Allergy Asthma Immunol Res. 2024 May;16(3):291-299
https://doi.org/10.4168/aair.2024.16.3.291
pISSN 2092-7355·eISSN 2092-7363

Allergy, Asthma & Immunology Research AAIR

Brief Communication

Check for updates

The Impact of Bronchiectasis on the Clinical Characteristics of Non-Severe Asthma

Kyung-Il Han ,[†] **Hyun Lee** ,[†] **Bo-Guen Kim** , **Yoomi Yeo** , **Tai Sun Park** , **Dong Won Park** , **Ji-Yong Moon** , **Sang-Heon Kim** , **Jang Won Sohn** , **Ho Joo Yoon** , **Tae Hyung Kim** [*]

Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Korea

Received: Aug 14, 2023
Revised: Jan 9, 2024
Accepted: Jan 27, 2024
Published online: Mar 22, 2024

Correspondence to
Tae Hyung Kim, MD, PhD
Division of Pulmonology and Critical Care Medicine, Department of Internal Medicine, Hanyang University Guri Hospital, Hanyang University College of Medicine, 153 Gyeongchun-ro, Guri 11923, Korea.
Tel: +82-31-560-2243
Fax: +82-31-553-7369
Email: drterry@hanyang.ac.kr

[†]Kyung-Il Han and Hyun Lee contributed equally to this work.

ORCID iDs
Kyung-Il Han
https://orcid.org/0009-0002-3204-8423
Hyun Lee
https://orcid.org/0000-0002-1269-0913
Bo-Guen Kim
https://orcid.org/0000-0003-0800-4324
Yoomi Yeo
https://orcid.org/0000-0002-2447-2067

ABSTRACT

Current literature primarily delves into the relationship between bronchiectasis and severe asthma, and only a few studies have evaluated the impact of bronchiectasis in patients with non-severe asthma. Therefore, this study investigated the clinical impact of bronchiectasis in patients with non-severe asthma. A prospective observational study of 140 non-severe asthmatic patients with (bronchiectasis group) and without bronchiectasis (control group) was conducted between September 2012 and February 2022. The bronchiectasis and control groups were compared in terms of demographics, lung function, asthma control test (ACT) results, exacerbation history, and respiratory medications. Among 140 non-severe asthmatic subjects, approximately 15.7% (n = 22) had bronchiectasis. The most common type of bronchiectasis was cylindrical type (90.7%). The left lingular division was the most frequently involved lung lobe (20.4%). There were no significant differences in the demographics (age, sex, body mass index, smoking history, and comorbidities) or ACT results between the 2 groups. The bronchiectasis group used inhaled corticosteroids/long-acting β2-agonists (P = 0.074) and mucolytics (P < 0.001) more frequently than the control group. Compared to the control group, the bronchiectasis group had lower forced expiratory volume in 1 second (FEV1) (L) (1.9 ± 0.7 L vs. 2.3 ± 0.9 L, P = 0.039) and FEV1%predicted (67.2 ± 22.2%predicted vs. 77.1 ± 20.0%predicted, P = 0.038). The rate of hospital admission to a general ward in the preceding year was significantly higher in the bronchiectasis group compared to those of the control group (23.8% vs. 3.5%, P = 0.005) with an adjusted odds ratio of 6.308 (95% confidence interval, 1.401–28.392). Patients with non-severe asthma and bronchiectasis had lower lung function and more frequent exacerbations requiring hospitalization than those without bronchiectasis. More attention is needed for asthmatic patients with bronchiectasis, even if the asthma is not severe.

Keywords: Asthma; bronchiectasis; comorbidity; prognosis; symptom flare up

INTRODUCTION

Asthma is a heterogeneous respiratory disease characterized by chronic airway inflammation and variable airflow limitations.[1] Many respiratory comorbidities are associated with asthma, which significantly influence its clinical characteristics and prognosis.[2-8] Therefore, it is

Tai Sun Park
https://orcid.org/0000-0001-7383-7934
Dong Won Park
https://orcid.org/0000-0002-4538-6045
Ji-Yong Moon
https://orcid.org/0000-0003-2459-3448
Sang-Heon Kim
https://orcid.org/0000-0001-8398-4444
Jang Won Sohn
https://orcid.org/0000-0001-7132-2988
Ho Joo Yoon
https://orcid.org/0000-0002-4645-4863
Tae-Hyung Kim
https://orcid.org/0000-0002-3863-7854

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

crucial to rapidly assess a patient's comorbidities, which may contribute to their respiratory symptoms, to plan a personalized treatment approach.

Bronchiectasis is known to be present in approximately 77% of patients with asthma, and bronchiectasis significantly affects the natural course of asthma.[7,19] Patients with severe asthma and bronchiectasis show lower lung function, more exacerbations, and higher mortality compared to those without bronchiectasis.[7,16-21] However, since previous studies focused on the impact of bronchiectasis on severe asthma, the impact of bronchiectasis on patients with non-severe asthma is not well known. Therefore, further studies are needed to establish the relationship between bronchiectasis and non-severe asthma. This study aimed to define the impact of bronchiectasis on the clinical characteristics of non-severe asthma.

MATERIALS AND METHODS

Study design

The HOPE study is a prospective, observational cohort study conducted at 2 centers in Korea that evaluates the clinical characteristics and courses of obstructive pulmonary diseases (asthma, bronchiectasis, and chronic obstructive pulmonary disease [COPD]). The inclusion criterion for the HOPE study was adult patients aged ≥ 18 years with a diagnosis of asthma, bronchiectasis, or COPD. Asthma was clinically diagnosed by attending physicians based on clinical symptoms, bronchodilator (BD) responses, excessive lung function change, and the results of a provocation test.[1] COPD was diagnosed in patients with respiratory symptoms, history of exposure to noxious particles (i.e., smoking), and post-BD forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) ratio < 0.7.[22] The diagnosis of bronchiectasis was based on chest computed tomography (CT) findings. The treatment duration was > 3 months for all patients. The exclusion criteria were patients 1) who are under treatment for active infectious conditions; 2) with interstitial lung disease; 3) with severe psychotic disorder; and 4) who were treated with systemic corticosteroids for diseases other than asthma or COPD ≥ 8 weeks before enrollment. Baseline data were obtained at the time of enrollment.

The study was approved by the Institutional Review Board of Hanyang University Guri Hospital Ethics Committee (No. HYGH-2012-01-057). Written informed consent was obtained from all participants.

Participants

In total, 636 participants with asthma, bronchiectasis, or COPD were enrolled in the HOPE study between September 2012 and February 2022. Out of these, 297 (46.7%) had asthma without physician-diagnosed COPD (asthma without asthma-COPD overlap). There were 86 (29.0%) patients with severe asthma (Global Initiative for Asthma [GINA] 4–5 treatments) and 211 (71.0%) patients with non-severe asthma (GINA 1–3 treatments). Of the 211 patients with non-severe asthma, 140 (66.4%) patients underwent CT scans. Of these, 22 patients (15.7%) had bronchiectasis, and 118 patients (84.3%) had no bronchiectasis (**Fig. 1**).

Data collection

The severity of asthma was classified as "severe" or "non-severe." Severe asthma was defined as an uncontrolled or partly controlled state despite using steps 4–5 of the GINA treatment guidelines. Mild-to-moderate asthma by GINA documents was classified as "non-

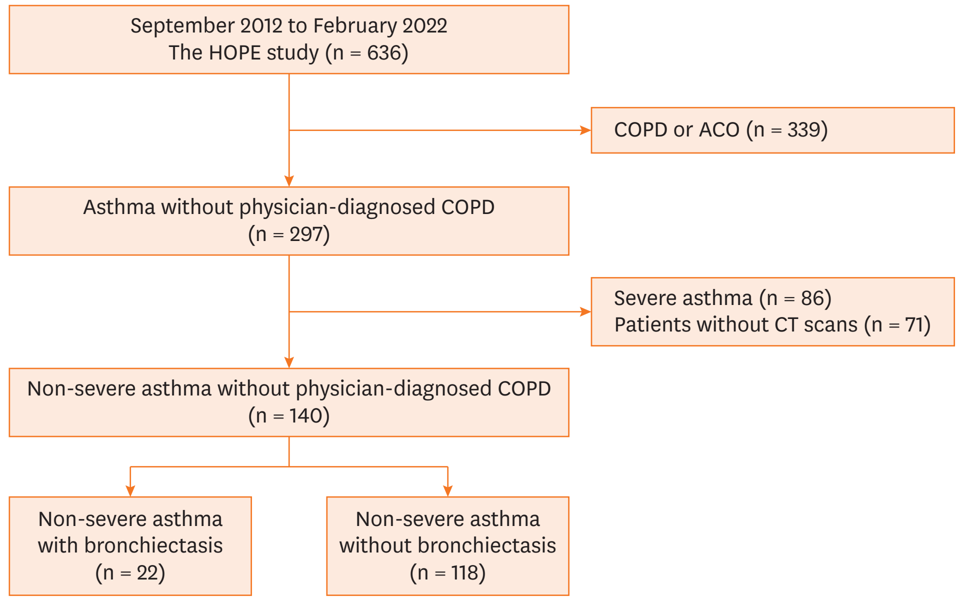

Fig. 1. Flow chart of the study.
COPD, chronic obstructive pulmonary disease; ACO, asthma-chronic obstructive pulmonary disease overlap; CT, computed tomography.

severe."[1] The following baseline data were collected for this study: demographics (age, sex, body mass index [BMI], and smoking status); comorbidities; exacerbation history; lung function; asthma control test (ACT); respiratory medications (inhalers, leukotriene receptor antagonist, methylxanthine, systemic corticosteroid, or mucolytics); and radiologic findings of bronchiectasis.

The presence or absence of bronchiectasis was determined using chest CT at the time of registration (within 1 year of registration). Chest CT was performed at the discretion of the attending physicians to assess any radiological findings suggestive of bronchiectasis, their distribution, dominant types (tubular, varicose, and cystic), and the number of involved lobes with bronchiectasis.[23]

Asthma exacerbation was defined as an unexpected event requiring a hospital visit for the treatment of worsening asthma symptoms (which may include the administration of systemic corticosteroids). We analyzed the patients' exacerbation history in the year preceding study enrollment, which was classified as follows: 1) any exacerbation; 2) unexpected visits to the outpatient department; 3) visits to the emergency room (ER); 4) admissions to the general ward; or 5) admissions to the intensive care unit. Treatments during acute exacerbation (e.g., systemic steroids, short-acting β2-agonist, or empirical antibiotics) and microbiological test results (sputum Gram stain/cultures and multiplex viral polymerase chain reaction [PCR] kit [Real-Q RV detection kit; BioSewoom, Seoul, Korea] for sputum) were also evaluated.

Statistical analyses

Continuous variables were described as mean values with standard deviations or as medians with interquartile ranges, as appropriate. The independent *t*-test was used for the former, whereas the Mann-Whitney *U* test was used for the latter. Categorical variables were described as numbers with percentages, and we used the χ^2 test or Fisher's exact test, whichever was appropriate. Univariate and multivariate logistic regression analyses were performed to evaluate whether bronchiectasis was independently associated with acute exacerbations leading to hospitalization. Factors included in the multivariate logistic regression analyses were demographics (age, sex, and BMI), asthma control (total ACT scores), pre-BD FEV1%predicted, and bronchiectasis. All statistical analyses were performed using the SPSS version 21.0 software (IBM Corp., Armonk, NY, USA). Statistical significance was set at $P < 0.05$.

RESULTS

Baseline characteristics

Of 140 patients with non-severe asthma, 22 (15.7%) patients had bronchiectasis, and 118 (84.3%) patients did not have bronchiectasis. Baseline characteristics of the study population are summarized in **Table 1**. There were no significant differences in age, sex, BMI, smoking history, total score on the ACT, GINA steps, or comorbidities ($P > 0.05$ for all).

Distribution and types of bronchiectasis

Fig. 2 shows the distribution and number of lobes in the bronchiectasis group. The lingula was the most frequently involved lobe (20.4%). Most of the lung lobes affected by bronchiectasis were of the cylindrical type (90.7%), followed by the varicose type (7.4%), and the cystic type (1.9%).

Pulmonary function tests

The bronchiectasis group had lower pre-BD FVC (2.9 ± 0.9 L vs. 3.4 ± 1.0 L, $P = 0.041$), %predicted FVC (80.5 ± 18.7%predicted vs. 89.2 ± 16.4%predicted, $P = 0.027$), FEV1 (1.9 ± 0.7 L vs. 2.3 ± 0.9 L, $P = 0.039$), and %predicted FEV1 (67.2 ± 22.2%predicted vs. 77.1 ± 20.0%predicted, $P = 0.038$) than did the control group (**Table 2**). However, the post-BD spirometry results were not significantly different between the 2 groups ($P > 0.05$).

Table 1. Baseline characteristics of patients with non-severe asthma

Characteristics	Bronchiectasis group (n = 22)	Control group (n = 118)	*P* value
Age (yr)	61.4 ± 7.6	57.5 ± 14.5	0.066
Male	13 (59.1)	71 (60.2)	0.924
BMI (kg/m^2; n = 113)	23.8 (22.9–25.4)	25.0 (22.4–27.1)	0.350
Smoking history			0.555
Never	11 (50.0)	49 (41.5)	
Ex-smoker	8 (36.4)	41 (34.7)	
Current smoker	3 (13.6)	28 (23.7)	
Asthma control test (n = 128)	24.0 (19.5–24.0)	23.0 (21.0–25.0)	0.865
GINA step			> 0.999
Step 2	19 (86.4)	98 (83.1)	
Step 3	3 (13.6)	20 (16.9)	
Comorbidities			
Allergic rhinitis (n = 139)	10 (45.5)	47 (40.2)	0.644
Allergic conjunctivitis (n = 137)	1 (5.0)	16 (13.7)	0.466
Atopic dermatitis	1 (4.5)	6 (5.1)	> 0.999
History of pneumonia (n = 139)	4 (18.2)	10 (8.5)	0.237
History of pulmonary TB (n = 138)	6 (27.3)	17 (14.7)	0.207
Hypertension (n = 139)	5 (22.7)	26 (22.2)	> 0.999
Angina (n = 139)	1 (4.5)	4 (3.4)	0.583
GERD (n = 138)	5 (22.7)	22 (19.0)	0.770
Osteoporosis	3 (13.6)	8 (6.8)	0.379

Continuous values are presented as means ± standard deviations or medians with interquartile ranges. Categorical values are presented as numbers (%).
BMI, body mass index; GINA, Global Initiative for Asthma; TB, tuberculosis; GERD, gastroesophageal reflux disease.

 https://doi.org/10.4168/aair.2024.16.3.291

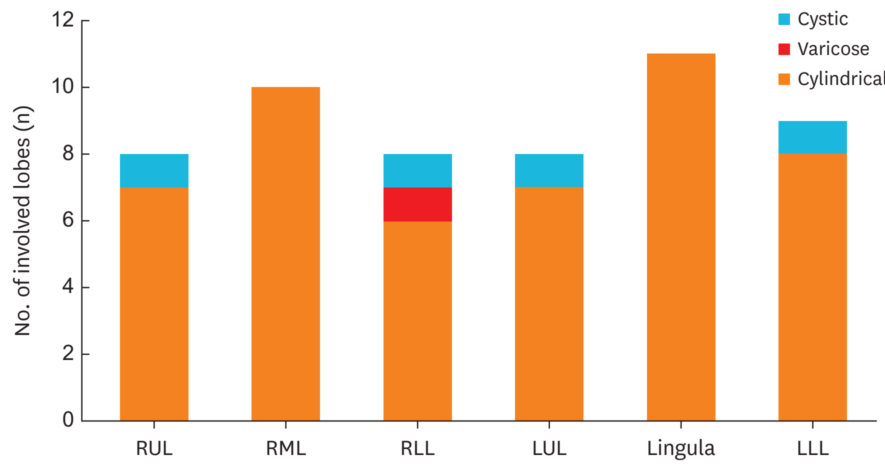

Fig. 2. The number of involved lung lobes and types in the bronchiectasis group.
RUL, right upper lobe; RML, right middle lobe; RLL, right lower lobe; LUL, left upper lobe; LLL, left lower lobe.

Table 2. Comparison of pulmonary function tests according to the presence or absence of bronchiectasis

Characteristics	Bronchiectasis group (n = 22)	Control group (n = 118)	*P* value
Pre-bronchodilator spirometry			
FVC (L)	2.9 ± 0.9	3.4 ± 1.0	0.041
FVC (%predicted)	80.5 ± 18.7	89.2 ± 16.4	0.027
FEV1 (L)	1.9 ± 0.7	2.3 ± 0.9	0.039
FEV1 (%predicted)	67.2 ± 22.2	77.1 ± 20.0	0.038
FEV1/FVC (%)	62.8 ± 12.4	65.9 ± 13.5	0.315
Post-bronchodilator spirometry			
FVC (L; n = 119)	3.1 ± 0.9	3.4 ± 0.9	0.091
FVC (%predicted; n = 119)	83.8 ± 19.7	90.0 ± 13.6	0.175
FEV1 (L; n = 119)	1.9 (1.3–2.4)	2.1 (1.6–2.8)	0.202
FEV1 (%predicted; n = 119)	73.2 ± 22.3	78.5 ± 18.0	0.238
FEV1/FVC (%; n = 119)	70.6 (57.3–74.9)	66.5 (58.6–76.8)	0.940
Bronchodilator response* (n = 126)	12 (54.5)	47 (45.2)	0.424
Airway hyperresponsiveness† (n = 69)	3 (42.9)	34 (54.8)	0.696

Continuous values are presented as means ± standard deviations or medians with interquartile ranges.
Categorical values are presented as numbers (%).
FVC, forced vital capacity; FEV1, forced expiratory volume in 1 second.
*An increase of ≥ 12% and ≥ 200 mL in FEV1 from the baseline.
†Methacholine, PC20 < 16 mg/mL or mannitol, PD15 < 635 mg.

Medications

As shown in **Fig. 3**, there were no significant differences in the use of inhaled corticosteroids with long-acting β2 agonists, leukotriene receptor antagonist, methylxanthine, or oral corticosteroids (OCS) ($P > 0.05$ for all) between the bronchiectasis and control groups. However, the use of mucolytics was significantly higher in the bronchiectasis group compared to the control group (68.2% vs. 19.5%, $P < 0.001$).

Exacerbation history

As shown in **Table 3**, there were no significant differences in the number of exacerbations, unexpected outpatient department visits, ER visits, or treatments during acute exacerbations (OCS administration, short-acting β-agonist use without OCS use, or antibiotic use) between the bronchiectasis and control groups. However, the bronchiectasis group demonstrated a higher rate of admission to the general ward in the previous year compared to the control group (23.8% [5/22] vs. 3.5% [4/118], $P = 0.005$). Of the 5 patients with bronchiectasis

https://doi.org/10.4168/aair.2024.16.3.291

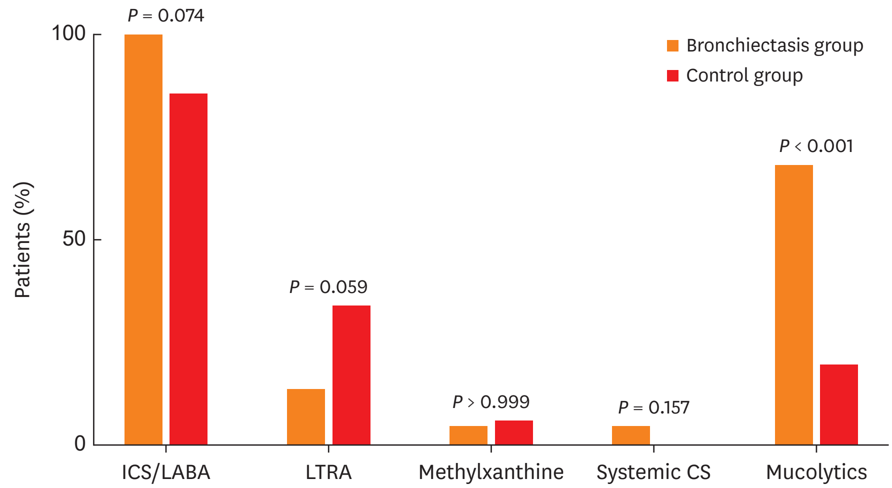

Fig. 3. Comparison of asthma-related medication use according to the presence or absence of bronchiectasis.
ICS, inhaled corticosteroid; LABA, long-acting β2-agonist; LTRA, leukotriene receptor antagonist; CS, corticosteroid.

Table 3. Comparison of exacerbations in the previous year according to the presence or absence of bronchiectasis

Characteristics	Bronchiectasis group (n = 22)	Control group (n = 118)	*P* value
All exacerbations (n = 136)	6 (25.0)*	18 (15.8)	0.223
Unexpected OPD visit (n = 134)	1 (4.8)	4 (3.5)	0.580
ER visit (n = 134)	1 (4.8)	10 (8.9)	0.691
Admission to the general ward (n = 134)	5 (23.8)*	4 (3.5)	0.005
Medications during exacerbations			
OCS use (n = 130)	5 (22.7)	12 (11.0)	0.163
SABA use without OCS use (n = 130)	0 (0.0)	6 (5.1)	0.277
Antibiotics use (n = 130)†	2 (9.1)*	2 (1.7)	0.251

Values are presented as numbers (%).
OPD, outpatient department; ER, emergency room; OCS, oral corticosteroid; SABA, short-acting β-agonist.
*One patient was considered to have bronchiectasis-related exacerbation, which was determined by sputum amount and purulence and improvement by antibiotic use. However, there was no bacterial growth in the sputum culture, and rhinovirus was identified in the multiplex viral polymerase chain reaction kit.
†Three patients received one dose of intravenous antibiotics at the emergency department without any evidence of respiratory infection.

who were admitted to the general ward, only one patient had a bronchiectasis-related exacerbation (determined by an increase in sputum amount and purulence).

Regarding viral/bacterial infection during exacerbation, 8 of the 24 patients who experienced acute exacerbations underwent sputum Gram staining and cultures. However, there was no bacterial growth. Of the 8 patients who underwent sputum Gram staining and culture, 4 (2 in the bronchiectasis group and 2 in the control group) received antibiotics. Of the 2 patients in the bronchiectasis group, one patient with bronchiectasis-related exacerbation showed rhinovirus in the multiplex viral PCR kit for sputum. Although one patient in the bronchiectasis group and 2 patients in the control group received one dose of empirical antibiotics in the ER, there was no evidence of respiratory infection.

Factors associated with acute exacerbations leading to hospitalizations

As shown in **Table 4**, the presence of bronchiectasis was the only factor associated with acute exacerbations leading to hospitalization (unadjusted odds ratio [OR], 8.516, 95% confidence interval [CI], 2.067–35.076; $P = 0.003$; adjusted OR, 6.308; 95% CI, 1.401–28.392; $P = 0.016$).

Table 4. Factors associated with acute exacerbation leading to hospitalization

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	*P* value	Adjusted OR (95% CI)	*P* value
Age (yr)	1.014 (0.962–1.069)	0.604	1.001 (0.936–1.070)	0.979
Males	0.806 (0.206–3.149)	0.756	0.555 (0.118–2.605)	0.455
BMI (kg/m^2)	1.031 (0.828–1.285)	0.784	1.046 (0.831–1.316)	0.702
Total ACT scores	1.043 (0.829–1.313)	0.717	1.021 (0.804–1.297)	0.863
Pre-BD FEV1 (%predicted)	1.003 (0.970–1.037)	0.857	1.013 (0.974–1.053)	0.514
Bronchiectasis	8.516 (2.067–35.076)	0.003	6.308 (1.401–28.392)	0.016

OR, odds ratio; CI, confidence interval; BMI, body mass index; ACT, asthma control test; BD, bronchodilator; FEV1, forced expiratory volume in 1 second.

DISCUSSION

This study investigated the clinical impact of bronchiectasis on non-severe asthma and showed that bronchiectasis was present in approximately 20% of non-severe asthma cases. Bronchiectasis in non-severe asthma is associated with poorer lung function and a higher rate of hospitalization (due to exacerbation) compared to patients with non-severe asthma without bronchiectasis.

Many prior studies have evaluated the prevalence and impact of bronchiectasis in asthma.[6-19,24,25] The reported prevalence of bronchiectasis in Korean asthmatic patients is highly variable, ranging from approximately 1.7% to 37.6%.[8,9,13,14,19] This wide range is probably due to patient characteristics or asthma disease severity.[8,9,13,14,19] Generally, bronchiectasis is known to be more common in patients with severe asthma than it is in those with non-severe asthma.[15,20,21,24] However, these previous studies mainly focused on severe asthma. Therefore, the prevalence and impact of bronchiectasis in patients with non-severe asthma were not well known. Our study provided insights into bronchiectasis and non-severe asthma. Our results demonstrated that approximately one-fifth of non-severe asthmatics have bronchiectasis on CT scans, suggesting that bronchiectasis is a common comorbidity, even in those with non-severe asthma.

Patients with severe asthma and bronchiectasis have more frequent exacerbations, fewer controlled symptoms, and poorer lung function than those without bronchiectasis.[6,17-20,26] However, the impact of bronchiectasis on the clinical course of non-severe asthma is poorly established. Our study showed that although pre-BD FEV1 was lower in non-severe asthmatics with bronchiectasis than in those without bronchiectasis, post-BD FEV1 was not significantly different. Moreover, the ACT score was slightly higher (not statistically significant) in patients with non-severe asthma and bronchiectasis than in those without bronchiectasis. These findings suggested that bronchiectasis may not significantly affect the severity of lung function and asthma control in patients with non-severe asthma, which differs from the impact of bronchiectasis in patients with severe asthma. However, similar to severe asthma, the number of exacerbations requiring hospitalization was higher in patients with non-severe asthma with bronchiectasis than those without bronchiectasis. Our study indicated that coexisting bronchiectasis can be accompanied by severe exacerbations in both severe and non-severe asthma. Despite the importance of the relationship between non-severe asthma and bronchiectasis, few studies have focused on this relationship. Further studies are required to confirm our findings.

Asthma and bronchiectasis share several pathophysiological characteristics, such as chronic airway inflammation, mucus accumulation, airway obstruction, and lung damage.[12] Airway inflammation and mucus accumulation play a significant role in acute exacerbations and impaired lung function in both asthma and bronchiectasis.[11] In addition, the presence of bronchiectasis can make the lungs vulnerable to viral/bacterial infections and air pollutants, which are the main causes of asthma exacerbation.[12,27] The presence of bronchiectasis, even in non-severe asthma, may increase the likelihood of rapid lung function decline and severe exacerbation, requiring hospitalization through these potential mechanisms.

The clinical implications of our study are as follows. When a patient's asthma is not controlled despite proper management, it is important to identify any extrapulmonary comorbidities (e.g., sinusitis, bronchiectasis, etc.) that may affect asthma symptoms.[4,28] However, a CT scan is not usually performed in patients with non-severe asthma; instead, it is more commonly performed in severe asthmatics with frequent exacerbations.[12] Contrary to this practice, our results suggested that identification of bronchiectasis with a CT scan is necessary in patients with non-severe asthma who experience severe exacerbations, regardless of good ACT results. However, since post-BD lung function and ACT scores were not significantly different, the usefulness of chest CT in patients with poor lung function or poor control is unknown.

Our study has several limitations. First, the number of participants was relatively small. Secondly, chest CT was performed at the discretion of the attending physicians. Accordingly, there might be selection bias, and it would be difficult to describe that the true prevalence of bronchiectasis in non-severe asthmatics is 20%. Future prospective studies incorporating routine CT scans in patients with non-severe asthma are needed to address this issue. Thirdly, due to the absence of microbiological data in the stable state, we could not determine the severity of bronchiectasis using quantitative severity assessment tools, such as the bronchiectasis severity index.

In conclusion, patients with non-severe asthma and bronchiectasis may have lower lung function and more frequent exacerbations requiring hospitalization than those without bronchiectasis.

REFERENCES

1. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention [Internet]. Fontana (WI): GINA; 2023 [cited 2023 Aug 14]. Available from: https://www.ginasthma.org/.
2. Moon SM, Choi H, Kang HK, Lee SW, Sim YS, Park HY, et al. Impacts of asthma in patients with bronchiectasis: findings from the KMBARC registry. Allergy Asthma Immunol Res 2023;15:83-93. PUBMED | CROSSREF
3. Lee H, Ryu J, Chung SJ, Park DW, Sohn JW, Yoon HJ, et al. Coexisting COPD increases mortality in patients with corticosteroid-dependent asthma: a nationwide population-based study. Allergy Asthma Immunol Res 2020;12:821-31. PUBMED | CROSSREF
4. Rogliani P, Laitano R, Ora J, Beasley R, Calzetta L. Strength of association between comorbidities and asthma: a meta-analysis. Eur Respir Rev 2023;32:220202. PUBMED | CROSSREF
5. Domínguez-Ortega J, Luna-Porta JA, Olaguibel JM, Barranco P, Arismendi E, Barroso B, et al. Exacerbations among patients with asthma are largely dependent on the presence of multimorbidity. J Investig Allergol Clin Immunol 2023;33:281-8. PUBMED | CROSSREF
6. Porsbjerg C, Menzies-Gow A. Co-morbidities in severe asthma: clinical impact and management. Respirology 2017;22:651-61. PUBMED | CROSSREF
7. Rogliani P, Sforza M, Calzetta L. The impact of comorbidities on severe asthma. Curr Opin Pulm Med 2020;26:47-55. PUBMED | CROSSREF

 https://doi.org/10.4168/aair.2024.16.3.291

8. Yeo Y, Lee H, Ryu J, Chung SJ, Park TS, Park DW, et al. Additive effects of coexisting respiratory comorbidities on overall or respiratory mortality in patients with asthma: a national cohort study. Sci Rep 2022;12:8105. PUBMED | CROSSREF

9. 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

10. 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

11. Crimi C, Ferri S, Crimi N. Bronchiectasis and asthma: a dangerous liaison? Curr Opin Allergy Clin Immunol 2019;19:46-52. PUBMED | CROSSREF

12. 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

13. Kang HR, Choi GS, Park SJ, Song YK, Kim JM, Ha J, et al. The effects of bronchiectasis on asthma exacerbation. Tuberc Respir Dis 2014;77:209-14. PUBMED | CROSSREF

14. Kim NY, Lee CH, Jin KN, Lee HW, Heo EY, Kim DK, et al. Clinical deterioration and lung function change in patients with concomitant asthma and bronchiectasis. J Allergy Clin Immunol Pract 2022;10:2607-2613.e4. PUBMED | CROSSREF

15. Luján M, Gallardo X, Amengual MJ, Bosque M, Mirapeix RM, Domingo C. Prevalence of bronchiectasis in asthma according to oral steroid requirement: influence of immunoglobulin levels. BioMed Res Int 2013;2013:109219. PUBMED | CROSSREF

16. Matsumoto H. Bronchiectasis in severe asthma and asthmatic components in bronchiectasis. Respir Investig 2022;60:187-96. PUBMED | CROSSREF

17. Dimakou K, Gousiou A, Toumbis M, Kaponi M, Chrysikos S, Thanos L, et al. Investigation of bronchiectasis in severe uncontrolled asthma. Clin Respir J 2018;12:1212-8. PUBMED | CROSSREF

18. García-Clemente M, Enríquez-Rodríguez AI, Iscar-Urrutia M, Escobar-Mallada B, Arias-Guillén M, López-González FJ, et al. Severe asthma and bronchiectasis. J Asthma 2020;57:505-9. PUBMED | CROSSREF

19. Choi H, Lee H, Ryu J, Chung SJ, Park DW, Sohn JW, et al. Bronchiectasis and increased mortality in patients with corticosteroid-dependent severe asthma: a nationwide population study. Ther Adv Respir Dis 2020;14:1753466620963030. PUBMED | CROSSREF

20. 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

21. Padilla-Galo A, Olveira C, Fernández de Rota-Garcia L, Marco-Galve I, Plata AJ, Alvarez A, et al. Factors associated with bronchiectasis in patients with uncontrolled asthma; the NOPES score: a study in 398 patients. Respir Res 2018;19:43. PUBMED | CROSSREF

22. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187:347-65. PUBMED | CROSSREF

23. Hill AT, Sullivan AL, Chalmers JD, De Soyza A, Elborn SJ, Floto AR, et al. British Thoracic Society Guideline for bronchiectasis in adults. Thorax 2019;74:1-69. PUBMED | CROSSREF

24. Ma D, Cruz MJ, Ojanguren I, Romero-Mesones C, Varona-Porres D, Munoz X. Risk factors for the development of bronchiectasis in patients with asthma. Sci Rep 2021;11:22820. PUBMED | CROSSREF

25. 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

26. Ferri S, Crimi C, Campisi R, Cacopardo G, Paoletti G, Puggioni F, et al. Impact of asthma on bronchiectasis severity and risk of exacerbations. J Asthma 2022;59:469-75. PUBMED | CROSSREF

27. Castillo JR, Peters SP, Busse WW. Asthma exacerbations: pathogenesis, prevention, and treatment. J Allergy Clin Immunol Pract 2017;5:918-27. PUBMED | CROSSREF

28. Cazzola M, Rogliani P, Ora J, Calzetta L, Matera MG. Asthma and comorbidities: recent advances. Pol Arch Intern Med 2022;132:16250. PUBMED | CROSSREF