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Original Research Article

Respiratory sequelae among children and adolescents post-tuberculosis treatment in Abuja, Nigeria

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ABSTRACT

Background: Despite successfully completed treatment, respiratory sequelae known as post-tuberculosis (TB) lung disease (PTLD) has been reported in 1% to 49% of children and adolescents TB survivors. Post-TB lung disease has been identified as a priority research area in Africa. However, available studies have been mainly among adults in developed countries. This study aimed to determine respiratory sequelae among children and adolescents previously treated for pulmonary TB by identifying persisting respiratory symptoms and lung function assessment.
Methods: A cross-sectional study among participants who had completed TB treatment within the last five years but not less than six months post-treatment. A proformer was used to document biodata, vital signs, anthropometric measurements, TB history, persisting respiratory symptoms, spirometry and incentive spirometry test results.
Results: Seventy-one names were extracted from records, 38 participated in the study. The mean age was 11.92 years, 23 (60.5%) underweight, 24 (63.2%) had at least one symptom sequela, mostly cough 23 (60.5%) and easy fatigability 23 (60.5%). Majority, 25 (65.8%) had abnormal spirometry results and 23 (60.5%) were able to sustain 600cc of air using the incentive spirometer. There was a significant association between symptom sequelae and nutritional status (p=0.002) and between symptom sequelae and age (p=0.001). Also, between lung function and age (p value<0.001) and between lung function and nutritional status (p value =0.002).
Conclusions: Majority had post-Tb sequelae. In order to improve health-related outcomes, children and adolescents should be followed up post-TB treatment and should include pulmonary and nutritional assessments.

Keywords: Adolescents, Post-tuberculosis lung disease, Respiratory sequelae, Spirometry, Children

INTRODUCTION

In 2023, Tuberculosis (TB) resulted in the morbidity of about 10.8 million people globally of whom six million were men, 3.6 million women and 1.3 million, children while 1.25 million people died from the disease making it the leading cause of mortality globally from a single infectious agent.[1] Nigeria has the highest TB burden in Africa.[2] Over 361,000 TB cases were reported in 2023, among which 9% of these were in children. The country also recorded a high treatment success rate of 93%.[2] Tuberculosis is a preventable, treatable and curable disease.[3] A six-month course of four anti TB drugs and adherence support is usually used in the treatment and cure.[3] However, the World Health Organization (WHO) recently introduced a new four month regimen for treatment of non-severe TB.[4] Despite successful completed treatment, respiratory sequelae known as post-tuberculosis lung disease (PTLD) occur. Post-TB lung disease is the occurrence of chronic respiratory

abnormality, in previously successfully treated pulmonary TB patients, presenting with or without symptoms.[5] A sizable proportion of the 155 million TB survivors in 2020, developed post-tuberculosis morbidity.[1] Features of PTLD include cough, sputum production, difficulty in breathing, pulmonary function test abnormalities, obstructive, restrictive and mixed patterns, bronchiectasis, pneumonia, chronic obstructive pulmonary disease colonization and infection with Aspergillus fumigatus and non-tuberculous mycobacteria amongst others.[6-13] Studies show that 1% to 49% of children and adolescents who survive TB, develop PTLD.[14]

There is also evidence supporting a shorter life expectancy after adequate treatment of TB.[15] When compared with the general population or matched controls, TB survivors who have been adequately treated are reported to have a three- to six-year higher risk of death.[16-19]

Post-TB lung disease has been identified as a priority research area in Africa.[20] Most of the few available studies on persons with previously treated TB or sequelae of TB disease have been carried out mainly among adults in developed countries. This study aims to determine the respiratory sequelae among children and adolescents previously treated for pulmonary tuberculosis at the University of Abuja Teaching Hospital (UATH), Gwagwalada, Abuja Federal Capital territory (FCT), Nigeria, by identifying persisting respiratory symptoms and assessing lung function.

METHODS

The University of Abuja Teaching Hospital is located in Gwagwalada, one of the six area councils in Abuja FCT, Nigeria. It is a 500-bedded tertiary healthcare facility with several departments and units. The hospital also accommodates the FCT School of Nursing and Midwifery, the Intensive Care Nursing Training Centre, the Faculties of Basic Clinical and Clinical Sciences of the University of Abuja. It serves the local community, the other five area councils in FCT, as well as the surrounding states. The Directly Observed Therapy Strategy (DOTS) clinic is located within the hospital's complex. Patients diagnosed with tuberculosis but without complications are managed on out-patient basis here. The clinic is manned by doctors, nurses and community health extension workers. It runs every weekday, from Monday to Friday and from 8am to 4pm, excluding public holidays.

This was a cross-sectional, descriptive study. The criteria for inclusion were children and adolescents who had previously been diagnosed and treated for pulmonary TB at the UATH DOTS clinic; had completed their anti-TB drugs within the last five years but not less than six months post treatment; had been certified cured; were aged 6 years or more in order to be able to use the spirometer and meet reproducibility and acceptability criteria for spirometry; were able to use an incentive spirometer; had caregivers who gave written consent for those less than 18 years, assent from participants aged less than 18 years; and written consent from those aged 18 and 19 years. Those who had been treated for extrapulmonary TB, had contraindications for spirometry or incentive spirometry who felt too ill to participate or incapacitated by mental or physical illness and so could not follow instructions, were excluded.[21-23]

The DOTS register was used to identify eligible participants who were then reached via phone calls to solicit willingness to participate after receiving information about the study. Those willing to participate were given dates to present to the hospital for the study. On presentation, the participant information sheets (PIS) were shared with them and consent forms signed. Verbal assent was obtained from participants less than 18 years old. Caregivers who had difficulty reading or could not understand English were assisted by the researchers or trained research assistants who either read out the PIS and questionnaire or translated in their local language. The study lasted from November, 2023 to July, 2025.

Contraindications to spirometry and incentive spirometry use were checked off to determine eligibility of the participant. A proforma developed by the researchers was used to obtain the participant's biodata, anthropometric measurements, blood pressure, oxygen saturation, HIV and smoking status. The patient's history of TB was obtained from the caregiver and confirmed from the DOTS clinic case notes. The weight, height, blood pressure and oxygen saturation were measured with a Seca© weighing scale, Seca© stadiometer, Omron© digital blood pressure monitor and Contec© pulse oximeter and recorded. They were calibrated as needed according to the manufacturers' recommendations. The nutritional status using weight, height, body mass index (BMI), BMI percentile, weight for height, height for age were assessed and calculated using Centre for Disease Control and Prevention (CDC) charts for children and teens aged 2 years to 19 years.

Spirometry was performed using Spirolab new MIR© according to the ATS/ERS recommendations and the lung function test results recorded in the proforma. Participants made three to eight attempts and the best values of the attempts were used for analysis. Only lung function measurements that met the ERS/ATS quality criteria for acceptable and repeatable were included. The results for forced expiratory volume in one second (FEV1), forced vital capacity (FVC) and FEV1 /FVC were documented in the proforma.

The participants then rested for 30 minutes and then were showed how to use the incentive spirometer. A flow-oriented incentive spirometer was used. The inspiratory volumes in the chambers were 600 cc per/sec, 900 cc per sec and 1,200 ml cc per sec, represented by one ball, two

balls and three balls staying afloat to the maximum level on inspiration, respectively. The participant held the incentive spirometer upright, while sitting upright, comfortably at the edge of a chair, then exhaled. The participant then placed his or her mouth on the mouthpiece forming a seal with the lips and then inhaled slowly and maximally, causing the ball to rise.[24,25] At the end of maximal inhalation, the breath was held for 5 seconds before slowly exhaling through the nose with the mouth removed from the mouthpiece.[24] The study participant then relaxed and took in a normal breath after each deep breath.[25] Each session consisted of 10 breaths, subsequently the participant was asked to cough two or three times at the end of the 10 breaths to clear the airway.[25,26] Having the three balls rise and sustained gives the maximum volume. The highest volume with the ball held up and sustained for five seconds on inspiration was recorded in the proforma.

The data was analysed using SPSS version 27 was used to analyses the data. Frequency tables have been used to show proportions, means calculated, Chi square and logistic regressions used to demonstrate associations between the variables, duration since treatment completion, nutritional status, age, and respiratory sequelae, symptoms and lung function. A p value<0.05 was taken as significant and the confidence interval set at 95%.

Ethical approval was obtained from the Research and Ethics Committee of the University of Abuja Teaching Hospital, Gwagwalada, Abuja FCT. Participants and caregivers were informed that they could decline consent at any time of the study without fear of repercussion or penalty. The participants confidentiality and privacy were ensured and no identifiers used. The principles of research ethics were maintained according to the Helsinki Declaration of 1975 as revised in 2013.

RESULTS

Seventy-one names with their contact details were extracted from the DOTS clinic records, 16 (22.5%) of them could not be reached via phone calls as the numbers had either been reassigned to other persons or were no longer valid, seven (9.9%) were deceased, six (8.5%) declined participation, three (4.2%) had moved out of Abuja and one (1.4%) excluded as a diagnosis of active TB was made while screening. A sample size of 38 was finally used for this pilot study.

General characteristics of participants

The age range of participants was seven years to nineteen years with a mean age of 11.92 SD±2.92. Majority were males 37 (97.4%), within the age group of 10 to 14 years 24 (63.1%), with mothers who mainly had secondary level of education 13 (34.2%) and fathers with tertiary level of education 24 (63.1%). All participants had results for chest radiographs, GeneXpert, sputum acid-fast bacilli smear and mantoux tests. The diagnosis of TB was made mainly using chest radiographs 21 (55.2%) and GeneXpert 20 (52.6%). Some were made using a combination of different investigations and clinical features; therefore, the sums do not add up to 100% as shown in Table 1. All had been treated according to the National Tuberculosis guideline. One (2.6%) participant who had drug-resistant TB was treated for seven months as the participant was initially started on first-line medications before switching in the second month to second-line medications when they became available. Others participants had been treated for 6 months. Only one (2.6%) participant was Human Immunodeficiency Virus positive. None of them had a history of smoking or exposure to second-hand smoke at home. About a third, 15 (39.5%) had completed treatment within 12 months (1 year) to 23 months prior to participating in the study. (Table 1).

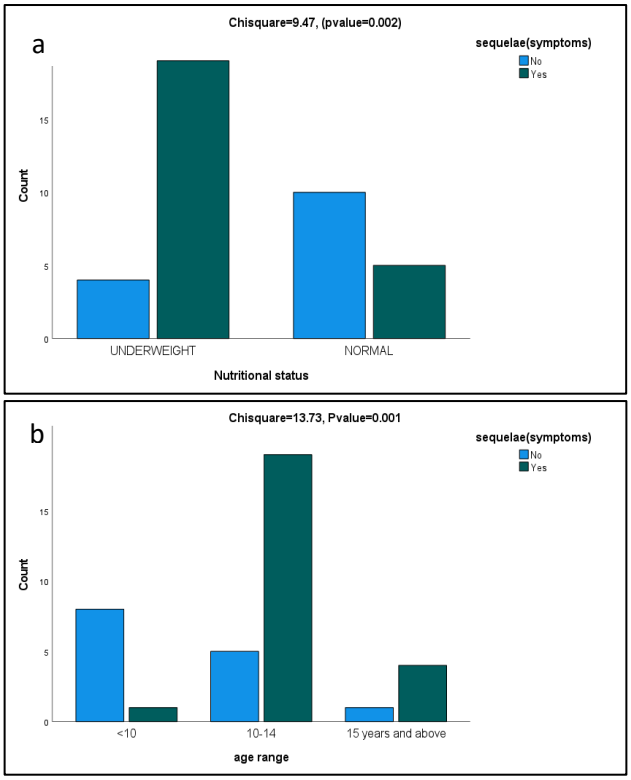

Figure 1: (a) Association between respiratory symptoms and nutrition and (b) association between respiratory symptoms and age.

Anthropometry and vital signs

The mean weight was 35.6 kg with SD±12.76 kg, the mean height 148.8 cm SD±21.87, mean BMI 15.48 kg/m^2 SD±2.21 and mean BMI percentile 15.84% SD±29.51. Majority of the participants were underweighted 23 (60.5%) while the others had normal weight 15 (39.5%). None of the participants were overweight, obese or stunted. All participants had normal blood pressure for age, sex and height, and normal oxygen saturation (SPO2) of 95% to 99%. (Table 2).

Post-tuberculosis respiratory sequelae

Respiratory symptoms

Twenty-four (63.2%) participants had at least one symptom. The most common recurrent respiratory symptom was cough 23 (60.5%) and easy fatigability 23 (60.5%). Chest pain was the next leading symptom 10 (26.3%). None of the patients had foul-smelling sputum, blood in sputum, cyanosis, weight loss, pneumonia or combination of symptoms suggestive of asthma: cough, difficulty in breathing, wheeze and chest tightness. (Table 3).

Spirometry and incentive spirometry

Assessing pulmonary lung function using spirometry, the median FEV1, FVC and FEV1/FVC were 1.63 SD±0.44, 1.77 SD±0.73 and 79.50±SD 8.74. Majority 25 (65.8%) had abnormal spirometry results with the restrictive pattern 11 (28.9%) being the most common abnormality. Using the incentive spirometer, majority 23 (60.5%) were only able to sustain one ball for five seconds on inspiration while only a few 5 (13.2) sustained three balls for 5 seconds (Table 3).

Association between nutritional status, age and respiratory symptom sequelae

There was a statistically significant association between respiratory symptom sequelae and nutritional status (weight) X 2 = 9.47, p= 0.002 (Figure 1a). There was also a statistically significant association between symptom sequelae and age X 2=13.73, p=0.001 (Figure 1b).

Association between lung function test, nutritional status and age

The association between lung function and age was statistically significant X2 34.4; p value<0.001 and between lung function and nutritional status (weight) X 2 14.99; p value =0.002 (Table 4).

Table 1: General characteristics of participants.

Variable	Frequency (%)
Gender	
Male	37 (97.4)
Female	1 (2.6)
Age (in years)	
<10	9 (23.7)
10-14	24 (63.1)
≥15	5 (13.2)
Education level of mothers	
No formal	8 (21.0)
Primary	5 (13.2)
Secondary	13 (34.2)
Tertiary	12 (31.6)
Education level of fathers	
No formal	5 (13.2)
Primary	0 (0)
Secondary	9 (23.7)
Tertiary	24 (63.1)
Method of TB diagnosis	
Chest X-ray	21 (55.3)
GeneXpert	20 (52.6)
Acid fast bacilli	5 (13.2)
Physician diagnosed using clinical features	4 (10.5)
Mantoux	2 (5.3)
WHO TB Scoring system	2 (5.3)
HIV status	
Negative	37 (97.4)
Duration since treatment completion	
6 months to 11 months (< 1 year)	6 (15.8)
1 year to < 2 years	15 (39.5)
2 years to <3 years	4 (10.53)
3 years to <4 years	4 (10.53)
4 years to 5 years	9 (23.7)

Table 2: Anthropometry and vital signs.

Variable	Frequency (%)
Weight	
Underweight	23 (60.5)
Normal weight	15 (39.5)
Overweight/obese	0 (0)
Height	
Normal	38 (100)
Blood pressure	
Normal	100%
SPO_2	
95% - 99%	100%

Table 3: Post-tuberculosis respiratory sequelae.

Variables	Frequency (%)
Respiratory symptoms	
Cough	23 (60.5)
Easy fatigability	23 (60.5)
Chest pain	10 (26.3)
Sputum production	5 (13.2)
Difficulty in breathing	4 (10.5)
Wheezing	3(7.9)
Foul-smelling sputum	2 (0)
Others[ł]	0 (0)
Lung function test	
Abnormal	25 (65.8%)
Normal	13 (34.2)
Restrictive	11 (28.9)
Obstructive	9 (23.7)
Mixed	5 (13.2)
Incentive spirometry	
One ball (600 cc/sec)	23 (60.5)
Two balls (900 cc/sec)	10 (26.3)
Three balls (1,200 cc/ sec)	5 (13.2)

Others[ł]: Blood in sputum, cyanosis, pneumonia, weight loss, asthma.

Table 4: Association between lung function test, nutritional status and age.

	Lung function test					P value
Variable	**Normal**	**Obstructive**	**Restrictive**	**Mixed**	X^2	
Age (in years)						
<10	8 (88.9)	0 (0)	1 (11.1)	0 (0)		
10-14	0 (0)	9 (37.5)	10 (41.7)	5 (20.8)	34.4	<0.001
≥ 15	5 (100)	0 (0)	0 (0)	0 (0)		
Total	13 (34.2)	9 (23.7)	11 (28.9)	5 (13.2)		
Nutritional status						
Underweight	4 (17.4)	9 (39.1)	5 (21.7)	5 (21.7)	14.99	0.002
Normal	9 (60)	0 (0)	6 (40)	0 (0)		
Total	13 (34.2)	9 (23.7)	11 (28.9)	5 (13.2)		

DISCUSSION

Childhood TB can be prevented by the use of the BCG vaccine given at birth. However, a study in Abuja among 414 mother/child dyad showed that only 35.2% of infants received the vaccine at birth.[27] Tuberculosis affects all ages and PTLD has been documented in children, adolescents and adult TB survivors. Although, there is

currently not much data on the short- and long-term effects of PTLD on the airways of a growing child, one may infer negative outcomes as seen in children who develop other lower respiratory tract infections such as pneumonia and bronchiolitis, at an early age.[28,29] Therefore, curbing TB infections, ensuring early diagnosis and treatment of TB are key to reducing the burden of PTLD. Making a diagnosis of TB in children can be quite challenging given the pauci-bacillary nature, lack of pathognomonic features, challenges in sample collection, and inequitable access of diagnostic tools.29 Bacteriologic testing for TB is the recommended standard for making a diagnosis.[29,30] Various samples such as stool, sputum, gastric aspirate and nasopharyngeal specimens can be used. The yield is higher in adolescents who tend to have disease similar to that in adults. Bacteriologic tests include Xpert, urine lateral flow-lipoarabinomannan (LF-LAM) assay, TB loop-mediated isothermal amplification (TB-LAMP), Truenat® MTB, line-probe assay (LPA), culture and drug susceptibility testing amongst others.[30,31]

Other non-bacteriologic tests for TB include chest X-ray, tuberculin skin tests such as mantoux and interferon-gamma release assays (IGRA) and sputum microscopy for acid-fast bacilli.[31] A combination of symptoms and signs are also used to develop various scoring systems and algorithms for diagnosis when the recommended investigations are not available as in some low- and middle-income countries.[30,31] In this study, TB diagnosis were made using mainly chest X-ray and bacteriologic confirmation with GeneXpert. Some other studies identified had a higher proportion diagnosed with bacteriological confirmation.[32,33] In a cross-sectional study in the Gambia, about two-third of the proportion had bacteriologic confirmation while another in South Africa among only adolescents used only bacteriologically confirmed participants.[33]

A high proportion of participants reported at least one symptom post-TB treatment. The proportion was higher than that reported in two studies among the same cohort in the Gambia where symptoms were assessed at completion of treatment in one study and after six months in the second study.[32,34] The authors documented an increase in the proportions with symptoms in the second study.[34] These findings may suggest that respiratory symptoms from PTLD may increase over time post-TB treatment, at least within the first few months to years. The proportion of participants with abnormal lung function was similar to that reported in a study in South Africa but higher than two studies reported in the Gambia which used the same cohort for an initial cross-sectional study and later followed them up and assessed again within six-months of completing TB medications.[32-34] Our study enrolled only those that were a minimum of six months post-TB treatment with majority being 12 months to 23 months post-treatment. Our study also had a higher proportion of adolescent participants compared with those in the Gambia. Adolescents tend to have more severe pulmonary TB compared with children so would be more likely to have abnormal lung function tests like adults.

In our study, the adolescent age group 10 to 19 years had the most proportion with respiratory symptoms and abnormal lung function test results post-treatment when compared with the younger children. They also made up a larger proportion of the study participants. This is similar to reports from study carried out in the Gambia.[34] The age range of study participants in these two studies were similar and a few of them in the study in the Gambia had a history of smoking while none in our study had any including second-hand smoke exposure at home. The higher proportion of symptoms in the adolescents may be due to the adult-type TB they were likely to have. Adolescents tend to have adult-like pulmonary TB which is usually more severe than that in children. There is a need to carry out studies on various age groups, separating adolescents from children in order to identify differences.

Cough and easy fatigability were the commonest reported post-treatment symptom sequelae in our study similar to cough as the commonest in other studies.[14,32,33,35] Easy fatigability as a symptom, was not assessed in these other studies. Majority of the participants were underweighted in our study, although none was stunted. Underweight and stunting were reported in other studies.[32,33] This highlights the need for continued nutritional support and rehabilitation all through treatment and post-treatment of TB patients especially considering that a significant association was reported between undernutrition and abnormal spirometry results in the studies. Interestingly, none of the participants in all the studies were overweight or obese. Patients who are underweight may require increased food intake but there is a need to further study the relationship between post-TB treatment and weight.

Abnormal lung function tests were reported in majority of the participants in this study with the most common abnormality being the restrictive pattern.[32-34] The mixed type was the least documented among the participants in our study while none were reported in another study.[32] Studies in adult populations have reported various proportions of the three different lung function abnormalities, obstructive restrictive and mixed pattern.[35-38] Studies in adult populations in Nigeria have reported restrictive and mixed as the leading lung function abnormality. Both studies reported cough as the major residual symptom.[35,38] However, there is still need for more research to determine the commonest pattern, pathophysiology and risks for developing the various lung function test abnormalities before arriving at a conclusion.

There was a significant association between duration of time post treatment and abnormal lung function test. This contrasts with the findings in the Gambia were there was no statistically significant association. The difference

could be that only participants who were at least six months post treatment were enrolled in this study while the other study used only participants within six months post-treatment.[34] More studies are needed to determine the short- and long-term effect of TB on lung function after completing treatment. The incentive spirometry revealed that majority of participants could only inspire and sustained about 600cc of air (one ball) for five seconds. A study in Indonesia among 32 adults previously managed for TB reported that pulmonary function test results and quality of life improved with the use of incentive spirometry and pursed lip breathing.38 Further studies with larger sample sizes are needed to determine if a similar effect will be obtained with children and adolescents.

The study however had some limitations. The small sample size and single-centre may not be enough to draw conclusions about PTLD in children and adolescents. There may have been selection bias given the non-randomization of participants, the number of eligible participants we couldn't reach or declined to participate, and the overly disproportionate male to female ratio of participants. This may suggest that mainly those who still had health challenges after completing TB treatment, presented for the study. Despite its limitations, this pilot study has demonstrated important findings about PTLD and exposed some shortcomings and challenges to be expected and overcome in a larger study. It has also added to the paucity of data available on PTLD in children and adolescents.

CONCLUSION

In conclusion, majority of the children and adolescents had post-Tb treatment sequelae with cough and easy fatigability being the commonest symptoms, restrictive pattern being the most common lung function abnormality and majority, underweight. A statistically significant association was found between respiratory symptoms and nutritional status as well as between lung function test and participants' age. Therefore, in order to improve morbidity and other health-related outcomes in survivors, children and adolescents with pulmonary TB should be followed up post-treatment and that pulmonary and nutritional assessments be included in their follow up assessments. Such patients may also benefit from pulmonary and nutritional rehabilitation.

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