

LSUHSC Non-TB Mycobacterial (NTM) - Bronchiectasis (BE) Center

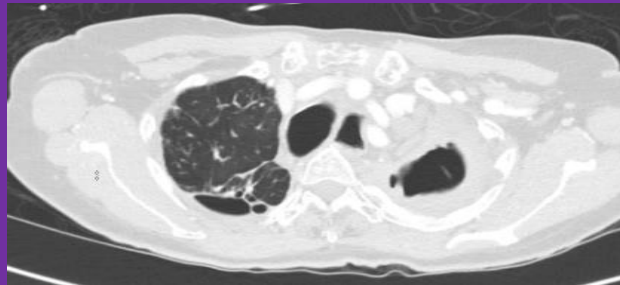
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Review

A multidisciplinary approach to the management of nontuberculous mycobacterial lung disease: a clinical perspective

[Juzar Ali](#)



Gastroesophageal Reflux Disease (GERD) and Pulmonary Exacerbation Frequency in Bronchiectasis Participants From the Bronchiectasis and NTM Research Registry (BRR)

Lapinel NC¹, Choate R², Aksamit TR³, Winthrop K⁴, Schmid A⁵, Metersky ML⁶ for the Bronchiectasis and NTM Research Registry Investigators



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Background and Aims

Existing evidence demonstrates conflicting results associating gastroesophageal reflux disease (GERD) with pulmonary exacerbation frequency in patients with bronchiectasis not associated with cystic fibrosis. Untreated GERD is believed to contribute to increased risk of pulmonary exacerbations. The impact of use of acid-suppressive medications is less clear. This study sought to analyze data from the United States Bronchiectasis and Nontuberculous Mycobacteria Research Registry (BRR) relating GERD and the use of acid-suppressive medication to determine if there is an association with frequency of pulmonary exacerbations in subjects with bronchiectasis.

Methods

- Data for this study was obtained from the BRR, a centralized database sponsored by the COPD Foundation, incorporating adult patients with bronchiectasis from 16 clinical sites throughout the United States.
- Baseline enrollment information for included subjects was collected between 2008-March 2020 and analyzed relative to GERD diagnosis, GERD-specific testing and GERD-related treatment.
- Subjects with unknown/missing data relative to GERD testing and use of GERD-suppression medication were excluded from the analysis.
- Predetermined subgroups were further stratified according to exacerbation frequency (<2 versus ≥2) at baseline enrollment.



Results

- Data from a total of 1872 subjects were analyzed.
- Total of 1008 patients were excluded from the analysis for unknown / missing data pertaining to GERD testing and 304 excluded for missing acid suppression data (n=287 overlap).
- Overall cohort: mean age of 65.2 (±13.3); predominantly female (79.3%), white (92.2%) and never-smokers (58.0%).
- Patients with GERD were older than patients without GERD (65.9 vs 64.5, p=.0161)
- More patients with GERD had a history of smoking (45.1%, p=.0057)

Table 1. Demographics**

	Overall cohort N=1872	GERD		p-value
		No n=925 (49.4%)	Yes n=947 (50.6%)	
Age, years, mean (SD)	65.2 (13.3)	64.5 (14.7)	65.9 (11.7)	0.0161
Gender, female, n (%)	1480 (79.3)	737 (79.8)	743 (78.8)	0.6079
Hispanic, n (%)	83 (4.6)	40 (4.6)	43 (4.6)	0.9999
Race, n (%)				0.2879
White	1720 (92.2)	842 (91.1)	878 (93.3)	
Black or African American	30 (1.6)	15 (1.6)	15 (1.6)	
Other*	61 (3.3)	36 (3.9)	25 (2.7)	
Smoking history (current or former), n (%)	54 (2.9)	31 (3.4)	23 (2.4)	0.0057
Pre-bronchodilator FEV1 % pred, mean (SD)	72.1 (22.0)	71.8 (21.5)	72.5 (11.5)	0.5297
FEV (L), mean (SD)	1.9 (0.7)	1.9 (0.7)	1.8 (0.7)	0.2778

Disclosures: Dr. Lapinel serves as a consultant and a member of the Advisory Board Panel for Insmid Incorporated.

Results (cont.)

- Slightly more subjects within the overall cohort were identified as having GERD (50.6%) than not having GERD.
- A greater proportion of those with GERD (41.4%) had ≥2 exacerbations compared to those without (34.2%, p=0.0013).
- The majority of cohort participants were not taking gastric-acid-suppressive medication (63.6%), however significantly more subjects with GERD were on acid-suppressive medication (61.6%, p<.0001) compared to 10.6% of those without GERD.
- However, only 38.1% of all subjects underwent GERD-specific testing. 44.8% of those on gastric acid-suppressive medication had ≥2 exacerbations compared to 33.8% of those not on treatment (p<0.0001).
- When subjects with GERD were evaluated according to use of gastric acid suppression, subjects on treatment were more likely to have ≥2 exacerbations (45.6% vs 34.6%, p=.0008).
- Among subjects without and with GERD, those with no history of NTM, had suffered more frequent pulmonary exacerbations (without GERD: 37.6% vs 26.9%, p=0.0012; with GERD: 48.6% vs 31.3%, p<.0001, respectively).

Funding: The Bronchiectasis and NTM Research Registry is funded by the Richard H. Scarborough Research Fund, the Anna-Maria and Stephen Kellen Foundation, and the Bronchiectasis and NTM Industry Advisory Committee.

Results (cont.)

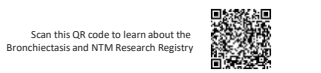
Table 2. Characterization of Gastroesophageal Reflux Disease, Testing and Treatment Relative to Pulmonary Exacerbations in Subjects with Bronchiectasis

	Gastroesophageal Reflux Disease (GERD)				p-value	
	No n=925 (49.4%)	Yes n=947 (50.6%)				
<2 exacerbations*, n (%)	609 (65.8)	555 (58.6)			0.0013	
≥2 exacerbations*, n (%)	316 (34.2)	392 (41.4)				
Gastric Acid Suppression Medication						
	No n=1191 (63.6%)	Yes n=681 (36.4%)			p-value	
<2 exacerbations*, n (%)	788 (66.2)	376 (55.2)			<.0001	
≥2 exacerbations*, n (%)	403 (33.8)	305 (44.8)				
GERD =No n=925 (49.4%) vs GERD =Yes n=947 (50.6%)						
	NTM (-) n=627	NTM (+) n=298	p-value	NTM (-) n=554	NTM (+) n=393	p-value
<2 exacerbations*, n (%)	391 (62.4)	218 (73.2)	0.0012	285 (51.4)	270 (68.7)	<.001
≥2 exacerbations*, n (%)	236 (37.6)	80 (26.9)		269 (48.6)	123 (31.3)	
GERD Test = Yes No vs GERD Test = Yes No						
	GERD Test = Yes n=84 (62.7)	GERD Test = No n=525 (66.4)	p-value	GERD Test = Yes n=347 (59.9)	GERD Test = No n=208 (56.5)	p-value
<2 exacerbations*, n (%)	59 (39.8)	277 (33.5)	0.2136	317 (54.4)	238 (65.4)	0.0008
≥2 exacerbations*, n (%)	39 (39.8)	277 (33.5)		266 (45.6)	126 (34.6)	
Gastric Acid Suppression Medication						
	Yes	No	p-value	Yes	No	p-value
<2 exacerbations*, n (%)	59 (60.2)	550 (66.5)	0.2136	317 (54.4)	238 (65.4)	0.0008
≥2 exacerbations*, n (%)	39 (39.8)	277 (33.5)		266 (45.6)	126 (34.6)	

* Baseline data included reported number of pulmonary exacerbations occurring 2 years prior to enrollment

Conclusions

The presence of GERD in patients with bronchiectasis is associated with increased exacerbation frequency. The use of acid-suppressive medication also appears to be associated with an increased frequency of exacerbations. However, the majority of subjects had not undergone GERD-specific testing. As this was a retrospective analysis, we are unable to determine causality, however, more studies are necessary to determine if GERD and GERD-related treatment meaningfully impact pulmonary exacerbations in bronchiectasis.



** 1. Dr. Nicole Lapinel, LSUHSC Faculty NTM-BE Program

Nontuberculous Mycobacteria (NTM) Isolation Status Relative to Pulmonary Exacerbation Frequency in Bronchiectasis Patients: Results From the Bronchiectasis and NTM Research Registry (BRR)



Lapinel NC, Choate R, Aksamit TR, Winthrop K, Schmid A, Metersky ML for the Bronchiectasis and NTM Research Registry Investigators

¹Section of Pulmonary/Critical Care & Allergy/Immunology, Louisiana State University, Health Sciences Center, New Orleans, LA ²Department of Epidemiology, University of Kentucky, Lexington, KY ³Division of Pulmonary & Critical Care Medicine, Mayo Clinic, Rochester, MN ⁴Division of Infectious Diseases, Oregon Health Sciences University ⁵Division of Pulmonary, Critical Care and Sleep Medicine, University of Kansas Medical Center, Kansas City, MO ⁶Division of Pulmonary, Critical Care and Sleep Medicine, University of Connecticut School of Medicine, Farmington, CT

Background and Aims

Bronchiectasis not associated with cystic fibrosis, is characterized by chronic inflammation and airway injury due to heterogeneous etiologies, that is inconsistently progressive among those affected. Increased frequency of pulmonary exacerbations is a known cause of worsening bronchiectasis. NTM is a significant pulmonary pathogen associated with chronic inflammatory disease and frequently isolated in bronchiectasis patients. This study aimed to compare subjects with underlying bronchiectasis according to history of NTM isolation, to determine the association with pulmonary exacerbation frequency.

Methods

- Baseline data from the Bronchiectasis and NTM Research Registry (BRR) for patients followed clinically between 2008- March 2020 was used for this study.
- BRR is a centralized database sponsored by the COPD Foundation of adult patients with bronchiectasis, identified at 16 clinical sites throughout the United States.
- Cross-sectional statistical analyses were performed for baseline demographics, select comorbidities, and clinical characteristics.
- The cohort was stratified into two groups based on number of pulmonary exacerbations (PE) (<2 versus ≥2) and history of NTM isolation at enrollment.

Results

- A total of 2950 subjects (mean age=65.5±13.4, 78.9% female, 90.1% white) were included in the analysis.
- Subjects without NTM were more likely to experience ≥2 PE than those with NTM isolation (67.4% vs 32.6%, p<.0001)
- Subjects with NTM were younger (mean age 62.0 vs 68.5, p<.0001) and were diagnosed with bronchiectasis at an earlier age (mean 53.3 vs 60.1) p<.0001).
- A greater proportion of participants with a ≥2 PE, but no history of NTM, had asthma (37.7% vs 27.8%, p=.0016), and positive cultures for *Pseudomonas aeruginosa* (35.1% vs 20.4%, p<.0001) compared to those with NTM.

Results (cont'd)

Table 1. Demographics, Comorbidities and Microbiology Stratified by Exacerbations and NTM Isolation at Enrollment

	<2 exacerbations n=1905 (64.6%)			≥2 exacerbations n=1045 (35.4%)		
	NTM (+) n=913 (47.9%)	NTM (-) n=992 (52.1%)	p-value	NTM (+) n=341 (32.6%)	NTM (-) n=704 (67.4%)	p-value
Demographics						
Age, years (mean, SD) (n=2924)	66.8(11.3)	66.2(14.2)	0.3620	68.5(11.3)	62.0(14.8)	<0.001
Age at bronchiectasis diagnosis, years (mean, SD) (n=2203)	61.8(14.0)	59.2(17.0)	0.0031	60.2(14.8)	53.3(17.9)	<0.001
Duration of bronchiectasis, years (mean, SD) (n=2165)	5.8(8.1)	7.4(11.0)	0.0026	8.5(9.9)	9.2(11.8)	0.3629
Gender, n (%) (n=2943)						
Female	729 (80.1%)	772 (77.9%)	0.2379	280 (82.1%)	547 (78.0%)	0.1267
Male	181 (19.9%)	219 (22.1%)		61 (17.9%)	154 (22.0%)	
Race, n (%)						
White	835 (91.5%)	872 (87.9%)	<0.001	314 (92.1%)	638 (90.6%)	0.0336
Black/African	7 (0.8%)	40 (4.0%)		4 (1.2%)	23 (3.3%)	
Asian	39 (4.3%)	40 (4.0%)		10 (3.5%)	10 (1.4%)	
Other	14 (1.5%)	28 (2.8%)		7 (2.1%)	25 (3.6%)	
Unknown	18 (2.0%)	12 (1.2%)		4 (1.2%)	8 (1.1%)	
Hispanic ethnicity, n (%)						
No	669 (73.3%)	877 (88.4%)	<0.001	262 (76.8%)	648 (92.1%)	<0.001
Yes	32 (3.5%)	34 (3.4%)		19 (5.6%)	36 (5.1%)	
Unknown	212 (23.2%)	81 (8.2%)		60 (17.6%)	20 (2.8%)	
Smoking status, n (%)						
Ever smoker	406 (44.5%)	400 (40.3%)	0.1813	147 (43.1%)	274 (38.9%)	0.2784
Non-smoker	497 (54.4%)	579 (58.4%)		194 (56.9%)	428 (60.8%)	
Unknown	10 (1.2%)	13 (1.3%)		0 (0.00%)	2 (0.3%)	
Associated Comorbidities						
COPD, n (%) (n=2887)						
Yes	138 (15.5%)	172 (17.8%)	0.1743	70 (20.8%)	133 (19.2%)	0.5278
No	754 (84.5%)	793 (82.2%)		266 (79.2%)	561 (80.8%)	
Asthma, n (%) (n=2881)						
Yes	152 (17.1%)	230 (23.9%)	0.0003	93 (27.8%)	261 (37.7%)	0.0016
No	739 (82.9%)	733 (76.1%)		242 (72.2%)	431 (62.3%)	
GERD, n (%) (n=2897)						
Yes	382 (42.8%)	357 (36.7%)	0.0065	175 (52.4%)	324 (46.5%)	0.0755
No	510 (57.2%)	617 (63.4%)		159 (47.6%)	373 (53.5%)	
Pseudomonas aeruginosa, n (%) (n=2926)						
Yes	102 (11.2%)	171 (17.4%)	0.0001	69 (20.4%)	244 (35.1%)	<0.001
No	809 (88.8%)	810 (82.6%)		270 (79.7%)	451 (64.9%)	

- Spirometry didn't differ significantly between NTM & non-NTM subjects
- For respiratory symptoms during stable state/exacerbation, wheezing was more common among subjects with ≥2 PE and no NTM compared to those with NTM (42.8% vs 28.5%, p<.0001).
- Mean number of hospitalizations was higher among non-NTM subjects with more frequent PE versus those with NTM (0.66 vs 0.51, p=0.028).

Results (cont.)

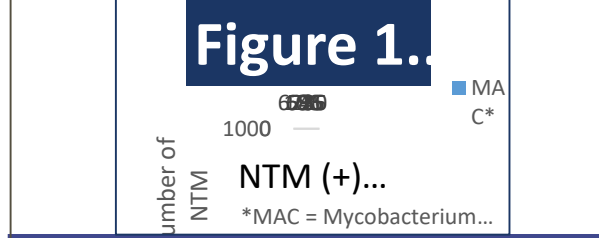


Table 2. Respiratory Symptoms and Spirometric Testing Stratified by Exacerbations and NTM Isolation

	<2 exacerbations n=1905 (64.6%)			≥2 exacerbations n=1045 (35.4%)		
	NTM (+) n=913 (47.9%)	NTM (-) n=992 (52.1%)	P value	NTM (+) n=341 (32.6%)	NTM (-) n=704 (67.4%)	P value
Respiratory symptoms						
Fatigue, n (%)						
Yes	398 (43.6)	375 (37.8)	0.0348	170 (49.9)	349 (49.6)	0.9583
No	486 (53.2)	585 (59)		161 (47.2)	332 (47.2)	
Unknown/Missing	29 (3.2)	32 (3.2)		10 (2.9)	23 (3.3)	
Regular coughing, n (%)						
Yes	639 (70.0)	669 (67.4)	0.4482	268 (78.6)	569 (80.8)	0.2612
No	262 (28.7)	311 (31.4)		71 (20.8)	125 (17.8)	
Unknown/Missing	12 (1.3)	12 (1.2)		2 (0.6)	10 (1.4)	
Hemoptysis, n (%)						
Yes	165 (18.1)	140 (14.1)	0.0083	93 (27.3)	177 (25.1)	0.1509
No	734 (80.4)	822 (82.9)		246 (72.1)	512 (72.7)	
Unknown/Missing	14 (1.5)	30 (3.0)		2 (0.6)	15 (2.1)	
Wheezing, n (%)						
Yes	146 (16.0)	233 (23.5)	0.0002	97 (28.5)	301 (42.8)	<0.001
No	748 (81.9)	740 (74.6)		239 (70.1)	387 (55.0)	
Unknown/Missing	19 (2.1)	19 (1.9)		5 (1.5)	16 (2.3)	
Spirometric tests						
Pre-Bronchodilator FEV1 (L) (mean, SD) (n=2474)	1.9(0.7)	1.9(0.7)	0.9384	1.8(0.7)	1.8(0.7)	0.7227
Pre-Bronchodilator FEV1 (%P) (mean, SD) (n=2467)	76.4(21.0)	74.7(21.6)	0.1285	72.2(23.0)	68.9(23.6)	0.0432
FEV1 (%P) < 50%, n (%)	75 (10.6)	102 (12.4)	0.2593	57 (18.8)	146 (23.2)	0.1304
FEV1 (%P) ≥ 50%, n (%) (n=2467)	636 (89.4)	721 (87.6)	0.2593	246 (81.2)	484 (76.8)	0.1304

Results (cont.)

Table 3. Modified Disease Severity Indices and Healthcare Resource Utilization Stratified by Exacerbations and NTM Isolation

	<2 exacerbations n=1905 (64.6%)			≥2 exacerbations n=1045 (35.4%)		
	NTM (+) n=913 (47.9%)	NTM (-) n=992 (52.1%)	P value	NTM (+) n=341 (32.6%)	NTM (-) n=704 (67.4%)	P value
Modified Disease Severity Indices						
Modified BSI (mean, SD)	5.58(3.0)	5.93(3.2)	0.0124	8.06(3.9)	7.97(3.9)	0.7168
Mild m-BSI, n (%)	372 (40.74%)	354 (35.69%)	0.0479	61 (17.89%)	126 (17.9)	0.9837
Moderate m-BSI, n (%)	387 (42.39%)	440 (44.35%)		143 (41.94%)	299 (42.5)	
Severe m-BSI, n (%)	154 (16.87%)	198 (19.96%)		137 (40.18%)	279 (39.6)	
Modified FACED (mean, SD)	1.9(1.4)	2.2(1.5)	0.0003	2.5(1.6)	2.4(1.7)	0.3258
Mild m- FACED, n (%)	604 (66.2)	599 (60.4)	0.0201	176 (51.6)	408 (58.0)	0.0892
Moderate m- FACED, n (%)	278 (30.5)	344 (34.7)		127 (37.2)	215 (30.5)	
Severe m- FACED, n (%)	31 (3.4)	49 (4.9)		38 (11.1)	81 (11.5)	
Healthcare Resource Utilization						
Number of hospitalizations in the past 2 years (mean, SD)	0.13(0.4)	0.13(0.5)	0.9920	0.51(1.0)	0.66(1.1)	0.0282

Conclusions

An increasing number of patients with bronchiectasis are recognized to have underlying NTM infection. Updated NTM-management guidelines emphasize NTM-specific treatment in select subjects. Results of this study suggest bronchiectasis patients without NTM have more frequent exacerbations, are diagnosed at an earlier age, more likely to have *Pseudomonas*, underlying asthma and a higher number of hospitalizations than those with NTM. More studies, particularly longitudinal data defining treatment paradigms between groups will better inform our understanding of what may be distinctive bronchiectasis phenotypes.

Dr. Nicole Lapinel



Disclosures:
Dr. Lapinel serves as a consultant and a member of the Advisory Board Panel for Insmid Incorporated

Funding:
The Bronchiectasis and NTM Research Registry is funded by the Richard H. Scarborough Research Fund, the Anna-Maria and Stephen Kellen Foundation, and the Bronchiectasis and NTM Industry Advisory Committee.

Scan this QR code to learn about the Bronchiectasis and NTM Research Registry



** 1. Dr. Nicole Lapinel , LSUHSC Faculty NTM-BE Program

[Respiratory Medicine Case Reports](#)

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Case report

A tale of two images: From mycobacterium avium complex-lung disease (MAC-LD) to mycobacterium avium complex-pleural disease [★](#)

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[Mary Rithu Varkey, Tania M.Kohal, Amit Barua, Nicole C.Lapinel, Juzar Ali
NTM-BE Program Team](#)

Wetmore TB clinic /OPH New Orleans
Baton Rouge TB clinic
Villa Felliaciana TB in pt unit

Consultant staff

TUBERCULOSIS

Watch Time: 13 mins

Juzar Ali, World TB Day 2022: Updates and Advances in Tuberculosis

Published Online: **March 11th 2022**

It was an honor to speak to valued editorial board member **Prof. Juzar Ali** (Louisiana State University Health Sciences Center, New Orleans, LA, USA) around the burden of TB worldwide, what stands in the way of elimination and what to look out for in the future.

<https://www.touchrespiratory.com/tuberculosis/conference-hub/juzar-ali-world-tb-day-2022-updates-and-advances-in-tuberculosis/>



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Recurrent Pulmonary Tuberculosis in Low Prevalence Settings:

Case Report & Review from OPH Louisiana

Amit Barua, Joseph Hubble, Kathryn Yoo, Michael Lacassagne,
John P. Areno, Louis Trachtman and Juzar Ali*

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Control, Louisiana, USA

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