

## Selected Summary

### Bronchiectasis in India: Results from the EMBARC and Respiratory Research Network of India Registry

Dhar R, Singh S, Talwar D, Mohan M, Tripathi SK, Swarnakar R, Trivedi S, Rajagopala S, D'Souza G, Padmanabhan A, Baburao A, Mahesh PA, Ghewade B, Nair G, Jindal A, Jayadevappa GDH, Sawhney H, Sarmah KR, Saha K, Anantharaj S, Khanna A, Gami S, Shah A, Shah A, Dutt N, Garg H, Vyas S, Venugopal K, Prasad R, Aleemuddin NM, Karmakar S, Singh V, Jindal SK, Sharma S, Prajapat D, Chandrashekaria S, McDonnell MJ, Mishra A, Rutherford R, Ramanathan RP, Goeminne PC, Vasudev P, Dimakou K, Crichton ML, Jayaraj BS, Kungwani R, Das A, Sawhney M, Polverino E, Torres A, Gulecha NS, Shteinberg M, De Soyza A, Mangala A, Shah P, Chauhan NK, Jajodia N, Singhal A, Batra S, Hasan A, Limaye S, Salvi S, Aliberti S, Chalmers JD. (Department of Chest and TB, Fortis Hospital, Kolkata, West Bengal; Institute of Respiratory Disease, SMS Medical College, Jaipur, Rajasthan; Department of Respiratory Medicine, Metro Centre for Respiratory Diseases, NOIDA, Uttar Pradesh; Mazumdar Shaw Medical Centre, Narayana Hrudayalaya, Bengaluru, Karnataka; Department of Respiratory Medicine, King George's Medical University, Lucknow, Uttar Pradesh; Department of Respiratory Medicine, Getwell Hospital and Research Centre, Nagpur, Maharashtra; Department of Respiratory Medicine, Jawaharlal Nehru Hospital and Research Centre, Bhilai Nagar, Chhattisgarh; Department of Pulmonology, PSG Institute of Pulmonary Medicine, Coimbatore, Tamil Nadu; Department of Pulmonary Medicine, St John Medical College, Bengaluru, Karnataka; Department of Respiratory Medicine, Kerala Institute of Medical Sciences, Trivandrum, Kerala; Department of Pulmonary Medicine, Kempegowda Institute of Medical Sciences, Bengaluru, Karnataka; Department of Respiratory Medicine, JSS Medical College, Mysuru, Karnataka; Department of Respiratory Medicine, Datta Meghe Institute of Medical Sciences, Wardha, Maharashtra; Department of Pulmonary Medicine, D.Y. Patil School of Medicine, Navi Mumbai, Maharashtra; Jindal Clinics, Chandigarh, Punjab and Haryana; Department of Respiratory Medicine, M.S. Ramaiah Medical College, Bengaluru, Karnataka; Department of Medicine, Government Multispeciality Hospital, Chandigarh, Punjab and Haryana; Department of Pulmonary medicine, Apollo Hospitals, Guwahati, Assam; Chest Medicine Department, Burdwan Medical College, Burdwan, West Bengal; Department of Pulmonary Medicine, Sundaram Medical Foundation, Chennai, Tamil Nadu; Department of General Medicine, SRM Institute of Medical Sciences, Chennai, Tamil Nadu; Department of Internal Medicine, Galaxy Hospital, New Delhi; Department of Internal Medicine, Yashoda Super Speciality Hospital Kaushambi, Ghaziabad, Uttar Pradesh; Department of Pulmonary Medicine and Critical Care, Unique Hospital—Multispeciality and Research Institute, Surat, Gujarat; Department of Respiratory Medicine, Dhiraj Hospital, Sumandeep University, Vadodara,

Gujarat; Department of Respiratory Medicine, Pranayam Lung and Heart Institute and Research Centre, Vadodara, Gujarat; Department of Pulmonary Medicine, All India Institute of Medical Sciences, Jodhpur, Rajasthan; Department of Respiratory and Sleep Medicine, Artemis Hospitals, Gurgaon, New Delhi; Department of Pulmonary Medicine, Dr S.N. Medical College, Jodhpur, Rajasthan; Department of Pulmonary Medicine, Government Medical College, Kottayam, Kerala; Department of Pulmonary Medicine, Era's Lucknow Medical College and Hospital, Lucknow, Uttar Pradesh; Department of Respiratory Medicine, Deccan College of Medical Sciences, Hyderabad, Telangana; Department of Pulmonary Medicine, All India Institute of Medical Sciences, Patna, Bihar; Department of Respiratory Medicine, Asthma Bhawan, Jaipur, Rajasthan—all in India; Department of Respiratory Medicine, Galway University Hospitals, Galway, Ireland; Department of Respiratory Disease, A Z Nikolaas, Sint Niklaas, Belgium; 5th Department of Pulmonary Medicine, Sotiria Chest Diseases Hospital, Athens, Greece; Scottish Centre for Respiratory Research, University of Dundee, Dundee, UK; Pneumology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; Thorax Institute, Institute of Biomedical Research August Pi i Sunyer, University of Barcelona, Barcelona, Spain; Pulmonary Division, Hospital Clinic of Barcelona, Barcelona, Spain; Pulmonary Institute, Carmel Medical Center, Haifa, Israel; Adult Bronchiectasis Service and Sir William Leech Centre for Lung Research, Freeman Hospital, Newcastle upon Tyne, UK; Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; Respiratory Research Network of India, Chest Research Foundation, Pune, Maharashtra, India; Department of Pathophysiology and Transplantation, University of Milan, Milan, Italy; Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy.) Bronchiectasis in India: Results from the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) and Respiratory Research Network of India Registry. *Lancet Global Health* 2019;7:e1269–e1279.

#### SUMMARY

This multicentric, prospective observational study aimed to look at the characteristics, severity of the disease, microbiology and treatment of patients with bronchiectasis in India. A total of 2195 patients with bronchiectasis were recruited across 31 centres in India over a period of 2 years. It included patients aged  $\geq 18$  years with the clinical syndrome of bronchiectasis defined by the constellation of cough, sputum production or recurrent respiratory infections and bronchiectasis confirmed on chest computed tomography. Patients unable to give informed consent and those with bronchiectasis secondary to cystic fibrosis and interstitial lung disorders were excluded from the study. The epidemiological and clinical data were collected using the European Multicenter Bronchiectasis Audit and Research Collaboration (EMBARC) platform. Further, a comparison of the demographic data was made with the established European and American registries. The median age of the patients was 56 years (interquartile range 41–66), and males were more likely to be affected (56.9%). Pulmonary tuberculosis (PTB) remained the most common cause of bronchiectasis compared to the idiopathic variety in the European and American registries. A high prevalence of allergic bronchopulmonary aspergillosis (ABPA) as a

cause was seen in the study population (8.9%). *Pseudomonas aeruginosa* was the most commonly isolated organism in sputum cultures (13.7%). Treatable causes of bronchiectasis were identified in 10.6% of the population. A low adherence to guideline-recommended standardized care was also noted.

#### COMMENT

Bronchiectasis is a chronic, progressive, debilitating, respiratory disease that causes cough with excessive sputum production and frequent chest infections, leading to a poor quality of life (QoL) and high utilization of healthcare resources. The prevalence of bronchiectasis is not accurately known, and data vary considerably throughout the world, with a higher incidence in less-affluent communities. However, no data exist to define the burden of bronchiectasis in India. This multicentric study is the first attempt to establish an Indian bronchiectasis registry collecting clinico-epidemiological data on the burden of bronchiectasis across different parts of India.

Among the several unique features, significant demographic differences were noted between Indian and European patients. Indian patients were younger (56 v. 67 years;  $p < 0.05$ ) and had a male preponderance (males 56.9% v. 38.9%;  $p < 0.05$ ) and lower body mass index (21.5 v. 24.8;  $p < 0.05$ ). Owing to the younger age of the population, there were fewer comorbid conditions in the Indian patients compared to their European counterparts, except for diabetes mellitus which is more common in India.

The aetiological data also followed a different pattern. Most cases of bronchiectasis worldwide are reported to be idiopathic, but post-infectious aetiologies dominate across Asia, especially post-tuberculous bronchiectasis.<sup>1</sup> This study reinforces this pattern, with the most frequent cause being TB (780 [35.5%] of 2195 patients), followed by post-infectious (491 [22.4%]) and idiopathic (470 [21.4%]). Overall, 41.7% of the study population had a history of PTB and 34 (3.7%) patients were still receiving treatment for active PTB at the time of enrolment. Post-infectious causes other than PTB were largely due to pneumonia (351 [71.5%]) and other childhood respiratory infections (143 [29.1%]), including pertussis in 9 (1.8%) patients. Besides the aetiological phenotypes, a distinct 'frequent exacerbator' and '*Pseudomonas aeruginosa*' phenotype was seen in the study.

ABPA, a pulmonary disorder caused by hypersensitivity to *Aspergillus fumigatus*, is a well-described cause of bronchiectasis.<sup>2</sup> Usually seen in poorly controlled asthmatics, cystic fibrosis and those with pre-existing cavities, prevalence rates described from India are 5.9%–20.5%.<sup>3,4</sup> The EMBARC study found ABPA as a cause of bronchiectasis in 8.9% (196 of 2195) of patients. Nearly 50% of patients tested for ABPA had the disease, suggesting either a high prevalence, or that testing was restricted only to those individuals with a strong clinical suspicion of ABPA. However, only 30.6% of these patients were on treatment for ABPA (21.4% with oral corticosteroids and 9.2% with antifungal medications).

In the study, the extent, site, type and lobar distribution of bronchiectasis were dependent on the underlying aetiology. Bronchiectasis had a predominant lower lobe involvement in patients with syndromes of impaired mucociliary clearance and upper lobe involvement of TB, radiation fibrosis, sarcoidosis and pneumoconiosis.<sup>5</sup> Radiologically, there was an equal lobar distribution of bronchiectasis between the upper, middle and lower lobes. Cystic dilatation was the predominant radiological pattern.

The microbiological profile of sputum culture from Indian

patients differed significantly from that of the western population. There was relatively infrequent sputum sampling obtained in routine practice in India. *P. aeruginosa* and *Enterobacteriaceae* spp. constituted the major pathogens, in contrast to *Haemophilus influenzae*, *Moraxella catarrhalis* and *Streptococcus pneumoniae* commonly reported from western cohorts.<sup>6</sup> *P. aeruginosa* was the most commonly isolated organism in sputum culture (13.7%). This study showed a low level of adherence to guideline-recommended care in India, which underscores the need for culture-guided treatment of bronchiectasis.<sup>7</sup>

The severity of bronchiectasis also differed in the Indian population. Indian patients were more likely to be classified as severe and have lower predicted forced expiratory volume in 1 second compared to European patients. The Bronchiectasis Severity Index score used to grade the severity of bronchiectasis found an equal distribution of mild, moderate and severe bronchiectasis (728 [33.2%] of 2195 with mild, 674 [30.7%] with moderate and 793 [36.1%] with severe bronchiectasis). Breathlessness, daily sputum production, exacerbations and chronic airway infection were independently associated with worse QoL scores in linear regression models and contribute to poor QoL in these patients.

The 'frequent exacerbator' phenotype ( $\geq 3$ /year) was seen in 529 (24.1%) of 2195 patients. A history of PTB was associated with more frequent exacerbations and suggested that PTB might be an important contributor to the severity of disease observed in our population.<sup>8</sup>

Treatment of bronchiectasis varied across India but included a highly frequent use of inhaled corticosteroids and long-acting  $\beta$  agonists. The European Respiratory Society (ERS) guidelines recommend adherence to selected quality standards in the management of bronchiectasis, as follows:

- Ascertaining an aetiological diagnosis (testing for ABPA and immunoglobulin levels)
- Eradication therapy in patients with new *P. aeruginosa* infection
- Long-term antibiotics (in patients with  $\geq 3$  exacerbations/year)
- Bronchodilators (patients with significant breathlessness should be prescribed long-acting bronchodilators)
- Respiratory physiotherapy
- Pulmonary rehabilitation in patients with significant breathlessness
- Sputum for bacterial culture at least once a year.

Using a threshold of 80% to indicate good compliance with guideline-based care, the EMBARC study found a low adherence to guideline-recommended care in India.

The EMBARC study noted that almost 63.2% (1387 of 2195) of bronchiectasis patients were on inhaled corticosteroids. This is contrary to the current treatment standards for bronchiectasis, likely related to the easy availability and low cost of these combination inhalers in India. This is in contrast to the scant use of other recommended modalities in bronchiectasis, with low use of oral and inhaled prophylactic antibiotics (odds ratio 0.58, 95% CI 0.44–0.68;  $p < 0.0001$ ).<sup>9</sup> Both long-term oral and inhaled antibiotic treatments were more commonly used in Europe than in India.

The number of exacerbations treated with oral antibiotics was relatively low in India, whereas hospital admission due to exacerbations was more common. This finding may reflect a healthcare system more dependent on hospital-based care in

India but can also suggest differences in the severity of disease and therefore risk of more severe exacerbations. Overall, the treatable causes of bronchiectasis as defined by the ERS were identified in 232 (10.6%) of 2195 patients, and this number increased to 571 (26%) in centres where specific IgE to *Aspergillus fumigatus* and immunoglobulins were tested routinely.

Although the ERS guidelines strongly recommend participation in a pulmonary rehabilitation programme, only a fraction of the eligible patients (Modified Medical Research Council Dyspnoea score  $\geq 2$ ) were referred to such a programme (355 [38.1%] of 932 patients).<sup>10</sup>

This study confirms again that bronchiectasis in Asian patients frequently follows an aggressive course, with earlier onset, more extensive lung damage and severe symptoms compared with populations in Europe and the USA.

Any registry of this kind is not without limitations. Although this was a multicentric study across different geographical regions of India, it is limited by the cross-sectional nature of the data collection and lack of long-term follow-up. Ongoing data collection should address these shortcomings. The study also has limited aetiological work-up of bronchiectasis, which is often a practical issue related to financial constraints in the Indian setting. Another criticism of the study is related to the lack of stringent criteria for the diagnosis of post-TB bronchiectasis, with microbiological verification of TB not mentioned, and diagnosis based on largely a prior clinical history of TB. A similar issue exists with the diagnosis of ABPA. A detailed workup for ABPA was done only in a limited subgroup, and patients with ABPA can be confused with TB in India if a detailed workup is not done. These aspects can alter the incidence of these major conditions, as reported in the registry.

To conclude, this report is the first multicentric effort and a wake-up call to comprehensively diagnose, treat and improve the quality of care for patients with bronchiectasis in India. This highlights the need for further studies into this common,

complex and debilitating disease affecting a relatively younger population.

*Conflicts of interest.* Nil

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KALPAKAM HARIPRASAD

SHYAM KRISHNAN

RAVINDRA M. MEHTA

*Department of Pulmonary,  
Critical Care and Sleep Medicine  
Apollo Hospitals  
Bengaluru  
Karnataka  
India  
hariprasadkalkpakam@yahoo.com*