

Non-cystic fibrosis bronchiectasis: A single-centre retrospective study in Johannesburg, South Africa

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Background. Bronchiectasis, once rarely encountered, appears to be increasing in prevalence in South Africa (SA) and globally. There is a lack of published data on non-cystic fibrosis (CF) bronchiectasis, specifically in low- to middle-income countries, despite the high rates of risk factors such as HIV, pulmonary tuberculosis, and other infections.

Objectives. Given this lack of data, to review the characteristics of adult patients with non-CF bronchiectasis at a tertiary academic hospital in Johannesburg, SA.

Methods. This was a single-centre, retrospective record review, including all cases of non-CF bronchiectasis that were in the records of the adult pulmonology clinic at Charlotte Maxeke Johannesburg Academic Hospital as of April 2017.

Results. There were 197 patients, with a slight predominance of males, and the patients were generally young. The HIV rate was higher than the national average (34.8% v. 13.7%), and the HIV-positive patients had a high TB prevalence (86.9%). *Pseudomonas* spp. were cultured from sputum in 15.3% of cases. Fewer than half of the cohort had the diagnosis of bronchiectasis confirmed by high-resolution chest tomography. Airway obstruction (forced expiratory volume in 1 second/forced vital capacity ratio <70%) was observed in 47.0% of patients. Treatment with a short-acting beta-2-agonist was prescribed in 62.9%, a long-acting beta-2-agonist in 43.6% and inhaled corticosteroids in 51.3%. Antibiotic therapy during exacerbations was used in 44.2%, mainly amoxycillin-clavulanate (66.7%).

Conclusion. While single centre and retrospective, this study adds to the data on non-CF bronchiectasis in sub-Saharan Africa and should encourage further research to increase our understanding of adult non-CF bronchiectasis in SA.

Keywords. Adult, non-cystic fibrosis bronchiectasis, sub-Saharan Africa.

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Study synopsis

What the study adds. This study adds to published data detailing the clinical characteristics of adult non-cystic fibrosis (CF) bronchiectasis in low- and middle-income countries (LMICs).

Implications of the findings. As a retrospective descriptive study, the findings summarise the characteristics of adults with non-CF bronchiectasis in a cohort from Johannesburg, South Africa. The findings suggest that the characteristics of bronchiectasis in this region appear to be similar in several ways to those in other LMICs, but quite different from those in the developed world.

Bronchiectasis, first reported in 1819 and once known as an orphan disease, is becoming increasingly prevalent globally.^[1-3] It is a clinical syndrome characterised by both cough and sputum production along with abnormal thickening and dilation of the bronchial wall visible on lung imaging. The pathophysiology has been described by Cole's 'vicious cycle' hypothesis, where chronic neutrophil inflammation promotes damage to the mucosa, submucosa and muscular components of the bronchial wall, eventually leading to airway dilation.^[4] This chronic inflammation, associated with hypersecretion of mucus, impairment of mucociliary clearance mechanisms and subsequent bacterial colonisation, continually perpetuates the cycle of airway damage.^[3,5] High-resolution chest tomography (HRCT) is considered the gold standard for imaging

diagnosis of bronchiectasis.^[6] While it is possible to diagnose bronchiectasis using a chest radiograph (CXR) alone, it is estimated that ~10% of cases will be missed.^[7]

Most published data on bronchiectasis come from high-income countries, where patient demographics show that mainly older females are affected, with ~40% having idiopathic disease. Other documented causes include infection, immunodeficiency, ciliary abnormalities and allergic bronchopulmonary aspergillosis (ABPA).^[3,8] The global burden of bronchiectasis has been documented to be increasing, particularly in the past two decades, as indicated in publications from Asia (China, Singapore, Korea, India), Europe (UK, Spain, Germany, Israel) and the USA.^[2,3,9-11] Of all countries with published large-scale studies, only India can be classed as a low- to middle-income country (LMIC).

There is therefore a paucity of adult data in LMICs, despite a high prevalence of risk factors for bronchiectasis, including frequent early childhood infections and high rates of pulmonary tuberculosis (TB) and HIV. A systematic review by Gao *et al.*,^[9] which investigated the aetiology of bronchiectasis in adults worldwide, identified a single study from Africa, and the majority of cases in this African cohort were either post-infective, most commonly TB, or idiopathic. In 2014, a branch of the European Respiratory Society partnered with the Respiratory Research Network of India in order to establish a bronchiectasis registry in India. This collaboration established what is to our knowledge the first adult bronchiectasis registry in any LMIC. The Indian findings were described and compared with data from a substudy of the European registry (the European Multicentre Bronchiectasis Audit and Research Collaboration (EMBARC) database), which included data from Europe and Israel.^[3,11] The data from India suggest a very different disease profile from that seen in high-income countries. In particular, the Indian study identified a high proportion of young male patients with bronchiectasis, often caused by previous TB.^[3] A subsequent study of patients with post-TB lung disease in Malawi showed that 44% of the patients had bronchiectasis in one or more lobes, and 9.4% had one or more destroyed lobes confirmed on HRCT imaging.^[12] Currently, there appears to be a single bronchiectasis registry in South Africa (SA) in paediatrics, and there have apparently been no such initiatives in adults.^[13]

Based on the above data, we wished to review the characteristics of adult patients with non-cystic fibrosis (CF) bronchiectasis seen at a tertiary academic hospital in Johannesburg, SA.

Methods

This was a single-centre, retrospective record review, including all cases of non-CF bronchiectasis that were in the records of the adult pulmonology clinic at Charlotte Maxeke Johannesburg Academic Hospital as of April 2017. Inclusion criteria were adult patients ³18 years of age, with a diagnosis of non-CF-related bronchiectasis made at the discretion of the treating physician. The study was approved by the Human Research Ethics Committee (Medical) of the University of the Witwatersrand (ref. no. M220771). A waiver of consent was approved because the study was retrospective in nature with no direct patient contact.

Patient records in the pulmonology clinic are duplicated, with one file held in the patient record system at the hospital and a separate copy of the file being held securely in the pulmonology department. The latter files were retrieved, and various patient details were entered into an electronic database, including demographic data, history of smoking, occupation, possible risk factor exposure, exposure to or previous diagnosis of TB, HIV status, putative cause according to the treating physician, clinical presentation, investigations performed for diagnostic purposes, radiographic features, results of lung function testing, microbiology and treatment. The database was deidentified and was handled only by the research team.

Lung function was assessed according to the European Community of Coal and Steel reference equations. Categorical variables were represented as frequencies and percentages. Continuous variables were represented as means and standard deviations (SDs) when normally distributed, or as medians and interquartile ranges (IQRs) when not normally distributed. Statistical analysis consisted of summary and

descriptive statistics, as well as comparative analysis of categorical data using the χ^2 test, and was performed using Python 3.10 (Python Software Foundation, USA).

Results

Overall, 197 patients ($n=101$ (51.2%) male) were enrolled in the study, with a median (IQR) age of 49 (38 - 60) years. Fifty-two patients (26.4%) reported that they were either current ($n=12$; 6.1%) or ex-smokers ($n=37$; 18.8%); 3 were identified as smokers, but it was not specified in the file whether they were current or ex-smokers. The remaining 145 patients either reported never smoking or had no recorded smoking status. The date of first bronchiectasis diagnosis was recorded in 196 patients. At the time the study ended, April 2017, the median duration of bronchiectasis among the patients was 48.0 (26.9 - 88.5) months. Body mass index (BMI) was recorded in 167 patients, with a median value of 20.9 (18.5 - 24.8).

Reported occupations among the cohort ($n=61$) were diverse, ranging from unemployment to managerial, and from office work to mining and pharmaceutical drug manufacturing, totalling 35 different occupations. In the total cohort, there were 9 patients (4.6%) who reported occupational exposure as a cause of their bronchiectasis. The occupations considered by the patients to be associated with that exposure were mining ($n=2$ patients), plumbing ($n=2$), cement work, pharmaceutical drug manufacturing, chemical manufacturing, spray painting and mechanic ($n=1$ each).

Table 1 shows the frequency of the various radiological methods used for confirmation of the diagnosis of bronchiectasis. While HRCT and a CXR are well-known methods for diagnosing bronchiectasis, bronchography is an older modality, not currently used, performed by instilling contrast material via a bronchoscope.^[14] Of note, only 86 patients (43.7%) had HRCT imaging done to confirm the diagnosis. Overall, 164 patients (83.2%) had a CXR; of these, 88 (44.6%) had only a CXR, 1 (0.5%) had a CXR and a bronchogram, and the remaining 75 (38.1%) had both a CXR and HRCT. Eleven patients (5.6%) had HRCT alone, and in 22 cases (11.1%) there was no record of what imaging was done.

In the 86 HRCT records, the main distribution of disease was recorded for 49 patients (57.0%). Twenty patients (40.8%) had upper-lobe involvement, 9 (18.4%) had lower-lobe involvement, and 20 (40.8%) had both upper- and lower-lobe involvement. Specifically for the study population that had a previous diagnosis of TB, 30 records existed. Twelve patients (40.0%) had upper-lobe involvement, 5 (16.7%) had lower-lobe involvement, and the remaining 13 (43.3%) had both.

Table 2 shows the frequency of reported aetiologies, based on reporting in the file by the attending physicians. Thirty-eight patients did not have a documented aetiology, while others had multiple potential aetiologies listed. There was a total of 187 reported aetiologies for the 159 patients. The most frequent aetiology documented was TB ($n=144$; 77.0%), followed by various other causes ($n=21$; 11.2%) and then recurrent infection ($n=10$; 5.3%).

The 21 aetiologies that fell under 'other causes' included asthma, second-hand smoke exposure, aspiration, cancer, epilepsy, essential thrombocythosis, human papillomavirus infection, gastro-oesophageal reflux, splenomegaly, kyphosis, porphyria, post-renal transplant, mycetoma and sarcoidosis. Some of these reported aetiologies may represent associated comorbid conditions rather than actual causes of the bronchiectasis.

Of the total cohort, 144 patients (73.1%) had a previous diagnosis of TB. There was no consistent record in the patient files as to how the diagnosis of TB had been made. For more than half of these patients ($n=81$; 56.3%), the file indicated that they had had only one episode of TB. However, recurrent episodes of TB were reported for some patients: two episodes for 28 patients (19.4%), three for 4 (2.8%), four for 4 (2.8%), and seven for 1 (0.7%). Twenty-six patients did not have a record of the number of their TB episodes.

HIV status was documented for 175 patients, with 61 (34.9%) being HIV positive. Of the HIV-positive patients, 53 (86.9%) had TB documented as the aetiology of bronchiectasis. Conversely, these 53 patients accounted for only 36.8% of the total TB cohort.

For the total cohort, a breakdown of patients into specific classifications based on lung function results is shown in Fig. 1.

Of the 144 patients with a previous diagnosis of TB, it was possible to categorise the findings on lung function studies for only 127 (88.1%), as some values were unrecorded. Of these 127 patients, 44 (34.6%) were categorised as having a possible restrictive defect, 40 (31.5%) as having obstruction with a low forced vital capacity (FVC), 20 (15.7%) as having obstruction alone, and 23 (18.1%) as having normal lung function.^[15] The mean (SD) reversibility of the lung function (% change in forced expiratory volume in 1 second (FEV_1)) for the total cohort was 7.84% (7.26%).

We also assessed clinical findings. The presence or absence of crackles in the chest was documented in the records of 172 patients, in 101 (58.7%) of whom crackles were noted and in 71 (41.3%) of whom they were not. The presence or absence of clubbing was documented in the

records of 157 patients, with clubbing present in 79 patients (50.3%) and absent in 78 (49.7%). In the TB cohort, crackles were present in 71 patients (49.3%) and clubbing was present in 66 (45.8%). Patients with a previous diagnosis of TB therefore accounted for 70.3% of the documented crackles and 83.5% of the documented clubbing found in the whole cohort.

Of the total cohort, 98 patients had at least one sputum microbiology sample recorded in their files, taken during a period of exacerbation. Of these 98 patients, 54 (55.1%) had no organism cultured. The micro-organism cultured most often was *Pseudomonas aeruginosa* ($n=15$ patients; 15.3%), followed by mixed flora ($n=11$; 11.2%). Other organisms cultured were *Mycobacterium tuberculosis* ($n=4$; 4.1%), *Haemophilus influenzae* ($n=3$; 3.3%), *Staphylococcus aureus* ($n=3$; 3.3%), *Escherichia coli* ($n=2$; 2.0%), *Mycobacterium avium-intracellulare* ($n=2$; 2.0%), fungi ($n=2$; 2.0%), *Moraxella catarrhalis* ($n=1$; 1.0%), *Klebsiella pneumoniae* ($n=1$; 1.0%) and human parainfluenza virus ($n=1$; 1.0%).

Exacerbations were recorded in 128 patients (64.9%), 26 (13.2%) did not experience exacerbations, and the remaining 43 had no record of presence or absence of exacerbations.

Of the total cohort, 124 patients (62.9%) were treated with a short-acting beta-2-agonist and 86 (43.6%) with a long-acting beta-2-agonist. Inhaled corticosteroid therapy was used in 101 patients (51.3%). These numbers add up to more than 197, as many patients were on multiple forms of treatment.

Eighty-seven patients (44.2%) received antibiotic therapy during exacerbations, mainly amoxycillin-clavulanate ($n=58/87$; 66.7%).

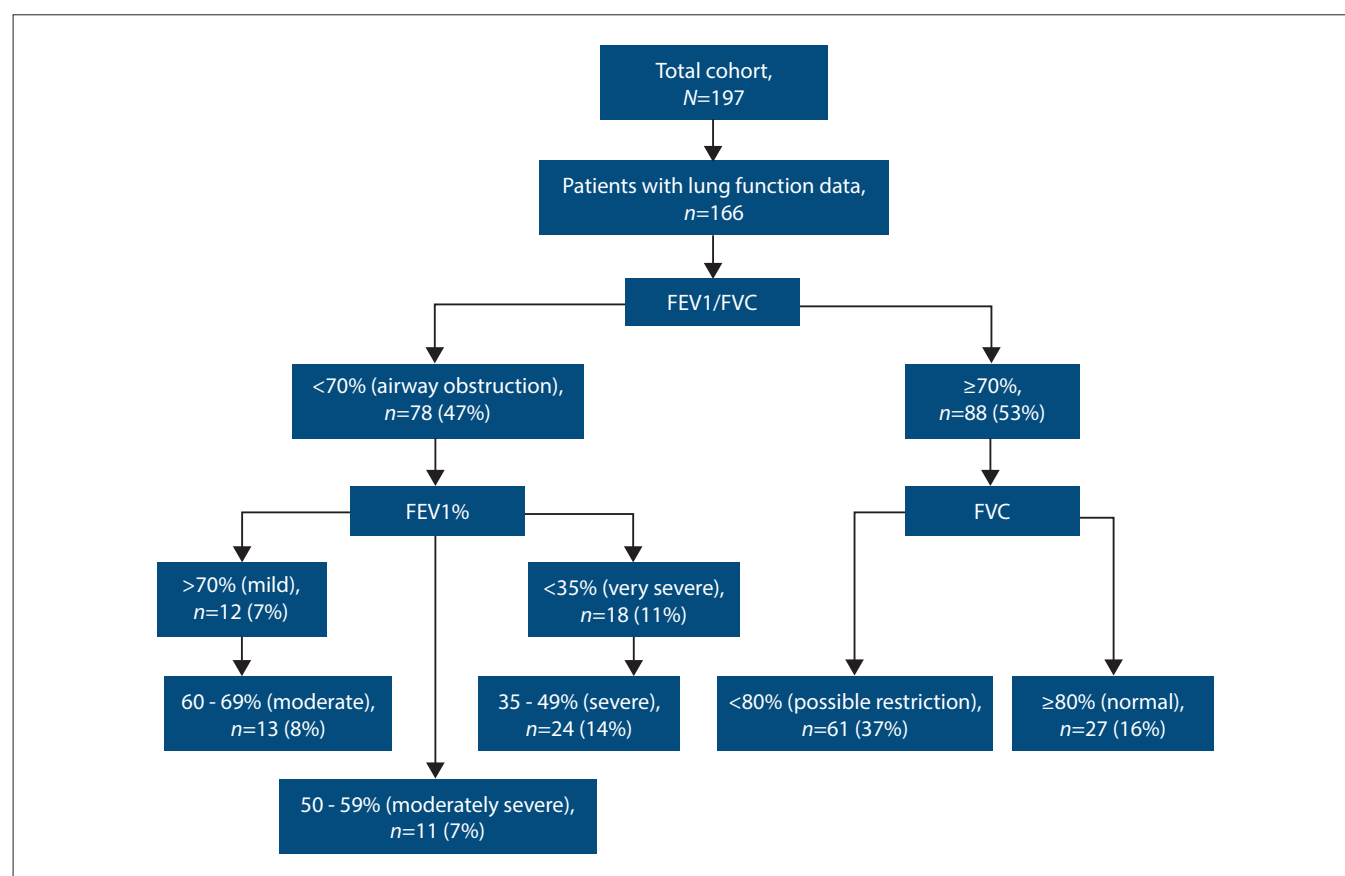


Fig. 1. Lung function results and classification. (FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; $FEV_1\%$ = % change in FEV_1 .)

Use of amoxicillin-clavulanate and macrolide therapy during exacerbations was recorded in 19 patients (9.6%). Use or non-use of a cephalosporin along with a macrolide during exacerbations was recorded in 36 of the total cohort, of whom 32 (88.9%) were noted to have received such therapy. Prophylactic macrolide therapy was recorded to have been used in 21 patients (10.7% of the total). No information on macrolide use was recorded in 161 patient files.

Long-term oxygen therapy was used for 19 patients (9.6%), and 12 (6.1%) underwent surgery. Of these surgical procedures, 7 were pneumonectomies, while in the remaining 5 the type of surgery was not specified.

Use or non-use of postural drainage was recorded in 170 patients, of whom 162 (95.3%) were noted to perform postural drainage.

Discussion

The major findings in this study of 197 patients diagnosed with and being followed up for bronchiectasis at a tertiary academic hospital in Johannesburg were that there was a slight predominance of males, the patients were generally young, the HIV rate was higher than the national population average, and by far the most common reported cause was TB. Additionally, fewer than half of the patients had HRCT imaging, which is considered the gold standard for diagnosis of bronchiectasis.

The slight predominance of males in the present study is similar to that in the cohort from India, but markedly different from the European study (Table 3) and from an additional EMBARC study from Europe, in which most patients were female.^[3,11]

In terms of age, the present cohort was somewhat younger than the cohort from India, and much younger than the European cohort. However, the IQRs were very similar between the present cohort and the Indian cohort, which suggests the two cohorts were generally in a similar range, while the IQR in the European study was higher (57 - 74), clearly suggesting a significantly higher age group for patients in the European study.^[3,11] The reason for the differences in age is uncertain, but may well relate to differences in the aetiology of the bronchiectasis in the different regions.

The BMI was recorded in 167 patients in the present study, with a median value of 20.9. This figure was very similar to that of the Indian cohort and lower than the European cohort.^[3,11] While bronchiectasis itself may be associated with a low BMI, which acts as a prognostic factor,^[1] the lower BMIs in the SA and Indian cohorts compared with the European cohort may also be associated with the fact that TB is the most common cause of bronchiectasis in the former regions.

The rates of smokers and ex-smokers in the present cohort and the cohort from India were similar, while both were significantly lower than the reported rate of smokers in the European cohort.^[3,11]

It should be noted that there is not yet clinical evidence of a direct causal link between occupational exposure and bronchiectasis, rather just associations. An advanced PubMed literature search for articles linking or evaluating bronchiectasis and occupation returned only two articles, one of which was a case study.^[16,17] Bronchiectasis therefore does not currently appear to be recognised as a work-related disease.

A major finding in the present study was that fewer than half of the patient cohort ($n=86$; 43.7%) appear to have had HRCT imaging done to confirm the diagnosis of bronchiectasis. This is probably because of resource constraints, which are also documented in other countries. HRCT is considered expensive in Nigeria, largely owing to poverty and lack of health insurance.^[18] Additionally, relatively few medical centres in SA are equipped with computed tomography scanners. It therefore appears likely that there may be financial reasons for the low rate of HRCT imaging. One patient had had a bronchogram as part of their imaging work-up, but this modality of imaging has long been discontinued worldwide.

The literature supports the finding of predominantly upper-lung involvement in post-TB bronchiectasis,^[19,20] and although there was significant upper-lobe involvement in our cohort, there were also a fair number of patients with lower-lobe and also mixed-lobe involvement.

Post-TB was the most commonly reported cause of bronchiectasis in both the SA and Indian cohorts (71.1% and 35.5%, respectively), and while aetiology was not reported at all in the European cohort (Table 3), TB was much less common in other European studies (4.9%).^(3,11) The high rate of post-TB aetiology documented in the SA cohort is not surprising given the prevalence of TB in our setting. Post-TB bronchiectasis has been documented as a distinct entity with higher rates of haemoptysis and non-tuberculous microbacteria isolation, more frequent exacerbations, and higher disease severity scores.^[10] Post-infective aetiology, but not TB-related, was reported more frequently in the Indian cohort and in other European studies (21.2%) compared with the lower rate in the SA cohort.^[3,11] ABPA was similarly reported at a higher rate in the Indian cohort (2.8% in European studies).^[3,11] Idiopathic disease was also reported at a higher rate in the Indian cohort and in European studies (38.1%) than in SA.^[3,11] Other diverse causes were reported more frequently in SA than in India or Europe (1.9%).^[3,11] Chronic obstructive pulmonary disease was reported in the Indian cohort and in European studies (8.1%), but not at all in the SA cohort.^[3,11] Conversely, autoimmune disease and immunodeficiency were reported in the SA and European studies (2.5% and 4.1%, respectively), but not at all in

Table 1. Radiological methods used to document bronchiectasis (N=197)

	<i>n</i> (%)
HRCT	86 (43.7)
CXR only	88 (44.6)
CXR + bronchogram	1 (0.5)
Not recorded	22 (11.1)

HRCT = high-resolution computed tomography; CXR = chest radiograph.

Table 2. Reported causes of non-cystic fibrosis bronchiectasis* (N=159)

	<i>n</i> (%)
Tuberculosis	144 (77.0)
Other causes	21 (11.2)
Recurrent infection	10 (5.3)
Allergic bronchopulmonary aspergillosis	6 (3.2)
Rheumatoid arthritis	3 (1.6)
Hypogammaglobulinaemia	3 (1.6)

*Sometimes multiple.

Table 3. Summary of comparative cohorts*

	South African study (the present study)	Indian study	European study [†]
Demographics			
Age (years), median (IQR)	49 (38 - 60)	56 (41 - 66)	67 (57 - 74)
Male, %	51.2	56.9	38.9
BMI, median (IQR)	20.9 (18.5 - 24.8)	21.5 (18.5 - 24.5)	24.8 (21.8 - 28.1)
Current/ex-smokers, %	26.4	28.2	38.1
Functional status			
FEV ₁ (% predicted) median (IQR)	52.0 (42.0 - 71.5)	61.4 (41.9 - 80.5)	73.8 (54.0 - 92.1)
Spirometry pattern, %			
Obstruction	47.6	34.8	-
Low FVC	36.3	26.7	-
Normal	16.1	38.5	-
Microbiology, %			
<i>Pseudomonas aeruginosa</i>	15.3	13.7	15.0
<i>Haemophilus influenzae</i>	3.3%	0.5	21.9
<i>Staphylococcus aureus</i>	3.3	2.3	6.0
<i>Moraxella catarrhalis</i>	1.0	1.0	5.9
<i>Enterobacteriaceae</i>	-	9.8	6.1
Treatment, %			
Long-term macrolide	10.6	6.2	NR
Aetiology, %			
Post-TB	71.1	35.5	NR
Idiopathic	0.5	21.4	NR
Post-infective (non-TB)	6.6	22.4	NR
ABPA	2.0	8.9	NR
COPD	-	5.3	NR
Asthma	3.0	2.5	NR
Other	7.0	4.1	NR
Autoimmune	1.5	-	NR
Immunodeficiency	1.0	-	NR

IQR = interquartile range; BMI = body mass index; FEV₁ = forced expiratory volume in 1 second; FVC = forced vital capacity; TB = tuberculosis; ABPA = allergic bronchopulmonary aspergillosis; COPD = chronic obstructive pulmonary disease; NR = not reported in the above European cohort – the data reported for aetiology of bronchiectasis in Europe, in the discussion section, are from the European Bronchiectasis Registry (EMBARC study).^[11]

*This table (Table 2 in Dhar *et al.*[3]) is reproduced with permission from *Lancet Global Health*, under a Creative Commons License Deed (Attribution-NonCommercial-NoDerivatives 4.0 international (CC BY-NC-ND 4.0)) (available from <https://creativecommons.org/licenses/by-nc-nd/4.0/legalcode>). The table has been modified to include some further data from the Indian cohort, and data from the present South African study have been added for comparison.

[†]Including cases from Israel.

the Indian cohort.^[3,11] Asthma as a cause was reported in the SA and Indian cohorts at similar levels, but was reported to occur more frequently in Europe (6.9%).^[3,11]

With reference to the post-TB aetiology detailed above, it is interesting to note the context of TB nationally in both SA and India. The latest World Health Organization country data (for 2021) documented an estimated TB prevalence in SA of 513 (95% confidence interval (CI) 348 - 709) patients per 100 000 population. For India, the prevalence was 210 (95% CI 178 - 244) per 100 000 population.^[21] This ratio of 513 to 210 for national TB prevalences (2.4:1) is very similar to the ratio of post-TB aetiology in the two cohorts (2.0:1).

FEV₁ % predicted values were different among the three cohorts. The SA cohort had the lowest FEV₁ % predicted (52.0) compared with the cohorts from India (61.4) and Europe (73.8). When comparing IQRs, it should be noted that the IQR for India completely encompasses the IQR for the SA cohort.^[3,11]

The HIV rate in the present cohort (34.8%) was higher than the national population average (13.7%).^[22] Additionally, the HIV cohort had a high prevalence of documented TB (86.9%). Further statistical analysis evaluating HIV status and TB aetiology indicated that they were linked rather than independent variables (χ^2 statistic = 8.01; two-sided *p*-value = 0.009).

Microbiological data were available for all three cohorts (Table 3). The prevalence of *P. aeruginosa* was relatively similar between the cohorts. The prevalence of *M. catarrhalis* was also similar in the SA and Indian cohorts, but slightly higher in the European cohort. However, the other organisms cultured differed among the cohorts. The SA population had a higher prevalence of *H. influenzae* than the Indian cohort, while the highest prevalence was in the European cohort. Conversely, the SA population had no reported cases of *Enterobacteriaceae*, whereas the Indian and European cohorts had similar prevalences.^[3,11]

The spirometry pattern in the SA cohort differed from the Indian cohort, with a higher percentage of obstructive findings with low FVC

and a much lower percentage of spirometry classified as normal.^[3,11]

The SA population had a higher prevalence of long-term macrolide use for exacerbations than the Indian cohort.^[3,11] The most common antibiotic used for exacerbations in the SA setting was amoxycillin-clavulanate. Others were amoxycillin-clavulanate plus a macrolide and a cephalosporin plus a macrolide.

Table 3 presents a summary of the above findings in the present cohort compared with those from India and Europe/Israel.

The present study does have some potential limitations. One major limitation is that some patients appear to have been diagnosed as having bronchiectasis without all the currently recommended investigations being done. In this respect, some clinicians appear to have made the diagnosis based on a CXR alone, without the use of HRCT. While HRCT is currently the gold standard for the diagnosis of bronchiectasis worldwide, it is often possible to diagnose bronchiectasis on CXR, although ~10% of cases will be missed without HRCT.^[7] It is known that most LMICs experience resource limitations, so there is a financial barrier to extensive investigations.^[16,18] A second limitation is that this was a single-centre study, so not all the findings can be extrapolated to other institutions and/or regions in SA. Thirdly, this was a retrospective record review, and details for some of the information were missing in the patient files. For example, there were no records in the database indicating how the previous diagnoses of TB, or some of the other diagnoses, had been made. Nevertheless, the strength of this study is that it is the first investigation of this sort of bronchiectasis in adults in SA, and would be useful as a base on which to plan future prospective studies in this region, and for improving the overall management of bronchiectasis.

Conclusion

While we acknowledge that this was a retrospective single-centre study, it is the first of its kind on bronchiectasis in adults in SA. The findings suggest that the characteristics of bronchiectasis in this region appear to be similar in several ways to those in other LMICs, but are quite different from those in the developed world. The study could function as a template for planning a future prospective study in this region, with the goal of improving the overall management of bronchiectasis.

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