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Research Article

Spirometric Assessment Of Post Tuberculosis Lung Disease Patients Attending Federal Teaching Hospital, Owerri, Imo State, South Eastern Nigeria

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Abstract

Background: Tuberculosis is a chronic lung disease that has remained a public health menace worldwide, especially in low and middle-income countries. It is a salient risk factor for long-term respiratory disease due to enduring lung damage. Post-tuberculosis lung disease is a major but unidentified chronic respiratory disease in countries with high tuberculosis disease such as Nigeria.

Objectives: The study was done to assess the spirometric indices of post pulmonary tuberculosis patients at the Federal Teaching Hospital, Owerri .

Methods: This was a hospital-based cross-sectional analytical study at the pulmonology out patient clinics of the Federal Teaching Hospital, Owerri, Imo State. Two hundred consenting participants consisting of 100 post-tuberculosis lung disease patients (aged 18 years and above) and 100 age-, sex- and height-matched apparently healthy controls had spirometry. The patients were contacted through phone calls from their phone contacts in the registers (including that of their relatives) and were invited to visit the clinic for follow up and participate in the research. On arrival, a written informed consent was extracted before inclusion from the participants and controls. A structured questionnaire developed for this study was administered to all patients to obtain data regarding sociodemographics. Spirometry was conducted using spirolab III. Data were entered first on Microsoft excel sheet and analysed using SPSS version 25.

Results: Two hundred participants consisting of 100 post-tuberculosis lung disease patients (aged 18 years and above) and 100 age-, sex- and height-matched apparently healthy controls, mean age for the case group was 48±15.2 years and 46.7±13.9 controls (18-90 years) were studied. The male to female ratios were 1:1.22 and 1:1.27 for cases and controls respectively. Respiratory lung function impairment occurred in 71% of cases and 12% of the control. The odds of lung function impairment were 18.0 (95% CI: 8.55 to 37.7, p<0.001) times higher in post-tuberculosis patients than controls. The pattern comprised – Obstruction 29%, Restrictive 28%, and Mixed 14%. These patterns were significant in cases compared to controls ($X^2=73.10$, p<0.001).

Conclusion: The prevalence of spirometric impairment was high in the post-tuberculosis patients, obstructive pattern was the most common abnormality followed by restrictive and mixed patterns. These findings help support the need for early follow up of tuberculosis patients after treatment, and spirometric assessments.

Key Words: Spirometry, Post-tuberculosis, lung function

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INTRODUCTION

Tuberculosis is an identified global health challenge.¹ It is a major cause of death in many countries.² Nigeria is one of the 14 high-burden countries for TB (Tuberculosis), TB/HIV (Tuberculosis/Human acquired Immunodeficiency virus) and MDR TB (Multi drug resistant tuberculosis) and was the first in Africa and 6th among the 30 high-TB burden countries, which collectively contribute to 87% of estimated TB cases globally.^{3,4,5}

The World Health Organization Global tuberculosis report 2022, reported an estimated 1.4 million deaths among HIV negative people and an additional 187000 deaths among HIV positive people making a combined total of 1.6 million.^{3,6} About six million people are noted to die every year due to HIV/AIDS, TB and malaria, of which, nearly 2 million deaths are due to tuberculosis.^{3,8,50,51}

Tuberculosis is usually evident as pulmonary disease which is responsible for about 80% of cases of TB.^{4,19} The resultant effect of pulmonary tuberculosis is the destruction of lung parenchyma caused by exaggeration of proteases and an aberrant regulation of protease control manifest in mycobacterium infections.^{5,7,57}

There are diversified forms of lung involvement in pulmonary tuberculosis. It can present as parenchymal lesions which include tuberculoma, thin-walled cavities, cicatrization, aspergilloma, end-stage lung destruction and bronchogenic carcinoma; airway lesions which include bronchiectasis, tracheobronchial stenosis and broncholithiasis;^{5,41,42} vascular lesions which include pulmonary or bronchial arteritis and thrombosis, bronchial artery dilatation and Rasmussen aneurysm; mediastinal lesions which include lymph node calcification and extranodal extension, oesophagomediastinal or oesophagobrachial fistula, constrictive pericarditis, fibrosing mediastinitis; pleural lesions which include rib tuberculosis and tuberculous spondylitis.^{5,6,43,49} Bronchiectasis and fungal diseases with subsequent haemoptysis are severe, potentially life threatening complications after successful treatment.^{8,23,24} These bequeath to endless morbidity and mortality as well as considerable strain of medical cost.^{9,78,79}

In spite of satisfactory treatment and clinical response, a good majority of patients are left with residual pulmonary sequelae.^{10,11,53,55}

A substantial number of pulmonary TB survivors have some form of persistent lung function defects despite bacteriological cure which impacts on their subjective well-being, reduce economic productivity as well as cause greater use of healthcare facilities.^{12,45,47} Post-tuberculosis lung disease is identified by abnormal spirometry and recurrent symptoms that are often mistakenly treated as recurrent TB infection with some patients experiencing significant adverse effects from unnecessary TB treatment due to drug toxicity.^{13,14,16} There have been scarcity of data on impaired

pulmonary function in pulmonary tuberculosis survivors, post-tuberculosis lung dysfunction often goes unrecognised despite its relative high prevalence and its association with reduced quality of life.^{5,17,19}

Pulmonary function tests are important in respiratory medicine. They are used to diagnose airway obstruction, assess the severity and prognosis, detect early lung disease and monitor for normal lung growth and lung function decline.^{21,25,26}

Spirometry is the most common pulmonary function test that measures the maximal volume of air that an individual can inspire and expire with maximal effort.^{22,28,29} The primary signal in spirometry is either volume or flow as a function of time. Spirometry is essential in the evaluation of general respiratory health.^{30,31} It is broadly used in the assessment of lung function to provide objective information used in the diagnosis of lung disease and monitoring lung health and enables measurement of the effect of the disease on lung function, assesses airway responsiveness, monitors disease course and determining a prognosis for pulmonary conditions.^{33,34,36,37} It is a beneficial tool that provides important information to clinicians which is used together with other physiological findings, symptoms and history to reach a diagnosis.⁴⁹

Studies of pulmonary function in post-tuberculosis lung disease patients have shown varying patterns and severity of impairment.^{35,38,39} Pulmonary function studies can range from normal to severe impairment and can show restrictive, obstructive, or mixed patterns.^{28,29,30} Those who survive pulmonary TB can come down with post treatment sequelae in the lung that may contribute to increased disability and mortality

METHODS

Study design: This was a hospital based cross sectional comparative study conducted over a seven-month period among post pulmonary tuberculosis patients attending Federal Teaching Hospital, Owerri, Imo state, south Eastern Nigeria. The study recruited about 100 patients aged more than 18 years who had completed treatment for TB and certified cured at the time of treatment completion down to 2 years previously and 100 age-, height- and sex-matched apparently healthy adults comprising individuals within the locale, and patients relatives.

Study instrument and administration:

Information regarding sociodemographics and comorbidities were obtained using an interviewer based questionnaire developed for this study (see supplementary file). Spirometry was carried out on the participants by the researcher who had undergone training in spirometry using a desk top spirometer (MIR Spirolab III version 3.4 ROME ITALY) in an open area with adequate ventilation. Calibration of the spirometer was carried out daily according to ATS/ERS recommendation before the first patient of the day,

after every 4 hours, after a temperature change of 2°C and after every 8th to 10th person using a certified 3 litre calibration syringe, the syringe handle was pulled out completely and about 3 litre volume pushed into the spirometer at the correct flow, the calibration check was repeated at least three different times at different flows to ensure the results were within calibration limit. The participants' data (name, height, weight) were uploaded into the machine and the reference equation chosen. The researcher and assistant wearing face masks and shield carefully explained the procedure to the participants including the forced inspiratory and expiratory manoeuvres; with the participants seated comfortably upright with both feet on the floor with legs uncrossed after it was ensured they were off vigorous exercise, eating and smoking in the preceding one hour (to avoid acute bronchoconstriction from smoke inhalation); consumption of toxicants in the preceding 8 hours (to avoid problems with coordination and comprehension) and clothed in a loose clothing that will not restrict full chest and abdominal movement, the participants were urged to inhale maximally to total lung capacity and after nose clips were applied, to momentarily hold their breath while a tight seal was formed around the disposable mouth piece after which the participants were encouraged to blow out air as forcibly and as fast as possible until their lungs were empty. The participants were given verbal encouragements such as 'you are doing well', 'good', 'good', 'continue', 'one more time' etc particularly towards the end of each manoeuvre to achieve the best possible effort. The test was repeated with a rest interval of about 2 minutes in between manoeuvres until three identical efforts were recorded though not exceeding 8 trials. The researcher also ensured that there were no leaks, no cough, no glottis closure and obstruction of the mouthpiece, no additional breath taken during the manoeuvre, that they kept going until a plateau is seen, no leaning forward during the test and vigorous effort ensured right from the start of the manoeuvre and continuing until no air can be expelled. Acceptability and repeatability of trials were determined using ATS/ERS 2019 guideline.²⁵ The disposable mouth piece was used only once and discarded thereafter.

Obstructive ventilatory defect was defined as forced expiratory volume in one second divided by forced vital capacity less than lower limit of normal with forced vital capacity greater than lower limit of normal.

Restrictive ventilatory defect was defined as forced expiratory volume in one second divided by forced vital capacity greater than lower limit of normal with forced vital capacity less than lower limit of normal.

Mixed ventilatory defect was defined as forced expiratory volume in one second divided by forced vital capacity less than lower limit of normal with forced vital capacity less than lower limit of normal.

Severity of Obstructive, Restrictive and Mixed ventilatory defects were determined using FEV₁ z-score as follows⁹³

For obstructive ventilatory defects.

- Mild: FEV₁/FVC < LLN and FEV₁ z-score ≥ -2
- Moderate: FEV₁/FVC < LLN and FEV₁ z-score between -2.5 and -2
- Moderately severe: FEV₁/FVC < LLN and FEV₁ z-score between -3 and -2.5
- Severe: FEV₁/FVC < LLN and FEV₁ z-score between -4 and -3
- Very severe: FEV₁/FVC < LLN and FEV₁ z-score less than -4

For restrictive ventilatory defects.

- Mild: FEV₁/FVC > LLN and FEV₁ z-score ≥ -2
- Moderate: FEV₁/FVC > LLN and FEV₁ z-score between -2.5 and -2
- Moderately severe: FEV₁/FVC > LLN and FEV₁ z-score between -3 and -2.5
- Severe: FEV₁/FVC > LLN and FEV₁ z-score between -4 and -3
- Very severe: FEV₁/FVC > LLN and FEV₁ z-score less than -4

Lung function impairment was defined as the presence of at least one of these three abnormalities based on the 2012 Global Lung Initiative reference equations for 'others' category as the equations for blacks was largely derived from AfroAmericans.²¹

Data analysis:

Data obtained were entered into Microsoft Excel spreadsheet, assessed for correctness, coded, and subsequently analysed using the IBM Statistical Product and Services (IBM SPSS Statistics) version 25 software (Armonk, NY: IBM Corp). Frequency tables and charts were generated from the results as descriptive statistics. The continuous variables were subjected to the Shapiro-Wilk test of normality to determine whether they were normally distributed or skewed. Continuous variables such as age, oxygen saturation, FEV₁, FVC etc were presented as mean $\pm$ standard deviations (SD) where normally distributed, or medians (interquartile range [IQR]), where skewed. Categorical variables (such as gender, pattern of lung function impairment etc) were expressed as percentages. The independent Student t-test was used to compare continuous data.

A p value of < 0.05 was considered significant.

RESULTS:

The base line data of the participants studied includes the gender distribution, age parameters, anthropometric indices (body mass index). The study participants comprised 100 participants in the case and control group. The post-TB group consisted of 54 (54%) females and 46 (46%) males and the control group consisted of 56 (56%) females and 44 (44%) males, with a M:F ratio of 1:1.22 for the cases and 1:1.27 for the controls ($\chi^2=0.08$, $p=0.776$). There was no statistically significant difference in the mean age of the post-TB patients and the control group (48.0 ± 15.2 years vs 46.7 ± 13.9 years, $t=0.660$; $p=0.510$). The

modal age group was 45 – 54 years for both the post-TB patients (31%) and the control group (28%).

The two groups were comparable in their marital status ($\chi^2=3.81$, $p=0.432$), with married people constituting most of the study population both among the post-TB

patients (47%) and the control group (49%). The case group had a significantly lower level of education, with 16 (16%) individuals in the case group compared to 56 (56%) controls having attained a tertiary education (χ^2 (df) = 39.54 (3), $p<0.001$) as shown in Table 1.

Table 1: Distribution of sociodemographic characteristics of study participants

	Cases n = 100, (%)	Control n = 100, (%)	Chi-square (p-value)
Gender			
Female	54 (54.0)	56 (56.0)	0.08 (0.776)
Male	46 (46.0)	44 (44.0)	
Mean age $\pm$ SD (years)	48.0 $\pm$ 15.2	46.7 $\pm$ 13.9	0.660 (0.510) [†]
Age groups (in years)			
<25	8 (8.0)	6 (6.0)	1.97 (0.894)
25 – 34	11 (11.0)	14 (14.0)	
35 – 44	18 (18.0)	24 (24.0)	
45 – 54	31 (31.0)	28 (28.0)	
55 – 64	18 (18.0)	15 (15.0)	
≥ 65	14 (14.0)	13 (13.0)	
Education			
No formal education	9 (9.0)	0 (0)	39.54 (<0.001)
Primary	39 (39.0)	25 (25.0)	
Secondary	36 (36.0)	19 (19.0)	
Tertiary	16 (16.0)	56 (56.0)	
Marital status			
Single	24 (24.0)	25 (25.0)	3.81 (0.432)
Married	47 (47.0)	49 (49.0)	
Divorced	5 (5.0)	1 (1.0)	
Separated	1 (1.0)	0 (0)	
Widowed	23 (23.0)	25 (25.0)	3.79 (0.052)
Smoking	8 (8.0)	2 (2.0)	
Alcohol	16 (16.0)	0 (0)	17.39 (<0.001)
Comorbidities			
Diabetes	1 (1.0)	1 (1.0)	0 (1.000)
Hypertension	5 (5.0)	1 (1.0)	2.75 (0.097)
HIV	19 (19.0)	6 (6.0)	7.73 (0.005)

[†] independent Student-t test

The post-TB cases had similar heights to their controls. However, the participants in the control group had a statistically significantly higher body mass indices ($25.5 \pm 4.7 \text{ kg/m}^2$ vs $22.3 \pm 4.1 \text{ kg/m}^2$, $p<0.001$) than those in the post-TB group ($t -4.14$, $p<0.001$). Obesity

was similarly more prevalent in the controls than in the post-TB cases (15 (15%) vs 4 (4%); $\chi^2=19.82$, $p<0.001$) as summarised in Table 2.

Table 2. Distribution of anthropometry and other clinical indices in study participants

	Cases n = 100 mean $\pm$ SD	Control n = 100 mean $\pm$ SD	Student t (p-value)
Mean weight $\pm$ SD (kg)	62.1 $\pm$ 10.9	69.3 $\pm$ 13.6	-4.14 (<0.001)
Mean Height $\pm$ SD (meters)	1.67 $\pm$ 0.10	1.65 $\pm$ 0.08	1.82 (0.07)
BMI (kg/m²)	22.3 $\pm$ 4.1	25.5 $\pm$ 4.7	-5.03 (<0.001)
BMI categories			
Underweight	18 (18.0)	3 (3.0)	19.82 (<0.001) [¶]
Normal	57 (57.0)	50 (50.0)	
Obesity	4 (4.0)	15 (15.0)	
Overweight	21 (21.0)	32 (32.0)	

Systolic blood pressure (mmHg)	121.5 ± 14.8	123.1 ± 10.6	-0.90 (0.368)
Diastolic blood pressure (mmHg)	74.3 ± 8.4	72.4 ± 4.9	1.88 (0.062)
Pulse rate (bpm)	82.0 ± 12.2	78.9 ± 10.3	1.95 (0.053)
Respiratory rate (cpm)	20.7 ± 1.8	20.3 ± 1.4	1.82 (0.07)
Oxygen saturation (%)	97.4 ± 1.6	97.9 ± 1.4	-2.65 (0.009)

† Chi-square test

The mean FEV₁ among the post-TB cases was 1.93 ± 0.73L (median z-score -2.06) comparatively lower to that of the control group with mean FEV₁ of 2.40 ± 0.64L (median z-score -0.7) and the difference was statistically significant (t -4.79, p<0.001). Similarly, the mean FVC among the post-TB cases was 2.72 ± 0.87L (median z-score -2.27) which was lower compared to the control group with mean FVC of 3.12

± 0.88L (median z-score -0.31) and the difference was statistically significant (t -3.22, p=0.001). Also the mean FEV₁/FVC of 69 ± 12.4 among the post-TB cases (t -5.62, p<0.001), mean FEF₂₅₋₇₅ of 1.57 ± 0.83 (t -4.67, p<0.001) and mean PEFR of 4.66 ± 1.92 (t -5.34, p<0.001) were statistically significantly lower in the post-TB cases compared to the control group as shown in table 3

Table 3. Lung function indices of study participants with their z-scores

	Cases n = 100 mean ± SD	Control n = 100 mean ± SD	Student t (p-value)
FEV₁ (litres)	1.93 ± 0.73	2.40 ± 0.64	-4.79 (<0.001)
FEV₁ z-score	-2.06 (-2.80 – -0.55) †	-0.71 (-0.96 – -0.27) †	2769 (<0.001) ‡
FVC (litres)	2.72 ± 0.87	3.12 ± 0.88	-3.22 (0.001)
FVC z-score	-2.27 (-2.30 – -0.24) †	-0.31 (-0.84 – -0.26) †	3417 (<0.001) ‡
FEV₁/FVC (%)	69.5 ± 12.4	77.7 ± 7.9	-5.62 (<0.001)
FEV₁/FVC z-score	-1.38 (-2.33 – -0.94) †	-1.34 (-1.38 – -1.21) †	4137 (0.035) ‡
FEF₂₅₋₇₅ (l/sec)	1.57 ± 0.83	2.09 ± 0.75	-4.67 (<0.001)
PEFR (l/sec)	4.66±1.92	6.16±2.04	-5.34 (<0.001)

† median (interquartile ranges), ‡ Mann-Whitney U test

The prevalence of lung function impairment was 71% among the post-TB cases compared to 12% in the controls ; this was statistically significant as the odds of lung function impairment were 18.0 (95% CI: 8.55 to

37.7, p<0.001) times higher in the post-tuberculosis patients than in their controls as shown in figures 1, 2 and 3 respectively.

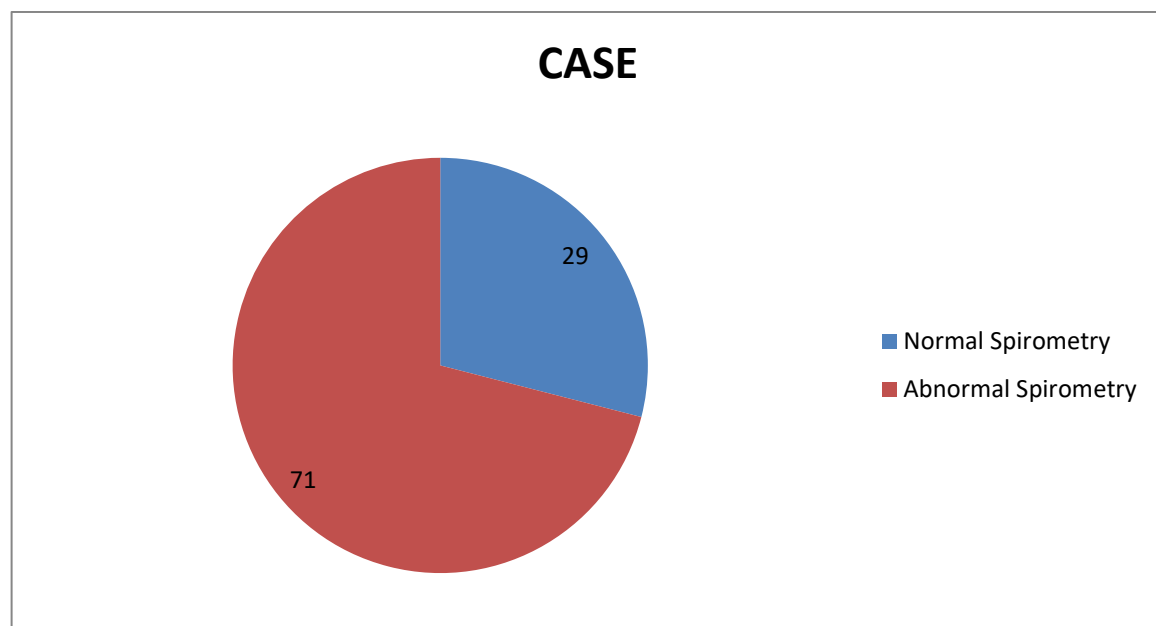


Figure 1. Prevalence of abnormal spirometry among cases

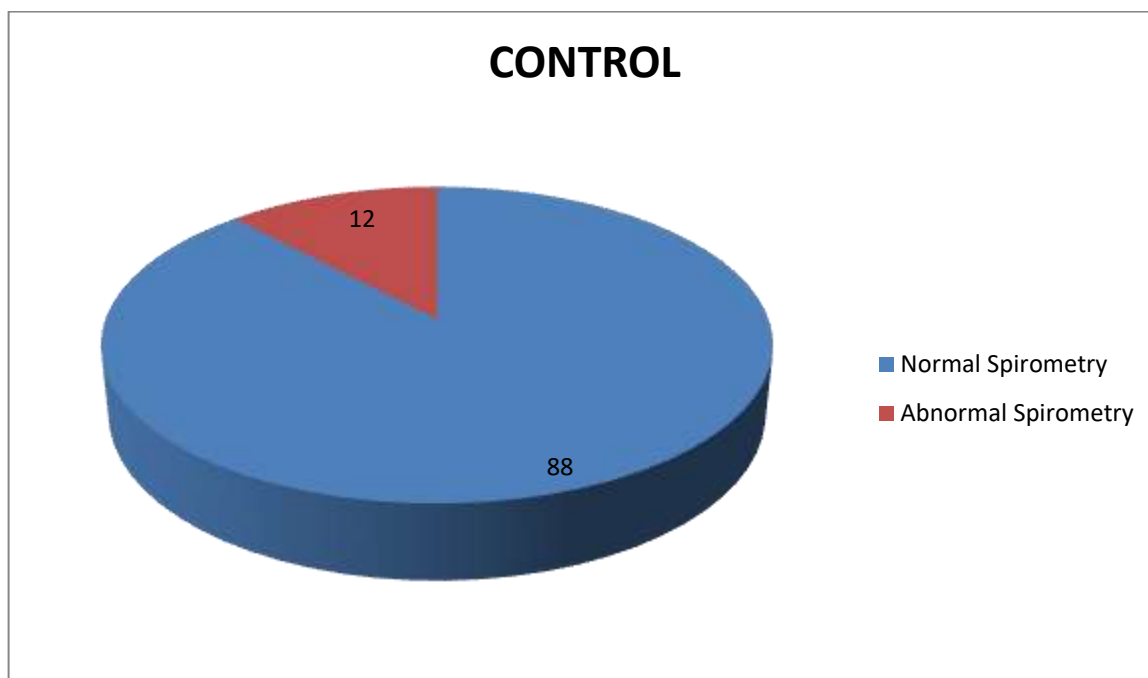


Figure 2. Prevalence of abnormal spirometry among controls

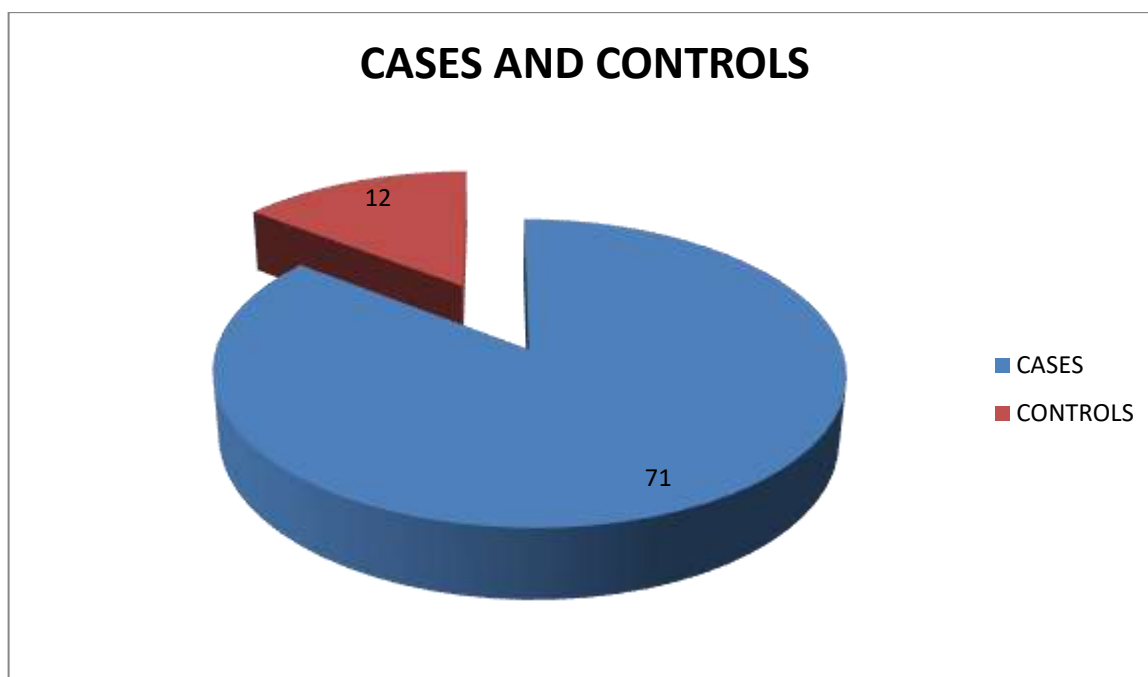


Figure 3. Abnormal lung function in study participants

Obstructive ventilatory pattern was the commonest ventilatory pattern seen in 29 (29%) post-TB patients, followed by the restrictive 28 (28%), and then mixed 14 (14%) compared with obstructive 8(8%), restrictive

3(3%) and mixed 1(1%) in the control group; the difference was statistically significant ($\chi^2=73.10$, $p<0.001$), as summarised in tables 4 and 5 below

Table 4. Lung function indices of study participants with their z-scores

	Cases <i>n</i> = 100 mean $\pm$ SD	Control <i>n</i> = 100 mean $\pm$ SD	Student t (<i>p</i> -value)
FEV₁ (litres)	1.93 $\pm$ 0.73	2.40 $\pm$ 0.64	-4.79 (<0.001)
FEV₁ z-score	-2.06 (-2.80 – -0.55) †	-0.71 (-0.96 – -0.27) †	2769 (<0.001) ‡
FVC (litres)	2.72 $\pm$ 0.87	3.12 $\pm$ 0.88	-3.22 (0.001)
FVC z-score	-2.27 (-2.30 – -0.24) †	-0.31 (-0.84 – -0.26) †	3417 (<0.001) ‡

FEV₁/FVC (%)	69.5 ± 12.4	77.7 ± 7.9	-5.62 (<0.001)
FEV₁/FVC z-score	-1.38 (-2.33 – -0.94) [†]	-1.34 (-1.38 – -1.21) [†]	4137 (0.035) [‡]
FEF₂₅₋₇₅ (l/sec)	1.57 ± 0.83	2.09 ± 0.75	-4.67 (<0.001)
PEFR (l/sec)	4.66±1.92	6.16±2.04	-5.34 (<0.001)

[†] median (interquartile ranges), [‡] Mann-Whitney U test

Table 5. Distribution of lung function patterns in study participants

Lung Function Pattern	Cases (n, %)	Control (n, %)	Chi-square (p-value)
Normal	29 (29.0)	88 (88.0)	73.10 (<0.001)
Obstructive	29 (29.0)	8 (8.0)	
Restrictive	28 (28.0)	3 (3.0)	
Mixed	14 (14.0)	1 (1.0)	
Total	100 (100.0)	100 (100.0)	

Majority of the post-TB cases with obstructive 20 (69%) and restrictive 17 (60.7%) spirometric patterns had moderate severity with a mean FEV1 z-scores of -2.22 ± 0.34 and -2.41 ± 0.4 respectively, followed by those with mild severity noted 9 (31%) and 5 (17.9%)

of those with obstructive and restrictive patterns, respectively. The least frequency was observed with very severe restrictive pattern in 2 (7.1%) post-TB cases as depicted in tables 6 and 7.

Table 6. Distribution of lung function impairment by severity in study participants

Severity of functional impairment	CASES			CONTROLS		
	Obstructive n=29 mean ± SD	Restrictive n=28 mean ± SD	Mixed n=14 mean ± SD	Obstructive n=8 median ± SD	Restrictive n=3 mean ± SD	Mixed n=1 mean±SD
Mild	-0.72 (-1.41 – 0.23) [¶]	-1.71 ± 0.45	-	-0.87 (-0.94 – 0.74) [¶]	-	-
Moderate	-2.22 ± 0.34	-2.41 ± 0.4	-2.31 ± 0.12	-2.23 ± 0.13	-2.1 ± 0.25	-
Severe	-	-3.65 ± 0.31	-3.48 ± 0.23	-	-	-3.4
Very severe	-	-4.35 ± 0.21	-	-	-	-

[¶] Median (interquartile range – IQR)

Severity of functional impairment	CASES				CONTROLS			
	Obstructive (n, %)	Restrictive (n, %)	Mixed (n, %)	Total (n, %)	Obstructive (n, %)	Restrictive (n, %)	Mixed (n, %)	Total (n, %)

Table 7 Distribution of severity of lung function patterns by FEV1 z-scores

Severity of functional impairment	CASES			CONTROLS		
	Obstructive n=29 mean ± SD	Restrictive n=28 mean ± SD	Mixed n=14 mean ± SD	Obstructive n=8 median ± SD	Restrictive n=3 mean ± SD	Mixed n=1 mean±SD
Mild	-0.72 (-1.41 – 0.23) [¶]	-1.71 ± 0.45	-	-0.87 (-0.94 – -0.74) [¶]	-	-
Moderate	-2.22 ± 0.34	-2.41 ± 0.4	-2.31 ± 0.12	-2.23 ± 0.13	-2.1 ± 0.25	-
Severe	-	-3.65 ± 0.31	-3.48 ± 0.23	-	-	-3.4
Very severe	-	-4.35 ± 0.21	-	-	-	-

[¶] Median (interquartile range – IQR)

DISCUSSION

Pulmonary tuberculosis is a communicable disease that is a major cause of ill health and one of the leading causes of death worldwide.^{2,14,80,81} The burden of post-tuberculosis lung disease seems to be on the rise resulting in debilitation among survivors. The post-tuberculosis condition is poorly defined with

respect to chronic respiratory impairment in TB survivors.

This study was a cross sectional comparative study that evaluated the prevalence and patterns of spirometric abnormality post-treatment TB patients in comparison to apparently healthy controls who were matched for age, sex and height.

This study showed a higher percentage of females (54%) compared to males (46%) similar to the findings by Ozoh et al²¹ and Halal et al¹⁴. This observation could be attributable to women having better health care seeking behaviour than men even though tuberculosis is said to generally affect more males than females.^{74,76,77} A smaller proportion of the post-TB patients 16 (16%) had tertiary education compared to the control where 56 (56%) had a tertiary education and this was statistically significant across the two groups, higher educational status could have contributed to higher socio-economic and better health status which could minimise the risk of contracting tuberculosis.^{66,67,68} Tuberculosis has been linked with environmental risk factors that go hand in hand with poverty, indoor air pollution, tobacco smoke, malnutrition, overcrowded living conditions and low educational status.^{70,72,73} Other studies had corroborated a similar association between tuberculosis and low educational status.⁹⁴⁻⁹⁶ This study also showed a statistically significant difference in the mean weight between the cases and the controls as evidenced by lower body mass index in the cases when compared with the control group and may suggest that adequate nutrition may enhance the body's immune system and provide a better defensive mechanism against tuberculosis.^{75,97} A similar observation was noted by Aaron et al where he observed a correlation between BMI and tuberculosis.⁹⁸ Association between malnutrition and tuberculosis is well established, malnutrition adversely affects both innate and adaptive immunity of individuals making them susceptible to a variety of infections such as tuberculosis.^{90,91,99} Tuberculosis contribute to malnutrition through various mechanisms which include cytokine activation, abnormal protein metabolism, loss of lean tissue and body reserves which could present as fever, anorexia, sweating and weight loss.^{93,101,103}

This study showed that the prevalence of lung function impairment was statistically significantly higher in post-TB patients than those of the controls. The overall prevalence of lung function impairment in post-TB patients in the study population was 71% in the cases which is comparable to 72% reported in Ilorin,⁹² 74% reported in Tanzania,³⁰ 76% reported in Egypt²⁰ and 68.2% reported in Mozambique.¹³ The different prevalence rates could be as a result of different geographical locations, possible effects of topography and ambient temperatures as the present study was carried out in Owerri, South Eastern Nigeria which is located in a valley with higher ambient temperature and could give rise to lower values of FEV₁ and FVC than obtained in areas of lower ambient temperatures.¹⁰⁴ A study on post-TB patients in Lagos reported higher prevalence rate of 88.7%.²¹ The higher prevalent rate in the later study could be as a result high population density, overcrowding and high level of pollution in the study area. However, other studies have reported lower rates such as 48% in the Breede Valley district of South Africa,⁸² 45% in Cotonou Benin,¹⁰² 34.4% in Malawi,⁸⁸ The lower prevalence rate could be because younger participants (≥ 15 years) with a median age of 35 years

was recruited in the later study contrary to this study that recruited older participants (≥ 18 years) with a mean age of 48 years as lung function has been known to decline with age. The local ecology of mycobacterial genotypes/strains could account for geographic variation in TB disease. In West Africa, *M. tuberculosis* strains co-circulate with *M. Africanum* and both pathogens cause pulmonary disease in humans;^{63,64,65} almost half of all TB cases in West African countries eg Nigeria are caused by infection with a member of the mycobacteria tuberculosis complex, *M. Africanum* and could contribute to higher prevalence rates in the affected areas,^{83,89} however, the concept of mycobacterial genotyping is beyond the scope of this work. Some prospective cohort studies have reported declining prevalence rates across varying weeks of TB treatment.^{84,85} A prospective cohort study of 69 patients in Mozambique reported the prevalence of lung impairment at 8, 26, and 52 weeks after treatment completion to be 78%, 68.9% and 64.5% respectively.¹³ This finding is contrary to Chung et al who reported lower spirometry values 18 months post-treatment; however their study included patients who were treated for non-tuberculous mycobacteria.¹⁰⁵ Hnizdo et al similarly reported decreased lung volume 6 months after treatment with stabilization of the changes between 7-12 months despite the fact that their sample was composed of coal miners and included more than one episode of PTB,⁸⁶ where as a longitudinal study by Allwood et al reported that lung volumes improved and CT fibrosis score decreased, but features of chronic airflow obstruction and gas trapping emerged after PTB treatment.¹⁰⁶ The discrepancies in the various reported prevalence rates may be attributable to the duration from tuberculosis infection to commencement of treatment and the severity of lung damage. It can also be due to differences in the geographical region, value cut off and reference equations used as a Russian study used FEV₁ below 60% as a cut-off for abnormality, use of fixed reference equations may over predict abnormality especially in older people. Countries with high TB burden like Tanzania, Egypt and Malawi reported higher prevalence than was reported in areas of low TB burden.^{22,27}

Immune mediators and pathways that promote caseous necrosis and pulmonary cavitation can give rise to airway obstruction during tuberculosis disease and later progress to fibrosis.⁵⁸⁻⁶²

This study found the obstructive ventilatory pattern as the predominant abnormality, similar to reports by Patil,³² Fiogbe,¹⁰² Manji³⁰ and Allwood et al³⁵ which demonstrated obstructive pattern as the predominant impairment in around 42%, 32.8%, 42% and 38% of the study population respectively as well as an Egyptian study that reported obstruction in 31.98%.²⁰ There is however a great difference in the proportion of obstructive lung disease between this study and the Ilorin study which reported 5.8%.⁹² The extent of lung affection as well as the predominant mechanism of lung involvement at the time of spirometric assessment may explain the observed differences in the

predominant ventilatory patterns reported in different studies. Majority of the patients with obstructive spirometric patterns in this study had moderate severity followed by those with mild obstruction in contrast to a Nigerian study that reported most of the study population having very severe ventilatory impairment.²¹ Some other studies have found restrictive ventilatory defect to be the main spirometry abnormality.^{87,92} Restriction in patients with tuberculosis may be explained by structural changes in the lungs as a result of aberrant lung tissue repair such as bronchovascular distortion, fibrotic bands and pleural thickening. There is also reduced ability to inhale fully as a result of extensive fibrosis and stiffening of the lung parenchyma. This study reported restriction in 28% of the study population lower than 36.1% reported by Mbatchou et al in Cameroun⁸⁷ and 42.2% reported in Ilorin, Southwestern Nigeria.⁹² There could be significant overlap of obstructive and restrictive impairment mechanisms in those with tuberculosis with some researchers suggesting that immune mediators and pathways that drive caseous necrosis and pulmonary cavitation which can lead to airflow obstruction during the disease and may also set up for later fibrosis. This study reported mixed ventilatory pattern as the least spirometric abnormality occurring in 14% of the study population. A previous study in Nigeria reported mixed pattern as the predominant spirometric impairment in 30% of the study population.²¹ There was a significant reduction in the mean lung volumes of post-TB patients compared to the controls. These findings are similar to a Tanzanian study that reported significant reduction in mean lung volumes of post-TB patients.³⁰ The lower lung volumes post-tuberculosis treatment may occur due to destruction of lung parenchyma leading to reduction in lung volumes. Studies by Chuskin,²⁹ Taylor¹⁰⁷ and Ojuawo et al⁹² have corroborated the findings in this study.

The limitations to this study is that Chest x-rays and Chest CT scan that could characterize the extent of lung damage were not done, as this research was self-funded. These investigations are expensive in resource poor countries like Nigeria. Also, Participants' baseline lung function before commencement of treatment for tuberculosis was not done as it could have helped to further strengthen the causal relationship between TB and post-TB sequelae. This was a cross-sectional rather than a longitudinal study.

CONCLUSION

The prevalence of Spirometric abnormality was high in post-TB patients and respiratory function impairment after tuberculosis as one of the chronic lung diseases appears underestimated. Lung function patterns occurring in Post-Tuberculosis clients include Obstructive, Restrictive and Mixed, but could be normal. Post-Tuberculosis Chronic Respiratory Disease is prevalent among post-treatment/cured Tuberculosis clients.

RECOMMENDATIONS

Based on the findings in this study, the following are recommended

- 1) A routine follow up evaluation of lung function of patients after treatment for tuberculosis to detect those with a residual respiratory impairment who might benefit from respiratory clinic follow up such as Chest Physiotherapy and Rehabilitation.
- 2) Prospective and longitudinal follow-up studies are advised to understand further, the disease trajectory over time.
- 3) Increased community advocacy, sensitization and awareness programs with emphasis on timely hospital presentation and early commencement of anti-tuberculosis medications.

LIST OF ABBREVIATIONS

AFB:	Acid fast bacilli
ANOVA:	Analysis of Variance
ATS:	American Thoracic Society
AIDS:	Acquired immune deficiency syndrome
CD:	Cluster designation
COPD:	Chronic obstructive pulmonary disease
DNA:	Deoxyribonucleic acid
ERS:	European Respiratory society
FEV ₁ :	Forced expiratory volume in one second
FVC:	Forced vital capacity
FIVC:	Forced inspiratory vital capacity
FEF:	Forced expiratory flow
GDP:	Gross Domestic Product
HIV:	Human Immunodeficiency virus
IFN:	Interferon
IQR:	Interquartile range
IGRA:	Interferon gamma release assay
IL:	Interleukin
mRNA:	messenger RNA
MIR:	Medical International Research
MMP:	Matrix metalloproteinase
PTB:	Pulmonary Tuberculosis
TGFB:	Transforming growth factor beta

Declarations

Ethics approval and consent to participate

This study was carried out in compliance with the Declaration of Helsinki. Ethical approval and consent to participate: Approval from the Ethics and Research Committee of the Federal Teaching Hospital, Owerri (FMC/OW/HREC/VOL.11/78) was sought and obtained before the commencement of the study,. Informed consent was obtained from all the participants. On arrival, a written informed consent was extracted before inclusion. Written, informed consent was obtained from each participant prior to recruitment

into the study and participants were at liberty to withdraw from the study at any stage without consequences.

Consent for publication: not applicable as no identifying images or personal details of participants are presented

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Authors' Contributions

CV envisioned the study, collated data, interpreted results, and wrote the manuscript.

CC assisted with study attainment, revision and supervision of the manuscript, GC supervised the manuscript, COU analysed and generated data, CF assisted with data collation.

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