ig, immunoglobulin; RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity.

https://doi.org/10.4168/aair.2023.15.1.83

Comparison of bronchiectasis severity, quality of life, and AEs in the previous year in BE with and without asthma

Bronchiectasis severity measured using the BSI (median 6; IQR, 4–9) and FACED (median 2; IQR, 1–3) scores were comparable between the 2 groups ($P = 0.230$ for BSI and $P = 0.089$ for FACED). However, BE with asthma showed significantly lower total BHQ scores than those without asthma (61.6 vs. 64.8, $P < 0.001$). Items regarding fatigue ($P = 0.020$), slower than others ($P = 0.007$), shortness of breath ($P < 0.001$), sleep disruption ($P = 0.007$), and coughing ($P = 0.048$), showed significant difference between the 2 groups (**Fig. 2**). The proportion of experiencing any AEs and severe AEs in the previous year did not differ between the 2 groups (55.2% vs. 53.9% for any AEs, $P = 0.783$; 23.9% vs. 21.6% for severe AEs, $P = 0.567$). However, the rate of AEs treated with antibiotics among the BE with AEs requiring secondary care was lower in BE with asthma than in those without asthma (77.3% vs. 94.1%, $P = 0.026$) (**Table 3**).

Table 3. Bronchiectasis severity, quality of life, and acute exacerbations

Variables	BE with asthma (n = 134, 22.4%)	BE without asthma (n = 464, 77.6%)	*P* value
Disease severity			
BSI (n = 581)	6 (4–10)	6 (4–9)	0.230
FACED (n = 467)	2 (1–3)	2 (1–3)	0.089
Quality of life (n = 591)			
BHQ	61.6 (54.8–66.6)	64.8 (57.4–70.8)	< 0.001
AEs in the previous year			
Any AEs (n = 598)	74 (55.2)	250 (53.9)	0.783
Severe AEs (n = 598)	32 (23.9)	100 (21.6)	0.567
AEs not requiring secondary or tertiary care (n = 598)	41 (30.6)	140 (30.2)	0.925
AEs requiring secondary or tertiary care, except for ER visit or admission (n = 462)	22 (23.2)	101 (27.5)	0.391
Use of antibiotics	17/22 (77.3)	95/101 (94.1)	0.026
AEs requiring visiting ER without admission (n = 598)	10 (7.5)	35 (7.5)	0.975
Use of antibiotics	9/10 (90.0)	26/32 (81.3)	> 0.999
AEs requiring admission (n = 598)	27 (20.1)	82 (17.7)	0.526
Use of antibiotics	26/27 (96.3)	69/72 (95.8)	> 0.999

Values are presented as numbers (percentages) or medians (interquartile ranges).
BE, bronchiectatic patients; BSI, Bronchiectasis Severity Index; BHQ, Bronchiectasis Health Questionnaire; AE, acute exacerbation; ER, emergency room.

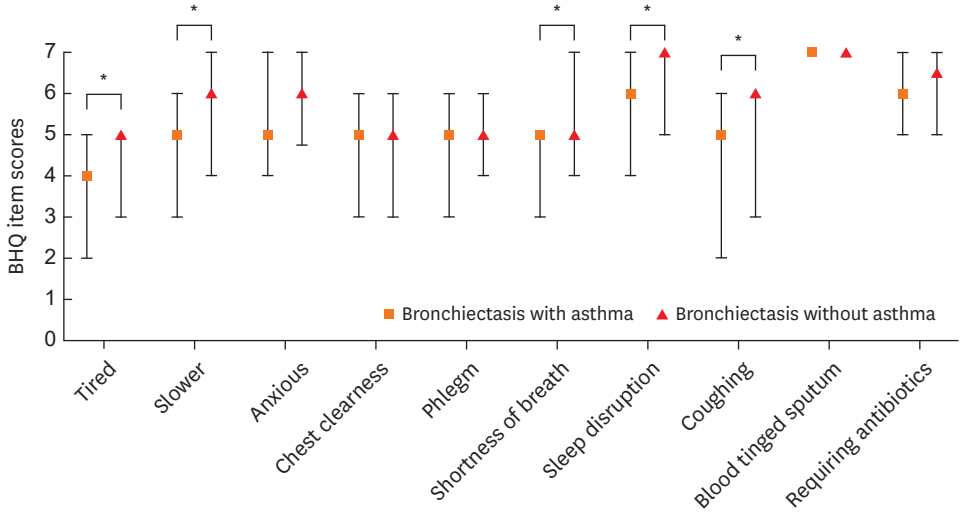

Fig. 2. Comparison of each BHQ item score based on the presence or absence of asthma.
BHQ, Bronchiectasis Health Questionnaire.
*$P < 0.05$.

https://doi.org/10.4168/aair.2023.15.1.83

Effects of asthma on quality of life and AEs

The relationship between asthma and quality of life measured based on the BHQ scores was investigated using multivariable linear regression analyses. Asthma was significantly associated with a lower BHQ score (β-coefficient = −3.957, $P < 0.001$). After adjusting for potential confounders, asthma remained associated with lower total BHQ scores (β-coefficient = −4.105, $P < 0.001$ in Model 1 and β-coefficient = −2.579, $P = 0.014$ in Model 2). Other factors that were significantly associated with BHQ included BMI (β-coefficient = 0.329, $P = 0.012$) in Model 1, and sputum volume (β-coefficient = −0.049, $P < 0.001$) and mMRC dyspnea scale ≥ 2 (β-coefficient = −6.913, $P < 0.001$) in Model 2 (**Table 4**).

The effect of asthma on any AEs and severe AEs in the previous 12 months was evaluated using univariable and multivariable logistic regression analyses. A significant association was not observed between asthma and the number of any AEs and severe AEs ($P = 0.528$ and $P = 0.149$, respectively). After adjusting for other clinical variables, a significant association was not observed between asthma and the frequency of any AEs and severe AEs (Models 1 and 2). Factors that were significantly associated with any AEs included female sex (odds ratio [OR], 1.595, $P = 0.042$) in Model 1, and female sex (OR, 1.984, $P = 0.003$), the number of involved lobes (OR, 1.251, $P = 0.004$), and BHQ score (OR, 0.975, $P = 0.032$) in Model 2. In addition, factors that were significantly associated with severe AEs included female sex (OR, 3.144, $P = 0.007$) and $FEV_{1\%}$predicted (OR, 0.966, $P = 0.010$) in Model 2 (**Table 5**).

DISCUSSION

In the present study, the clinical impacts of asthma in BE were evaluated. BE with asthma had more respiratory symptoms including a larger amount of sputum and more severe dyspnea and lower lung function than those without asthma. Inhalers such as ICS, ICS/LABA, and LAMA and leukotriene receptor antagonists were more frequently used in BE with asthma than in those without asthma. Although significant intergroup differences in radiological extent, disease severity scores, and exacerbation history were not observed, BE with asthma showed significantly poorer quality of life than those without asthma.

Table 4. Effect of asthma on the quality of life measured by Bronchiectasis Health Questionnaire

Variables	β-coefficient (95% CI) for asthma	*P* value
Unadjusted model		
Asthma	−3.957 (−5.978, −1.935)	< 0.001
Model 1		
Asthma	−4.105 (−6.203, −2.007)	< 0.001
Age	0.065 (−0.033, 0.164)	0.194
Female	−1.133 (−2.909, 0.642)	0.210
BMI	0.329 (0.072, 0.586)	0.012
Model 2		
Asthma	−2.579 (−4.644, −0.514)	0.014
Age	0.041 (−0.059, 0.141)	0.418
Female	−1.628 (−3.377, 0.120)	0.068
BMI	0.066 (−0.186, 0.319)	0.606
FEV_1 %predicted	0.035 (−0.019, 0.088)	0.202
Sputum volume	−0.049 (−0.067, −0.031)	< 0.001
mMRC dyspnea scale ≥ 2	−6.913 (−9.170, −4.655)	< 0.001
No. of involved lobes	−0.537 (−1.130, 0.056)	0.076

Model 1: adjusted for age, sex, and BMI. Model 2: adjusted for variables included in Model 1, $FEV_{1\%}$predicted, sputum volume, mMRC dyspnea scale ≥ 2, and number of involved lobes.
CI, confidence interval; FEV_1, forced expiratory volume in 1 second; mMRC, modified Medical Research Council; BMI, body mass index.

https://doi.org/10.4168/aair.2023.15.1.83

Table 5. Effects of asthma on acute exacerbations in the previous year

Variables	Any AEs		Severe AEs	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Unadjusted model				
Asthma	1.159 (0.732, 1.836)	0.528	1.630 (0.840, 3.161)	0.149
Model 1				
Asthma	1.134 (0.698, 1.845)	0.611	1.748 (0.883, 3.461)	0.109
Age	0.991 (0.969, 1.014)	0.449	1.015 (0.980, 1.052)	0.391
Female	1.595 (1.075, 2.366)	0.042	1.736 (0.889, 3.390)	0.106
BMI	0.964 (0.911, 1.021)	0.212	0.908 (0.825, 1.000)	0.050
Model 2				
Asthma	1.039 (0.602, 1.796)	0.890	1.112 (0.478, 2.588)	0.806
Age	0.995 (0.969, 1.021)	0.695	1.015 (0.972, 1.061)	0.501
Female	1.984 (1.264, 3.115)	0.003	3.144 (1.370, 7.212)	0.007
BMI	0.986 (0.925, 1.052)	0.676	0.978 (0.877, 1.089)	0.681
FEV_1 %predicted	0.996 (0.984, 1.009)	0.588	0.966 (0.940, 0.992)	0.010
Sputum volume	1.000 (0.995, 1.005)	0.967	0.996 (0.986, 1.006)	0.426
mMRC dyspnea scale ≥ 2	1.225 (0.667, 2.249)	0.513	1.464 (0.601, 3.564)	0.401
No. of involved lobes	1.251 (1.073, 1.459)	0.004	1.151 (0.890, 1.489)	0.285
BHQ scores	0.975 (0.953, 0.998)	0.032	0.985 (0.949, 1.023)	0.436

Model 1: adjusted for age, sex, and BMI. Model 2: adjusted for variables included in Model 1, FEV_1%predicted, sputum volume, mMRC dyspnea scale ≥ 2, number of involved lobes, and BHQ scores.
AE, acute exacerbation; OR, odds ratio; CI, confidence interval; BMI, body mass index; FEV_1, forced expiratory volume in 1 second; mMRC, modified medical research council; BHQ, Bronchiectasis Health Questionnaire.

BE with asthma showed different clinical characteristics, including higher BMI, more respiratory symptoms, and more use of inhaler treatment compared with those without asthma. Similar findings were also observed in a previous research performed in China.[27] However, data regarding the characteristics of bronchiectatic population with asthma are limited. Because bronchiectasis-asthma overlap is not yet clearly defined,[2,6,18,28] the diagnosis of asthma in BE is challenging since it is made at the discretion of attending physicians. However, the present study provided meaningful results showing the clinical characteristics of asthma in terms of bronchiectasis cohorts in actual clinics. However, BE with asthma-like features and patients with long-confirmed asthma history plus concomitant bronchiectasis may be different populations,[6] which was not distinguished in this study. Thus, further studies using various cohorts (bronchiectasis and asthma cohorts) are warranted to characterize bronchiectasis-asthma overlap.

Notably, the existence of asthma was independently associated with a poorer quality of life in BE even when adjusting for potentially confounding factors. In agreement with our results, in a previous study, the EMBARC cohort showed a similar result when the quality of life was measured using a different tool (quality of life-bronchiectasis scale).[29] The present study also provided detailed aspects of quality of life because the score for BHQ each item was evaluated, which supports previous findings. BE with asthma were more hampered by the following than those without asthma: dyspnea, sleep disruption, coughing, tiredness, and much slower in performing tasks. The impaired dyspnea, sleep disruption, and coughing indicate that more attention should be given to the proper control of respiratory symptoms in BE with asthma. Furthermore, the present study results provide insights into pulmonary rehabilitation potentially benefitting tiredness and slow task performance, which may improve quality of life and long-term outcomes in BE with asthma.

Unexpectedly, asthma was not significantly associated with an increased rate of AEs in the prior year in BE. Conversely, identified asthma was considered a relevant risk factor for bronchiectasis exacerbation in previous studies.[13,18,29] In studies with asthmatic patients,

https://doi.org/10.4168/aair.2023.15.1.83

bronchiectasis was also associated with increased risk of exacerbations.[11,17,30] The discordant result of our study might be explained by the following reasons: exacerbation was assessed during a relatively short period (initial questionnaires on exacerbations in a previous year); regional differences in study populations affected different clinical outcomes[18]; a very high proportion of regular asthma-related medications, especially ICS, may have affected the results. Proper therapeutic intervention such as asthma medication in asthma-bronchiectasis overlap patients may reduce the risk of exacerbations requiring antibiotics,[2,28] and because we used the definition of AE for bronchiectasis, mild AEs requiring a short-acting beta agonist only might not have been counted.

Notably, BE with asthma showed lower frequency of exacerbation requiring antibiotics than BE without asthma (77.3% vs. 94.1%). Clinicians might prescribe systemic corticosteroids instead of antibiotics when their BE with asthma experience AEs. Currently, biomarkers do not exist to guide the use of antibiotics or corticosteroids for the treatment of BE with asthma. Because identifying therapeutic traits can improve the clinical outcomes of BE,[31,32] evaluating whether eosinophilic endotypes are higher in BE with asthma than in BE without asthma is important. Because the KMBARC is an ongoing registry, future longitudinal data could help elucidate the exacerbation risk and appropriate treatment strategies when considering eosinophilic endotypes in BE with asthma.

The current study had several limitations. First, the study population was limited to Korean patients. Thus, the results of this study should be carefully adapted to different clinical settings considering geographic and racial/ethnic diversity. Second, some values were missing, including microbiological data. Third, the diagnosis of asthma was based on physicians' diagnosis and patients' reports in this study. Thus, there is a possibility that BE with more symptoms may have reported having asthma, which could lead to an error of circular reasoning. In addition, a recall bias could affect the asthma diagnosis. However, the study results have the advantage of reflecting real practice.

In conclusion, BE with asthma had more respiratory symptoms, lower lung functions, and poorer quality of life, which was not reflected by disease severity, than those without asthma. A better understanding of the impacts of asthma in BE will guide appropriate management in this population. Further studies are warranted to gain a better understanding of BE with asthma.

ACKNOWLEDGMENTS

The authors would like to thank members of the Korean Multicenter Bronchiectasis Audit and Research Collaboration (KMBARC) registry for collecting data: An-Soo Jang, Bumhee Yang, Byoung Soo Kwon, Chang Youl Lee, Chang-Hoon Lee, Changhwan Kim, Chin Kook Rhee, Deog Kyeom Kim, Eun Hye Lee, Eun Kyung Kim, Hyun Kuk Kim, Hyun-Kyung Lee, Ina Jeong, Jae Ha Lee, Jae Seung Lee, Jae Sung Choi, Ji Soo Choi, Ji Ye Jung, Ji-Ho Lee, Ji-Hyun Lee, Junghyun Kim, Jung-Kyu Lee, Juok Na, Ki Uk Kim, Kwang Ha Yoo, Sang Ha Kim, Sang Haak Lee, Se Hee Lee, Seung Jun Lee, Seung Won Ra, Shinhee Park, Sooim Sin, Soo-Jung Um, So-Young Park, Sung-Yoon Kang, Tae-Hyung Kim, Woo Jin Kim, Yee Hyung Kim, Yong Bum Park, Yoonki Hong, Youlim Kim, Young-Jae Cho, Young-Soon Yoon, Yu-Il Kim, and Yun-Jeong Jeong.

Part of this article was presented in the form of an abstract at the American Thoracic Society International Conference 2020.

https://doi.org/10.4168/aair.2023.15.1.83

This work was supported by a National Research Foundation of Korea (NRF) grant funded by the Ministry of Science, Information, and Communications Technologies (No. 2020R1F1A1070468 and 2021M3E5D1A01015176 to HL) and the Korean Ministry of Education (No. 2021R1I1A3052416 to HC). This work was also supported by the Korea Medical Device Development Fund grant funded by the Korean government (the Ministry of Science and ICT, the Ministry of Trade, Industry and Energy, the Ministry of Health & Welfare, the Ministry of Food and Drug Safety) (No. Project Number: 1711138447, KMDF_PR_20200901_0214). The funders had no role in the design of the study, the collection and analysis of the data, or the preparation of the manuscript.

REFERENCES

1. Chalmers JD, Goeminne P, Aliberti S, McDonnell MJ, Lonni S, Davidson J, et al. The bronchiectasis severity index. An international derivation and validation study. Am J Respir Crit Care Med 2014;189:576-85.
PUBMED | CROSSREF
2. Martinez-Garcia MA, Polverino E, Aksamit T. Bronchiectasis and chronic airway disease: it is not just about asthma and COPD. Chest 2018;154:737-9.
PUBMED | CROSSREF
3. Loebinger MR, Wells AU, Hansell DM, Chinyanganya N, Devaraj A, Meister M, et al. Mortality in bronchiectasis: a long-term study assessing the factors influencing survival. Eur Respir J 2009;34:843-9.
PUBMED | CROSSREF
4. McDonnell MJ, Aliberti S, Goeminne PC, Restrepo MI, Finch S, Pesci A, et al. Comorbidities and the risk of mortality in patients with bronchiectasis: an international multicentre cohort study. Lancet Respir Med 2016;4:969-79.
PUBMED | CROSSREF
5. Choi H, Yang B, Kim YJ, Sin S, Jo YS, Kim Y, et al. Increased mortality in patients with non cystic fibrosis bronchiectasis with respiratory comorbidities. Sci Rep 2021;11:7126.
PUBMED | CROSSREF
6. Polverino E, Dimakou K, Hurst J, Martinez-Garcia MA, Miravitlles M, Paggiaro P, et al. The overlap between bronchiectasis and chronic airway diseases: state of the art and future directions. Eur Respir J 2018;52:1800328.
PUBMED | CROSSREF
7. Lonni S, Chalmers JD, Goeminne PC, McDonnell MJ, Dimakou K, De Soyza A, et al. Etiology of non-cystic fibrosis bronchiectasis in adults and its correlation to disease severity. Ann Am Thorac Soc 2015;12:1764-70.
PUBMED | CROSSREF
8. Aksamit TR, O'Donnell AE, Barker A, Olivier KN, Winthrop KL, Daniels ML, et al. Adult patients with bronchiectasis: a first look at the US bronchiectasis research registry. Chest 2017;151:982-92.
PUBMED | CROSSREF
9. Choi H, Yang B, Nam H, Kyoung DS, Sim YS, Park HY, et al. Population-based prevalence of bronchiectasis and associated comorbidities in South Korea. Eur Respir J 2019;54:1900194.
PUBMED | CROSSREF
10. Lee H, Choi H, Chalmers JD, Dhar R, Nguyen TQ, Visser SK, et al. Characteristics of bronchiectasis in Korea: First data from the Korean Multicentre Bronchiectasis Audit and Research Collaboration registry and comparison with other international registries. Respirology 2021;26:619-21.
PUBMED | CROSSREF
11. Lee SC, Son KJ, Park HJ, Jung JY, Park SC, Jeong SH, et al. Long-term prognosis of asthma-bronchiectasis overlapped patients: a nationwide population-based cohort study. Allergy Asthma Immunol Res 2021;13:908-21.
PUBMED | CROSSREF
12. Ni Y, Shi G, Yu Y, Hao J, Chen T, Song H. Clinical characteristics of patients with chronic obstructive pulmonary disease with comorbid bronchiectasis: a systemic review and meta-analysis. Int J Chron Obstruct Pulmon Dis 2015;10:1465-75.
PUBMED | CROSSREF
13. Mao B, Yang JW, Lu HW, Xu JF. Asthma and bronchiectasis exacerbation. Eur Respir J 2016;47:1680-6.
PUBMED | CROSSREF

14. Venning V, Bartlett J, Jayaram L. Patients hospitalized with an infective exacerbation of bronchiectasis unrelated to cystic fibrosis: clinical, physiological and sputum characteristics. Respirology 2017;22:922-7.
PUBMED | CROSSREF

15. Oguzulgen IK, Kervan F, Ozis T, Turktas H. The impact of bronchiectasis in clinical presentation of asthma. South Med J 2007;100:468-71.
PUBMED | CROSSREF

16. Porsbjerg C, Menzies-Gow A. Co-morbidities in severe asthma: clinical impact and management. Respirology 2017;22:651-61.
PUBMED | CROSSREF

17. Coman I, Pola-Bibián B, Barranco P, Vila-Nadal G, Dominguez-Ortega J, Romero D, et al. Bronchiectasis in severe asthma: clinical features and outcomes. Ann Allergy Asthma Immunol 2018;120:409-13.
PUBMED | CROSSREF

18. Mäntylä J, Mazur W, Törölä T, Bergman P, Saarinen T, Kauppi P. Asthma as aetiology of bronchiectasis in Finland. Respir Med 2019;152:105-11.
PUBMED | CROSSREF

19. Lee H, Choi H, Sim YS, Park S, Kim WJ, Yoo KH, et al. KMBARC registry: protocol for a multicentre observational cohort study on non-cystic fibrosis bronchiectasis in Korea. BMJ Open 2020;10:e034090.
PUBMED | CROSSREF

20. Pasteur MC, Helliwell SM, Houghton SJ, Webb SC, Foweraker JE, Coulden RA, et al. An investigation into causative factors in patients with bronchiectasis. Am J Respir Crit Care Med 2000;162:1277-84.
PUBMED | CROSSREF

21. Sim YS, Lee JH, Lee WY, Suh DI, Oh YM, Yoon JS, et al. Spirometry and Bronchodilator Test. Tuberc Respir Dis 2017;80:105-12.
PUBMED | CROSSREF

22. Martínez-García MA, de Gracia J, Vendrell Relat M, Girón RM, Máiz Carro L, de la Rosa Carrillo D, et al. Multidimensional approach to non-cystic fibrosis bronchiectasis: the FACED score. Eur Respir J 2014;43:1357-67.
PUBMED | CROSSREF

23. Spinou A, Siegert RJ, Guan WJ, Patel AS, Gosker HR, Lee KK, et al. The development and validation of the Bronchiectasis Health Questionnaire. Eur Respir J 2017;49:1601532.
PUBMED | CROSSREF

24. Kim HK, Lee H, Kim SH, Choi H, Lee JH, Lee JS, et al. Validation of the Korean version of the Bronchiectasis Health Questionnaire. Tuberc Respir Dis 2020;83:228-33.
PUBMED | CROSSREF

25. Hill AT, Haworth CS, Aliberti S, Barker A, Blasi F, Boersma W, et al. Pulmonary exacerbation in adults with bronchiectasis: a consensus definition for clinical research. Eur Respir J 2017;49:1700051.
PUBMED | CROSSREF

26. Pasteur MC, Bilton D, Hill AT; British Thoracic Society Bronchiectasis non-CF Guideline Group. British Thoracic Society guideline for non-CF bronchiectasis. Thorax 2010;65 Suppl 1:i1-58.
PUBMED | CROSSREF

27. Liu BC, Huang TX, Yang D, Yang L, Liu CT. Asthma-associated bronchiectasis: more attention needed! Respir Med 2020;161:105789.
PUBMED | CROSSREF

28. Crimi C, Ferri S, Campisi R, Crimi N. The link between asthma and bronchiectasis: state of the art. Respiration 2020;99:463-76.
PUBMED | CROSSREF

29. Polverino E, Traversi L, Martinez-Garcia M, Shteinberg M, Bossios A, Dimakou K, et al. Asthma as a co-morbidity and cause of bronchiectasis: data from the European Bronchiectasis Registry (EMBARC). Eur Respir J 2020;56:2364.
CROSSREF

30. Bendien SA, van Loon-Kooij S, Kramer G, Huijgen W, Altenburg J, Ten Brinke A, et al. Bronchiectasis in severe asthma: Does it make a difference? Respiration 2020;99:1-9.
PUBMED | CROSSREF

31. Rademacher J, Konwert S, Fuge J, Dettmer S, Welte T, Ringshausen FC. Anti-IL5 and anti-IL5Rα therapy for clinically significant bronchiectasis with eosinophilic endotype: a case series. Eur Respir J 2020;55:1901333.
PUBMED | CROSSREF

32. Flume PA, Chalmers JD, Olivier KN. Advances in bronchiectasis: endotyping, genetics, microbiome, and disease heterogeneity. Lancet 2018;392:880-90.
PUBMED | CROSSREF