



**A retrospective review of lung disease in adolescent patients living with Human
Immunodeficiency virus**

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Declaration

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Format and contributions.

This manuscript is in a publication ready format. JN designed the study, collected data and performed data analysis. RP supervised JN in the study design and data analysis. RvZS recruited the GSH Respiratory Adolescent clinic patients and supervised the study design, data collection and data analysis.

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Acronyms and Abbreviations

ART	Antiretroviral therapy
SA	South Africa
HIV	Human immunodeficiency virus
CLD	Chronic lung diseases
ALHIV	Adolescents living with HIV
TB	Tuberculosis
CR	Chest radiograph
FVC	Forced vital capacity
LIP	Lymphocytic interstitial pneumonitis.
FEV1	Forced expiratory volume in one second
LRTI	Lower respiratory infections
MRSA	<i>Methicillin-resistant staphylococcus aureus</i>
IQR	Interquartile range
BMI	Body mass index
FEV1%	FEV1 as a percentage of predicted
BDR	Bronchodilator response
DLCO	Diffusing capacity of the lungs for carbon monoxide.
IeDEA	International Epidemiology Databases to Evaluate AIDS
ICS	Inhaled corticosteroids
PI	Protease inhibitors

Publication ready manuscript

A retrospective review of lung disease in adolescent patients living with Human Immunodeficiency Virus

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Abstract

Background

Chronic lung disease (CLD) is common in adolescents living with Human Immunodeficiency Virus (ALHIV), many of whom have survived early childhood respiratory infections and immune dysregulation. Little is known about the characteristics of ALHIV with significant CLD requiring

referral to a tertiary center. Understanding the characteristics of this population is key to guiding service design, informing preventative strategies, and identifying tailored therapeutic interventions for preserving lung function and optimizing respiratory health.

Methods

We retrospectively reviewed the clinical records of a historical cohort of adolescents aged 12 years to 20 years, diagnosed with vertically transmitted HIV and presenting with chronic lung disease to the Adolescent Respiratory Clinic of Groote Schuur Hospital between 1 January 2015, and 1 January 2023. Demographic data, details on HIV diagnosis, treatment history, lung function data, radiological data, clinical history and examination data, and microbiological data were analysed.

Results

Seventeen patient records were reviewed. The median age at first visit was 16.9 years (interquartile range (IQR) 15.2 to 18.7), and 58.9% (10/17) were female. The median age at HIV diagnosis was 1.1 years (IQR 1- 2), with a median duration of ART treatment of 13.2 years (IQR, 8.6- 15.6), reflecting early HIV diagnosis and treatment initiation. The median CD4 nadir was 243 cells/mm³ (IQR 140- 516) and 16/17 patients had more than two prior episodes of pulmonary tuberculosis (PTB). Growth stunting was a common feature with a median BMI 17.7 kg/m² (IQR 16.4- 19.8) and 16 /17 participants plotting below the 50th population centile of height-for-age. Radiological evidence of bilateral lung disease with bronchiectasis and cavitation was ubiquitous. Haemophilus influenzae was isolated in 12/17 (70.6%) patients and Methicillin-resistant staphylococcus aureus (MRSA) in 2/17 (11.7%) patients). The median FVC as a percentage of predicted values was 51.7% (IQR, 41.1- 60.8), and the median pre-bronchodilator FEV₁/FVC ratio was 65%, (IQR of 57.8 to 74.3). indicating mixed spirometric defects. There was no significant bronchodilator response in any of the participants.

Conclusion

Among ALHIV with CLD, there was a high prevalence of both airway and parenchymal lung disease, as well as severe growth impairment. Prior PTB was a common respiratory insult, and

participants did not have early access to ART as the median age of HIV diagnosis was 1 year. More needs to be done to prevent PTB, reduce the burden of recurrent respiratory infections, and to preserve long-term respiratory health in this vulnerable population. Additionally, perinatal HIV testing of infants born to HIV positive mothers and perinatal ART initiation needs to be evaluated at the community clinic level.

What the study adds:

This study characterised a cohort of adolescents living with HIV and chronic lung disease in South Africa. Prior tuberculosis was common, and extensive bilateral structural lung abnormalities were universal. A significant proportion of the cohort exhibited severe growth impairment. Taken together, this study identifies ALHIV and CLD as a population with a high burden of respiratory deficits. Evidence-based secondary prevention and therapeutic strategies are needed to ensure the long-term preservation of lung function in these individuals.

Background

The rollout of antiretroviral therapy (ART) in South Africa in 2004 resulted in the dawn of a new era in the management of human immunodeficiency virus (HIV) infection. Children with vertically acquired HIV on ART experience improved survival into adulthood, with some entering their 5th decade of life in high-income countries(1). This has brought with it the challenge of caring for a generation of adolescents with a spectrum of pulmonary disorders associated with vertically acquired HIV. Chronic lung diseases (CLDs) are the most common chronic conditions affecting adolescents living with HIV(ALHIV) (2). These include non-cystic fibrosis bronchiectasis, post-tuberculosis (TB) lung disease, and HIV-related chronic airflow limitation.

The UNAIDS 2023 data approximated that 1.65 million adolescents (aged 10- 19 years) are living with HIV globally. In 2022, 740 children were infected with HIV daily. The estimated vertical transmission rate in South Africa, although on the decline, is estimated at 3% per childbirth in a mother with HIV(3)

The spectrum of CLD differs in ALHIV who receive ART in early life compared to those in whom treatment is delayed. Bronchiectasis, post-infectious bronchiolitis and idiopathic interstitial pneumonias are common conditions in patients with advanced immunosuppression who commence ART late in childhood, whilst asthma and chronic obstructive pulmonary disease are the most common lung diseases that occur in those who commence treatment perinatally (2). A recent local study conducted in Tygerberg Hospital by Gie et al. found that initiating ART in early infancy resulted in preserving lung function in individuals with perinatally acquired HIV (4).

Respiratory disease is a leading cause of mortality and morbidity in developing countries, particularly in Africa. Several studies have illustrated that adolescents in sub-Saharan Africa have a high rate of tuberculosis, with a higher incidence in ALHIV(5, 6). Little is known about the clinical characteristics of CLD in ALHIV, Schaaf et al. reported that HIV and TB co-infected children in the Western Cape were more likely to present with lymphadenopathy, alveolar opacification, cavitary disease, and hyperinflation on chest radiographs (CR) than HIV-uninfected children with thoracic tuberculosis (7). An observational longitudinal study in Kenya found ALHIV to commonly present with exertional breathlessness, chronic cough, respiratory complaints in the preceding year, tachypnoea, finger clubbing, exercise limitation and oxygen desaturation during exercise(8). This study was however confounded by majority of participants being exposed to polluting cooking fuel. Additionally, the same study found that CLD in ALHIV was associated with prior TB or pneumonia, delayed initiation of ART, delayed cotrimoxazole prophylaxis or delayed initiation of TB prophylaxis(8).

There is a paucity of information regarding the epidemiology and aetiology of chronic lung disease affecting adolescents in developing countries. A prospective study conducted in Harare by Ferrand et al. found that recently diagnosed or undiagnosed vertically acquired HIV was the leading cause of hospital admissions and in-hospital deaths amongst adolescents. Respiratory failure and a history suggestive of acute-on-chronic lung disease were the commonest causes of in-hospital mortality in these individuals (9). Additionally, a history of hospitalization for pneumonia or pulmonary tuberculosis was more common in ALHIV than in HIV-uninfected adolescents with CLD(3).

Before the HIV epidemic, CLD in children was primarily due to congenital malformations, cystic fibrosis, immune deficiencies, and aspiration (10). In HIV-infected children during the pre-ART era, the commonest causes of CLD included recurrent respiratory tract infections, lymphocytic interstitial pneumonitis (LIP), herpes simplex virus infection, cytomegalovirus infection, and pulmonary tuberculosis(11-13). While LIP remains the most common respiratory illness in untreated ALHIV, it rarely occurs in ALHIV who have been successfully treated with ART and HIV-uninfected children (8). Instead, the most common causes of CLD in ALHIV on ART are small airway disease, bronchiolitis, and bronchiectasis (12-14). Often individuals with small airway disease will present in early adulthood with severe chronic obstructive pulmonary disease (2). The pathogenesis of chronic airflow limitation associated with HIV is not fully understood with a notable lack of histopathological studies. It is thought to be the result of longstanding systemic immune activation and inflammatory dysregulation, coupled with recurrent respiratory tract infections (13). Thus, there is no consensus or guideline for the management of HIV associated chronic airflow limitation.

Prior studies in sub-Saharan Africa have shown that approximately one-third of adolescents had abnormal spirometry, with ALHIV found to have a lower forced vital capacity (FVC) and forced expiratory volume in one second (FEV_1) compared to HIV-uninfected risk-matched controls, despite ART and virological suppression (5, 12, 15, 16). A late diagnosis of vertically acquired HIV and delayed initiation of ART are associated with abnormal spirometry (2, 16). Some studies reported a predominantly obstructive pattern(13, 17), while others have reported a restrictive pattern (16, 18). Notably, obstructive lung function patterns were seen more commonly in individuals with a history of previous lower respiratory infections (LRTI)(2). None of the studies reported significant bronchodilator responsiveness ((13, 16, 17).

A recent longitudinal study in Cape Town found that ALHIV had a lower FEV_1 , FVC, forced expiratory flow at 25% and 75% of FVC, and FEV_1/FVC values than their HIV-negative counterparts. Mixed obstruction and restriction as well as exclusively obstructive patterns were

seen more commonly in ALHIV. Additionally, lung function in the ALHIV tracked over two years showed neither deterioration nor recovery, suggesting relatively fixed insults (5).

Given the high burden of chronic lung disease in ALHIV despite effective ART, the care and prevention of long-term respiratory sequelae remains a challenge. The BREATHE trial conducted in Malawi and Kenya demonstrated that once weekly azithromycin dose is associated with a reduction in acute respiratory exacerbations in children and adolescents with perinatally acquired HIV and CLD by half(19). A further challenge is the interpretation of lung function in ALHIV due to the lack of reference data for lung function in African adolescents (2).

Several adolescents have been referred to the Respiratory Clinic at Groote Schuur Hospital for long-term follow-up with chronic lung disease. This study aims to describe the socio-demographic, pulmonary function, and radiological characteristics of this cohort of ALHIV and chronic lung disease.

Methods

The study is a retrospective cohort study, a single investigator collected all data directly from patient records, both paper-based and electronic. The study focused on adolescent patients aged 12 to 20 years diagnosed with HIV and referred with chronic lung disease to the Adolescent Respiratory Clinic at Groote Schuur Hospital Respiratory Clinic (E16) from January 1, 2015, to January 1, 2023. Data collection included variables such as age, sex, race, date of HIV diagnosis, antiretroviral therapy initiation, CD4 count, viral load, co-morbidities, height, weight, respiratory symptoms, spirometry data, diffusing capacity of the lungs for carbon monoxide, radiological data, and sputum culture that was entered directly onto an excel spreadsheet (supplementary 1). A total of 20 patients were recorded to have attended the Adolescent Respiratory Clinic at Groote Schuur Hospital Respiratory Clinic (E16) from January 1, 2015, to January 1, 2023. All patient records were available and 3 HIV-negative patients were excluded from the study. There was only one patient record with missing spirometry information and this was recorded as unavailable. Lung functions in the E16 Respiratory clinic were performed by experienced clinical technologists according to the American Thoracic Society/ European Respiratory Society guidelines. Chest X-

rays were reviewed by 2 medical practitioners, one of whom was a pulmonologist. Ethical oversight was provided by the University of Cape Town Human Research Ethics Committee (reference 668/2022).

Statistical analyses used descriptive statistics, unpaired t-tests, Mann-Whitney U tests, and chi-square tests.

Results

Demographics

The clinical records of 17 ALHIV with CLD were reviewed, with a median age of 15 to 20 years at first visit of 16.9 years (interquartile range (IQR) 15.2 to 18.7). Most of the participants were female (58.9%), and of black African descent (94%). The age at HIV diagnosis was a median of 1.1 years, and only 3 participants were above the age of 3 years at time of diagnosis. Participants had been on antiretroviral therapy (ART) for an average of 13.2 years, with only 3 participants receiving ART for less than 3 years. Immunological profiles showed a CD4 nadir during follow-up of 243 cells/mm³ and 5 participants had a CD4 nadir below 200 cells/mm³. The mean current CD4 count was 447 cells/mm³, and 5 of the participants had a most recent CD4 count below 200 cells/mm³. Notably, multiple prior PTB episodes was the most significant common respiratory insult in the study population, occurring in 16 (94%) participants.

Anthropometry

The anthropometric findings within the study population revealed a range of characteristics. The median weight was 44 kilograms, with an interquartile range (IQR) of 41 to 47 kg, while the median height of participants was 158 centimetres, IQR of 150 to 161 cm. The median calculated body mass index (BMI) was 17.7kg/m² and 6 participants had a calculated BMI below 17kg/m². Furthermore, height-for-age assessments revealed that a substantial portion of participants (35.3% and 6 participants) fell below the 3rd centile, signifying growth stunting. Additionally, 41.2% of participants were within the 3rd to 15th centile range, while 17.6% fell within the 15th to 50th centile range. Only 1 participant plotted above the 50th centile.

Chest radiographs

The chest radiograph (CR) findings revealed a range of pulmonary abnormalities among the study participants with bronchiectasis and cavitation note as the predominant abnormalities. Fibrosis was another common finding, affecting 94% of the participants. Bilateral lung disease was universal, but the extent of the disease was asymmetric in the majority (94%) of participants. The CR findings are presented in *Table 1*.

Table 1: Chest radiograph findings

Variable	n (%)
Bronchiectasis	17(100)
Cavitation	17 (100)
Fibrosis	16 (94)
Reticular infiltrates	9 (52.9)
Nodules < 2mm	2 (11.8)
Nodules ≥ 2mm	3 (17.6)
Ground glass opacification	1 (5.9)

Microbiological profile

The sputum microbiological profile revealed a variety of microorganisms in the study participants. *Haemophilus influenza* was the most prevalent, detected in 12 cases (70.6%), followed by *methicillin-resistant staphylococcus aureus* (MRSA) in 2 cases (11.8%). The sputum culture results are presented in Table 2.

Table 2: Sputum microbiology

variable	n (%)
<i>Haemophilus influenzae</i>	12 (70)
<i>Methicillin-resistant staphylococcus aureus</i>	2 (11.7)

<i>Moraxella catarrhalis</i>	1 (5.9)
<i>Streptococcus pneumonia</i>	1 (5.9)
<i>pseudomonas aeruginosa</i>	1 (5.9)

Lung function

In all participants the FVC and FEV₁ were significantly reduced, indicating mixed restrictive and obstructive patterns. Of the 17 participants; 1 participant had no documented spirometry, 1 participant had obstructive spirometry, 6 participants had restrictive spirometry and 9 participants had mixed defect spirometry. The median pre-bronchodilator FEV₁/FVC ratio was 65% (IQR 57.8 - 74.3). The median post-bronchodilator FEV₁ percentage predicted was 35.5% (IQR 30.1- 51.3). The median FVC as a percentage of predicted values (FVC% predicted) was 51.7% (IQR 41.1- 60.8).

The spirometry results are presented in Table 3.

Table 3: Spirometry and diffusing capacity of the lungs for carbon monoxide in ALHIV with CLD

Pulmonary functions	Median (IQR)
Pre- bronchodilator FEV ₁ , mL	1050 (760- 1583)
Pre- bronchodilator FVC, mL	1680 (1208- 1948)
Pre- bronchodilator FEV ₁ /FVC	65 (57.8- 74.3)
Post- bronchodilator FEV ₁ , mL	1070 (800- 1580)
Post- bronchodilator FEV ₁ percentage of predicted	35.5 (30.1- 51.3)
FVC percentage of predicted	51.7 (41.1- 60.8)
DLCO, percentage of predicted	68.9 (41.4- 83.7)

None of the participants demonstrated significant bronchodilator response (BDR).

There was evidence of an association between FEV₁% and age of HIV diagnosis; those with delayed HIV diagnosis (>2 years of age) had a lower FEV₁% as the age of HIV diagnosis increased (Figure 1). Additionally, a longer duration of ART use was associated with a higher FEV₁% predicted (Figure 2). Growth stunting was associated with a lower FEV₁% predicted (Figure 3).

There was no apparent association between current CD4 counts and FEV₁% predicted.

Commented [jn1]: Number of participants with mixed defect spirometry vs obstructive and restrictive spirometry added

Finally, the diffusing capacity of the lungs for carbon monoxide (DLCO) was only documented in 6 participants, and only 1 participant had a normal DLCO.

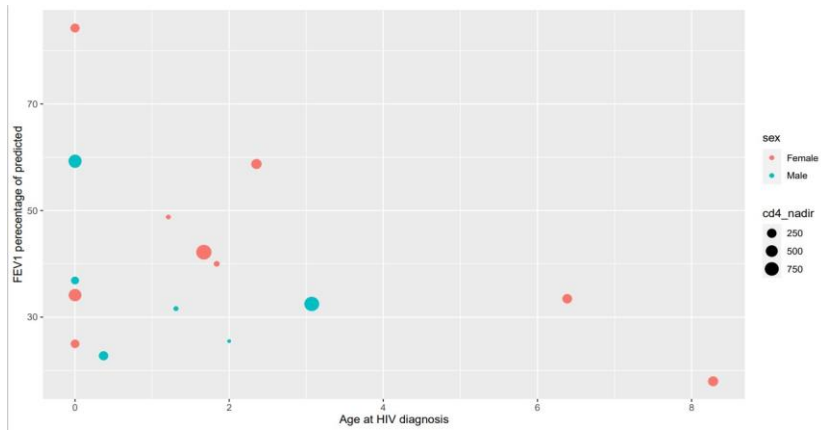


Figure 1 Relationship between current FEV₁ percentage predicted and age at HIV diagnosis.

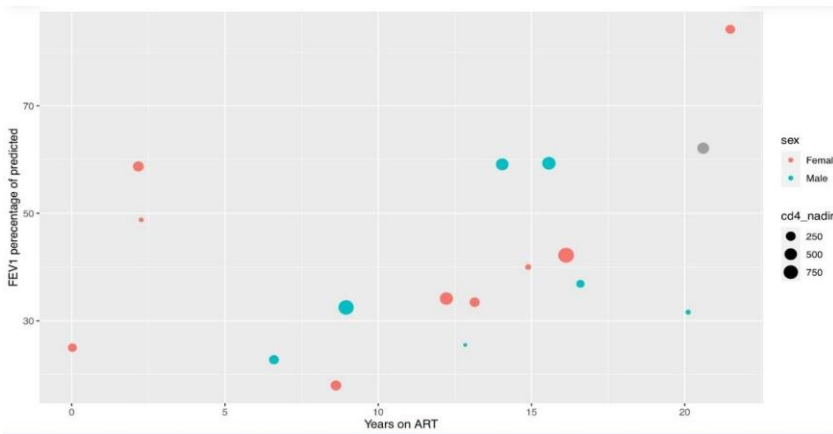


Figure 2: Relationship between current FEV₁ percentage predicted and duration of ART

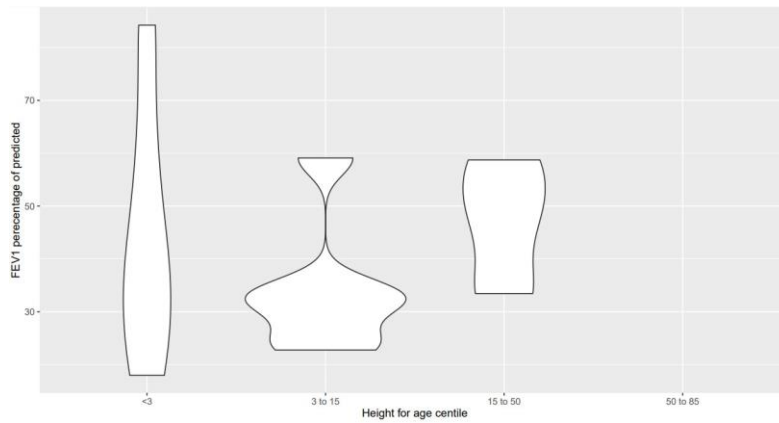


Figure 3: Modified violin plot displaying relationship between growth (height-for-age) and FEV₁ percentage predicted

Treatment

Inhaled bronchodilators, airway clearance techniques, and vaccinations for pneumococcal disease and influenza were universally prescribed. A total of nine participants were prescribed an immunomodulatory macrolide (azithromycin).

Discussion

This was a retrospective, descriptive study of 17 ALHIV at a single centre that provides valuable insights on the characteristics of ALHIV and CLD in South Africa. The principal findings in this study were i) growth restriction and stunting is common in ALHIV. ii) high prevalence of TB. iii) Grossly abnormal lung functions despite early ART initiation. iv) FEV₁% predicted was lower in patients for whom HIV diagnosis and ART initiation was delayed.

Our study confirmed that a significant portion of participants were stunted. The International Epidemiology Databases to Evaluate AIDS (IeDEA) reported that 41% of a global cohort of ALHIV were stunted, with no significant difference between males and females (20). Additionally,

Gebrie et al. similarly found that 28% of ALHIV on ART were stunted and that adolescent males were almost 2 times more likely to be stunted than their female counterparts (21). This study population was too small to establish a difference between male and female growth patterns. The relationship between HIV-associated CLD and growth stunting is multifactorial, involving a complex interplay of recurrent infections, impaired lung function, poor lung growth and chronic inflammation culminating in net energy deficits and ultimately growth restriction (figure 4). The reason behind severe growth restriction and CLD in patients who initiated antiretroviral therapy (ART) at a young age remains uncertain. However, one hypothesis suggests that this phenomenon could be attributed to the ART itself as ART may lead to decreased antioxidant tolerance, trigger immune reconstitution inflammatory syndrome, and potentially contribute to increased autoimmunity (14).

Prior studies have demonstrated an association between airway disease and HIV. The lung function findings in our study showcase substantial variability in all parameters, with most participants exhibiting mixed obstructive and restrictive defects. This is in keeping with the findings of Githinji et al. in sub-Saharan Africa, where ALHIV attending an ART clinic were found to have a high burden of obstructive airway disease [median FEV₁ 53% (IQR 5- 86%)] with the majority (78%) exhibiting no bronchodilator responsiveness.(22, 23).

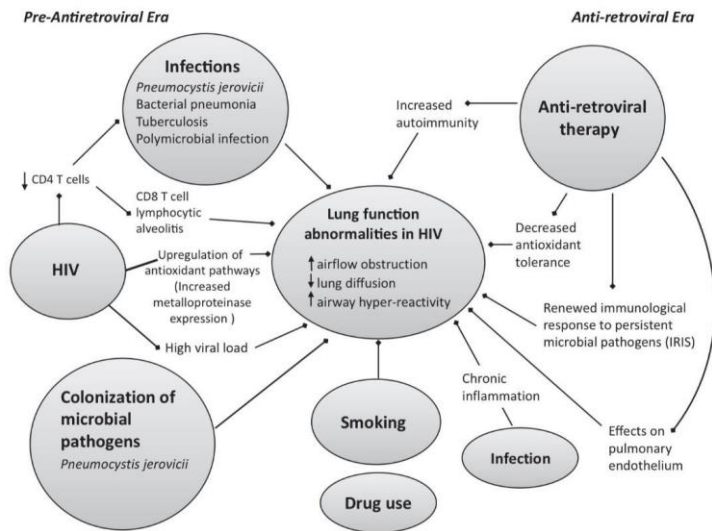


Figure 4: Factors underlying the interaction between human immunodeficiency virus (HIV) and chronic lung disease. Reproduced with permission (5756110396582)

The CR findings indicate a high prevalence of extensive bilateral disease, with all cases displaying features of bronchiectasis and cavitations. A large majority (94%) had evidence of fibrosis. Nodules and ground glass opacification were less prevalent. In a study of 75 ALHIV in Zimbabwe, Desai et al. similarly found that bronchiectatic changes were the predominant (>50%) CR findings. Whilst 74% of their study population had extensive disease on the CR (24). These results emphasize the severe burden of respiratory disease among ALHIV in South Africa, which can be attributed to various factors, including the high prevalence of infectious diseases such as tuberculosis.

Commonly isolated airway microbiota in patients with non-cystic fibrosis bronchiectasis are Haemophilus influenza, streptococcus pneumonia and Moraxella catarrhalis, regardless of antibiotic exposure (25). The sputum microbiome in this study was dominated by haemophilus influenza isolated in 12 participants, followed by methicillin resistant staphylococcus aureus. To

the best of our knowledge, no studies have evaluated the lung microbiome in ALHIV in the context of CLD. One of the challenges in this study was the lack of sputum cultures in some participant records, additionally, the clinical picture and indication at the time of sputum culture was unknown. Our study participants were managed on a combination of azithromycin, airway clearance techniques, vaccination, inhaled long-acting beta-agonists and inhaled corticosteroids (ICS), despite the lack of BDR. The use of ICS in ALHIV is an interesting topic as there have been numerous case reports of patients on protease inhibitors (PI) and ICS developing Cushing's syndrome due to steroid accumulation, as PI's are potent cytochrome P450 inhibitors (26, 27). Furthermore, there is an increased risk of pneumonia, pulmonary TB and hospitalization in HIV-negative patients using long-term ICS with CLD (28-30). To the best of our knowledge, there are no studies evaluating the risk of long-term ICS use in patients with HIV and CLD, but the risk is presumably similar, if not greater, than in individuals without HIV. The use of azithromycin in patients with severe bronchiectasis (≥ 3 exacerbations per year) who are not colonized with *Pseudomonas aeruginosa* reduces hospitalizations due to the drug anti-inflammatory and immunomodulatory effects and forms part of the European Respiratory Society guidelines for treatment of bronchiectasis in adults (31, 32). There is a lack of guidelines or consensus for the management of bronchiectasis specifically in ALHIV. In our study we were unable to ascertain the number of exacerbations per year, however, azithromycin was universally prescribed. This raises concerns of side effects such as hearing loss, cardiac and liver toxicity, necessitating long-term safety monitoring and pre-treatment screening of liver function tests, electrocardiogram and hearing assessment.

Limitations

There were several limitations to this study. As with most retrospective observational studies, it was not possible to obtain accurate data on medication history, smoking/ illicit substance use rates, and other information from the medical records. Details on the frequency of exacerbations and adherence to ART and inhaled therapies were not available. TB prophylaxis and basis of prior TB diagnosis and drug sensitivities was not documented in all folders. Spirometry results pre- 2019 were transcribed by the attending clinician into the clinical records as a result predicted values, height and weight were not always documented in the clinical records. Survival bias might have

influenced our results since this study included ALHIV who are still alive and receiving outpatient care. Consequently, those who may have died from more severe lung disease could be underrepresented in this study. The COVID-19 pandemic resulted in the closure of outpatient clinics for approximately two years at Groote Schuur Hospital, therefore affecting the number of study participants and limiting the availability of spirometry and radiography. This was a descriptive study conducted at a single tertiary centre therefore results may not be generalisable to the broader population as these study participants significant lung damage requiring sub-specialist intervention. Despite these limitations, the study offers valuable insights into a unique population, serving as a reference point for future studies.

Conclusion

This study characterised a cohort of adolescents living with HIV and chronic lung disease in South Africa. Prior tuberculosis was common, and extensive bilateral structural lung abnormalities were universal. A significant proportion of the cohort exhibited severe growth impairment. Taken together, this study identifies ALHIV and CLD as a population with a high burden of respiratory deficits. Evidence-based secondary prevention and therapeutic strategies are needed to ensure the long-term preservation of lung function in these individuals. Further research is required to understand the long-term trajectory of lung function, growth, and overall health with the aim to develop effective management strategies.

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Supplementary 1

	A	B	C	D	E	F	G	H	I	J	K	L	M	
1	participant	Sex	Age	DOB	Date of first visit	Race	Smoker	Cannabis	HIV	Date of HIV Dx	Date of ART initiation	Duration on ART	Initial ART regimen	Present An
2		2												
3		3												
4		4												
5		6												
6		7												
7		8												
8		10												
9		12												

	O	P	Q	R	S	T	U	V	W	X	Y	Z
1	participant	Prior ART regimen	Nadir CD4	Current Current CD4	CXR findings(cavitation)	CXR- fibrosis	CXR infiltrates	CXR nodules<2mm	CXR nodules> 2mm	CXR mass	CXR collapse	CXR ground glass
2		2										
3		3										
4		4										
5		6										
6		7										
7		8										
8		10										
9		12										

	Z	AA	AB	AC	AD	AE	AF	AG	AH	AI	AJ
1	participant	CXR ground glass	CXR volume loss	CXR pneumothora	CXR bronchiectasi	CXR pleural eff	CXR bilat disease	CXR unilateral dx	CXR air fluid level	Right lung not involed	Right lung involvement
2		2									
3		3									
4		4									
5		6									
6		7									
7		8									
8		10									
9		12									

	AK	AL	AM	AN	AO	AP	AQ	AR	AS
1	participant	Right lung involved 25- 50%	Right lung 50- 75%	Right lung severity >75%	Left lung not involved	Left lung <25% involved	Left lung 25-50% involved	Left lung 50- 75% involved	Left lung > 75% invc
2		2							
3		3							
4		4							
5		6							
6		7							
7		8							
8		10							
9		12							

	AT	AU	AV	AW	AX	AY	AZ
1	participant	Completed TB treatmen	Micro result haemophilus influenzae	Micro result MRSA	Micro result moraxella catarrhali	Micro result streo oneumoniae	Micro pseudomonas aeruginos
2		2					
3		3					
4		4					
5		6					
6		7					
7		8					
8		10					
9		12					

	AZ	BA	BB	BC	BD	BE	BF	BG	BH	BI	BJ
1	participant	Height for age centile	Height	Weight	BMI	lung Fx FEV1 actual	FEV1 post bronchodilator	FEV1 predicted	FEV1 % predicted	FEV1 % post bronchodilator	FVC actual
2		2									
3		3									
4		4									
5		6									
6		7									
7		8									
8		10									
9		12									

Commented [jn2]: CRF added

