

Evaluation of Post-Treatment Health- Related Quality of Life (HRQoL) Lung Function and Exercise Capacity in A Cured Tuberculosis Population: A Prospective Cohort Study

Amsha Ghazi

Masters in Cardiopulmonary Physiotherapy (MSCPPT), Riphah International University, Gulberg Green Campus, Islamabad. Amshaghazi05@gmail.com

Tahir Latif

Loralai Medical College, Loralai, Professor Community Medicine. drtahirmusakhail1988@gmail.com ORCID: 0009-0006-9692-7135

Sahifa Fatima Memon

Genetic Engineering and Biotechnology, University of Sindh. sahifa.memon24@gmail.com

Mustafa Zaveri

Karachi Institute of Physiotherapy and Rehabilitation Sciences, Saifee Burhani University. principal.kiprs@gmail.com

Rida Noor

Karachi Institute of Physiotherapy and Rehabilitation Sciences, Karachi, Pakistan. ridanoorkhan2024@gmail.com

Author Details

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Corresponding E-mail & Author*:

Tahir Latif (Corresponding)

Loralai Medical College, Loralai, Professor Community Medicine. drtahirmusakhail1988@gmail.com ORCID: 0009-0006-9692-7135

Abstract

Background: Many survivors of tuberculosis continue to have impaired lung function and diminished quality of life despite achieving microbiological cure.

Objective: To evaluate the level of post-treatment health-related quality of life (HRQoL), lung function and exercise capacity in a prospective cohort study of cured pulmonary TB patients.

Methodology: This was a prospective longitudinal cohort study carried out at the Federal Government Tuberculosis Center, Rawalpindi, Pakistan from June 2023 to May 2024. After completion of ATT, 68 eligible participants were enrolled and 52 patients completed all follow-up assessments and were included in the final analysis. Spirometry, chest radiography, 6MWT, Modified Borg Scale and SF-36 questionnaire were used to assess the participants at baseline, 3 months, and 6 months. Repeated Measures ANOVA was used for data analysis and p-values < 0.05 were deemed significant.

Results: The mean age of participants was 31.31 ± 11.87 years, with males and females equally represented (26; 50.0% each). Bilateral lung involvement was observed in 27 (51.9%) patients. Pulmonary function significantly declined during follow-up, with FEV1 decreasing from 31.98 ± 12.93 to 29.99 ± 15.75 and FVC from 37.19 ± 12.28 to 32.78 ± 11.40 ($p < 0.001$). Chest infiltrates improved from 52 (100%) patients at

baseline to 39 (75.0%) at 6 months, while consolidation reduced from 35 (67.3%) to 18 (34.6%). Exercise capacity showed no significant improvement, although dyspnea scores significantly improved ($p < 0.001$). SF-36 analysis demonstrated improvement in emotional well-being and pain domains, while most quality-of-life domains remained persistently impaired.

Conclusion: Patients with cured pulmonary TB still have significant long-term deficits in lung function, exercise capacity and quality of life and require rehabilitation and follow-up programs to address these deficits.

1. Introduction

Tuberculosis (TB) is still one of the biggest infectious diseases in the world and is a major public health problem, especially in low and middle-income countries where diagnosis is delayed, socioeconomic barriers to treatment contribute to ongoing transmission of TB and the scarcity of healthcare infrastructure leads to high burden of disease [1,2]. Although the treatment of pulmonary tuberculosis is effective and similar treatment regimens are used throughout the world, the disease remains a problem for millions of people every year, and causes significant morbidity even after the organism has been cured [3].

In the past TB management has been mainly about sputum conversion and stopping the spread of TB transmission. But there is growing evidence however that it is not always possible to achieve microbiological cure, which is synonymous with complete functional recovery [4]. Many people who reported themselves as "cured" still have a significant number of people that have ongoing symptoms in their respiratory system, decrements in lung function, and loss of exercise capacity. The observations suggest that TB not only be a treatable acute infectious illness but also a long-term functional and structural illness [5,6].

In spite of successful treatment, structural damage to the lungs due to TB (fibrosis, bronchiectasis, distortion of airways, destruction of parenchymal tissue) is common [7]. These structural changes are irreversible or at least partially irreversible and result in long lasting impairments of ventilatory mechanics, in the efficiency of gas exchange, and in the limitation of physical performance [8]. Thus, there are many people with long-term respiratory impairment after microbiological cure of the illness [9].

Post-tuberculosis sequelae not only impair the body function, but also significantly affect health-related quality of life (HRQoL) [10]. Fatigue and exertional dyspnea, decreased physical endurance, and social and emotional dysfunction are common patient-reported symptoms [11]. This emphasizes TB as a dual burden disease with not only infectious, but chronic disability-related consequences beyond treatment completion. Thus, assessment of HRQoL offers valuable information on the overall effects of disease recovery [12].

Pulmonary dysfunction can be quantified by objective measures, including spirometry; and exercise capacity measures, like the 6MWT, can assess integrated exercise cardiopulmonary function [13]. In a similar fashion, validated instruments like the SF-36 questionnaire offer multi-dimensional assessment of physical, psychological and social health domains. These two assessments provide a comprehensive and holistic assessment of post treatment recovery in TB survivors [14].

Although there is growing awareness of the morbidity of post-tuberculosis lung disease, few prospective longitudinal studies exist to evaluate the effects of treatment on lung function, exercise capacity, or quality of life following the end of treatment, especially in resource-limited areas where long-term follow-up has not been well established.

Research Objective

The objective of this study was to determine the post-treatment HRQoL, lung

function, and exercise capacity in a cured pulmonary tuberculosis population using a prospective cohort study design.

Methodology

Study Design

This study aimed to assess HRQoL, lung function and exercise capacity in a prospective longitudinal cohort study of those individuals who have finished therapy for pulmonary tuberculosis. The future design enabled multiple observations over time to evaluate functional recovery and ongoing impairments after microbiological cure.

Study Setting and Duration

This study was carried out at the Federal Government Tuberculosis Center, Rawalpindi, Pakistan in collaboration with Riphah International University, Islamabad. The data collection period was from 1st June 2023 to 1st May 2024. Follow-up assessments were conducted at baseline, 3 months, and 6 months after treatment completion.

Study Population and Sampling

In total 80 persons were tested for eligibility, 68 persons fulfilled the inclusion criteria and participated in the study. Eventually, 52 participants finished all follow-up assessments, and these were used in the final analysis. The attrition was largely due to loss to follow up and to the fact that some data were not collected, which was taken into account in the final data analysis.

Eligibility Criteria

Participants were adults 18 to 60 years of age and either male or female, who had completed standard anti-tuberculous therapy (SAT) according to World Health Organization (WHO) guidelines, had been confirmed to be microbiologically negative by sputum microscopy and/or GeneXpert MTB/RIF. The informed consent was obtained in writing before the participants were enrolled. Patients were excluded if they had an active history of tuberculosis, pre-existing chronic lung disease (such as chronic obstructive pulmonary disease and asthma), pulmonary malignancy, significant cardiovascular disease that precluded functional testing, pregnancy, physical handicap that would not allow for independent ambulation, or cognitive dysfunction that would interfere with functional testing.

Data Collection Procedure

After getting ethical approval, patients were recruited from the outpatient clinic of the post-treatment follow-up. A standard data collection form was used to capture baseline demographic and clinical parameters, such as age, gender, body mass index, occupation, vital signs, and duration of treatment. All subjects were assessed at baseline and at 3 and 6 months' follow-up on a standardized protocol.

Outcome Measures

The validated short form-36 (SF-36) questionnaire was used to measure HRQoL, which measures eight domains: physical functioning, role physical, role emotional, energy/fatigue, emotional well-being, social functioning, pain, and general health perception. Scores of 0-4 indicate low perceived health status and functional well-being while higher scores indicate better perceived health status and functional well-being. Digital spirometry was performed to measure pulmonary function according to the guidelines of the American Thoracic Society (ATS). Objective assessments of ventilatory impairment were made by measuring the forced expiratory volume in one second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio and peak expiratory flow rate (PEF). Six-minute walk test (6MWT) was used to measure exercise capacity. Distance walked, percentage of predicted distance, heart rate and changes in oxygen saturation were measured. Modified Borg Scale was used to quantify breathlessness before and after exercise testing to assess dyspnea. To correlate the functional outcomes with the radiologic features of the chest radiographs, assessment of residual post-tuberculous structural changes (fibrosis, infiltrates, consolidation) was made.

Statistical Analysis

Data were analyzed by using the software of Statistical Package for Social Sciences (SPSS) version 26. Values of continuous variables are described as mean \pm SD, and categorical variables as frequencies and percentages. Changes over baseline, 3-month and 6-month follow-up were evaluated using repeated measures analysis of variance (ANOVA). Pairwise comparisons were conducted as appropriate to determine specific differences at time points. Partial eta squared was used to determine the effect size of observed changes. A p value < 0.05 was deemed significant.

Ethical Considerations

The study was approved by the institutional ethical review committee before the study was started. Written informed consent was obtained after full explanation of study procedures after all participants. All of the participant data was kept confidential and anonymous throughout this study, and all methods were performed in accordance with the Declaration of Helsinki principles.

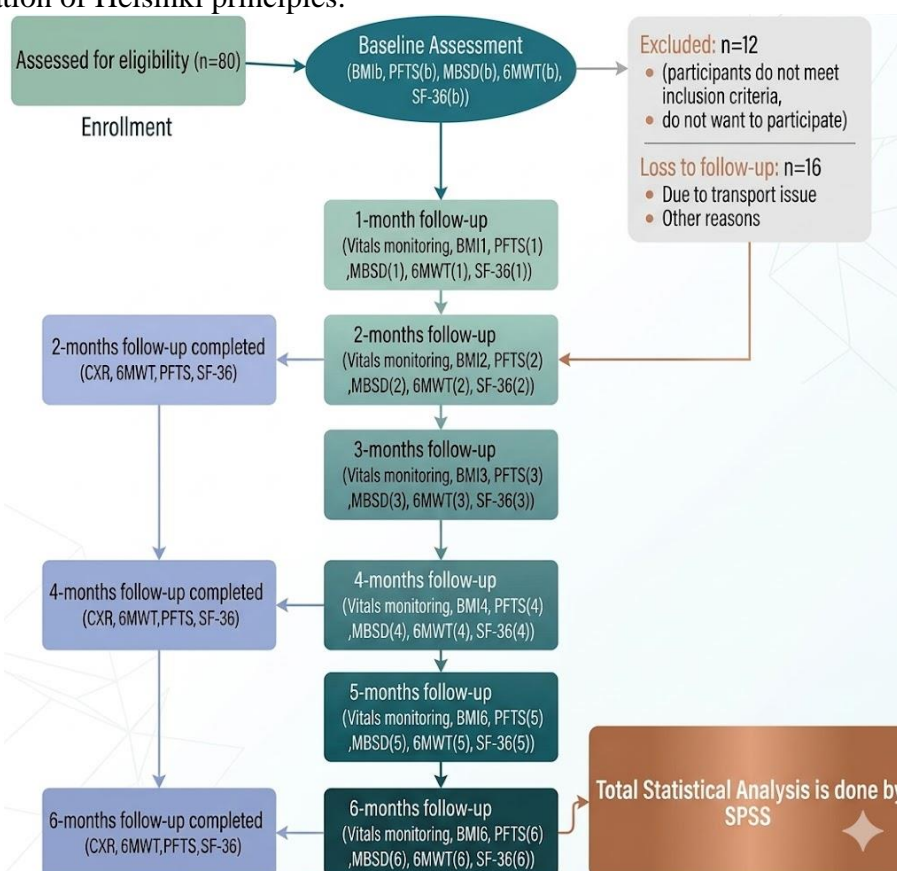


Figure 1. Flow Diagram of Participant Recruitment, Follow-up, and Outcome Assessment

Results

The baseline characteristics showed that the mean age of participants was 31.31 ± 11.87 years, with equal gender distribution including 26 (50.0%) males and 26 (50.0%) females (table 1). The mean BMI was low at 18.36 ± 4.80 kg/m², indicating undernutrition among many participants. Bilateral lung involvement was the most common finding in 27 (51.9%) patients, while right lung involvement was observed in 12 (23.1%) and left lung involvement in 13 (25.0%) participants. The average treatment duration was 6.69 ± 0.76 months.

Table 1. Baseline Demographic and Clinical Characteristics (n = 52)

Variable	Category	Frequency (n;%) / Mean \pm SD
Age (years)	Mean \pm SD	31.31 ± 11.87
Gender	Male	26 (50.0%)
	Female	26 (50.0%)
BMI (kg/m ²)	Mean \pm SD	18.36 ± 4.80

Lung involvement	Right lung	12 (23.1%)
	Left lung	13 (25.0%)
	Bilateral lungs	27 (51.9%)
Treatment duration (months)	Mean ± SD	6.69 ± 0.76

Pulmonary function tests demonstrated progressive decline during follow-up (table 2). Mean FEV1 decreased from 31.98 ± 12.93 at baseline to 29.99 ± 15.75 at 6 months, while FVC declined from 37.19 ± 12.28 to 32.78 ± 11.40. Similarly, PEF reduced from 26.01 ± 12.88 to 22.65 ± 12.65. All reductions were statistically significant ($p < 0.001$), indicating persistent deterioration in lung function after TB cure.

Table 2. Pulmonary Function Tests Over Follow-Up

Variable	Baseline	3 Months	6 Months	p-value	Interpretation
FEV1	31.98 ± 12.93	30.77 ± 14.27	29.99 ± 15.75	<0.001	Significant decline over time
FVC	37.19 ± 12.28	34.85 ± 11.94	32.78 ± 11.40	<0.001	
PEF	26.01 ± 12.88	24.03 ± 11.79	22.65 ± 12.65	<0.001	

Abbreviations: FEV1 = Forced Expiratory Volume in 1 second; FVC = Forced Vital Capacity; PEF = Peak Expiratory Flow.

Radiological assessment showed gradual improvement over time. Chest X-ray infiltrates decreased from 52 (100%) at baseline to 39 (75.0%) at 6 months (table 3). Mild fibrosis reduced from 35 (67.3%) to 31 (59.6%), while moderate fibrosis decreased from 13 (25.0%) to 7 (13.5%). Consolidation also improved markedly from 35 (67.3%) to 18 (34.6%), suggesting partial radiological recovery following treatment completion.

Table 3. Radiological Findings Over Follow-Up

Variable	Baseline	6 Months	Interpretation
CXR infiltrates present	52 (100%)	39 (75.0%)	Radiological improvement (reduction in infiltrates)
Mild fibrosis	35 (67.3%)	31 (59.6%)	Slight reduction in fibrotic changes
Moderate fibrosis	13 (25.0%)	7 (13.5%)	Marked reduction in moderate fibrosis
Consolidation present	35 (67.3%)	18 (34.6%)	Significant resolution of consolidation

Exercise capacity remained persistently reduced throughout follow-up (table 4). The mean 6MWT distance was 313.13 ± 104.84 meters at baseline and 300.92 ± 140.71 meters at 6 months, with no statistically significant change ($p = 0.16$). Expected walking distance percentages also remained low. However, dyspnea improved significantly, as the Modified Borg Scale decreased from 4.84 ± 1.17 to 3.96 ± 1.45 ($p < 0.001$), indicating symptomatic improvement despite limited functional recovery.

Table 4. Exercise Capacity and Dyspnea Over Follow-Up

Variable	Baseline	3 Months	6 Months	p-value	Interpretation
6MWT (meters)	313.13 ± 104.84	297.98 ± 124.12	300.92 ± 140.71	0.16	No significant change in exercise capacity
Expected distance (%)	43.05 ± 12.17	41.39 ± 15.30	41.85 ± 18.45	—	Persistently reduced exercise performance

Modified Borg Scale	4.84 ± 1.17	4.07 ± 1.26	3.96 ± 1.45	<0.001	Significant reduction in dyspnea (symptom improvement)
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SF-36 quality of life analysis showed mixed outcomes (table 5). Physical functioning, energy/fatigue, social functioning, and general health domains showed no significant changes ($p > 0.05$). Emotional well-being improved significantly from 43.73 ± 12.44 to 46.88 ± 13.12 ($p < 0.05$), while pain scores improved from 35.51 ± 13.14 to 41.36 ± 13.90 ($p < 0.05$). In contrast, role limitation due to emotional problems worsened from 24.30 ± 30.29 to 18.05 ± 23.04 ($p < 0.05$). Health change scores improved temporarily at 3 months from 37.11 ± 25.57 to 44.80 ± 21.60 before declining at 6 months.

Table 5. SF-36 Quality of Life Scores Over Follow-Up

Domain	Baseline	3 Months	6 Months	p-value	Interpretation
Physical functioning	45.76 ± 19.71	47.01 ± 16.00	47.59 ± 18.66	>0.05	No significant change
Role limitation (physical)	20.48 ± 25.57	20.28 ± 23.14	20.38 ± 20.28	>0.05	No significant change
Role limitation (emotional)	24.30 ± 30.29	25.49 ± 25.83	18.05 ± 23.04 ↓	<0.05	Significant deterioration at 6 months
Energy/Fatigue	41.73 ± 10.04	42.78 ± 10.81	42.69 ± 13.70	>0.05	No significant change
Emotional well-being	43.73 ± 12.44	46.00 ± 11.35	46.88 ± 13.12 ↑	<0.05	Significant improvement
Social functioning	35.44 ± 15.55	36.90 ± 12.52	34.57 ± 15.36	>0.05	No significant change
Pain	35.51 ± 13.14	37.05 ± 12.93	41.36 ± 13.90 ↑	<0.05	Significant improvement in perceived pain
General health	37.78 ± 11.93	38.46 ± 13.66	37.98 ± 15.53	>0.05	No significant change
Health change	37.11 ± 25.57	44.80 ± 21.60 ↑	38.94 ± 27.30	<0.05	Temporary improvement at 3 months

Repeated measures ANOVA confirmed significant decline in lung function over time, including FEV1 ($F = 6.356$, $p < 0.001$), FVC ($F = 26.524$, $p < 0.001$), and PEF ($F = 15.892$, $p < 0.001$), with the strongest effect observed for FVC (Partial $\eta^2 = 0.342$), shown in table 6. Exercise capacity measured by 6MWT showed no significant change ($F = 1.746$, $p = 0.16$), whereas dyspnea significantly improved on the Borg Scale ($F = 18.856$, $p < 0.001$). HRQoL analysis demonstrated significant improvement in emotional well-being and pain domains, but significant deterioration in emotional role limitation, while most other domains remained unchanged over time.

Table 6. Repeated Measures ANOVA for Outcomes

Outcome Domain	Variable	F-value	p-value	Partial η^2	Interpretation
Lung Function	FEV1	6.356	<0.001	0.111	Significant decline over time
	FVC	26.524	<0.001	0.342	Strong significant decline over time
	PEF	15.892	<0.001	0.238	Significant decline over time

Exercise Capacity	6MWT	1.746	0.16	0.033	No significant change over time
	Modified Borg Scale	18.856	<0.001	0.270	Significant improvement (reduced dyspnea)
HRQoL	Physical functioning	0.40	>0.05	0.008	No significant change
	Role limitation (physical)	0.00	>0.05	0.000	No significant change
	Role limitation (emotional)	3.03	<0.05	0.050	Significant deterioration
	Energy/Fatigue	0.22	>0.05	0.004	No significant change
	Emotional well-being	4.50	<0.05	0.080	Significant improvement
	Social functioning	0.52	>0.05	0.010	No significant change
	Pain	6.08	<0.05	0.107	Moderate significant improvement
	General health	0.06	>0.05	0.001	No significant change
	Health change	2.93	<0.05	0.054	Fluctuating post-treatment perception

Discussion

The current investigation confirmed the persistent decrease of pulmonary function even after microbiological cure in patients with TB. Mean FEV1 declined from 31.98 ± 12.93 at baseline to 29.99 ± 15.75 at 6 months, while FVC decreased from 37.19 ± 12.28 to 32.78 ± 11.40 ($p < 0.001$). The results indicate progressive ventilatory limitation is probably due to the irreversible structural changes in the lungs like fibrosis and airway remodeling. Few studies have reported similarly, Daniels et al. noted that 48% of their cured pulmonary TB patients had abnormal lung function, with restrictive and obstructive defects [15]. Both studies showed that the spirometric parameters remained impaired after TB, which is being recognized more as a chronic respiratory disease and not just a finished infectious process.

There was also some radiological abnormality in the current study but not as much as there was during follow-up which showed partial improvement. At 6 months, there was also a decrease from 100% to 75.0% in chest infiltrate, from 67.3% to 34.6% in consolidation, and from 25.0% to 13.5% in moderate fibrosis. These results suggest that recovery is incomplete even following successful treatment completion. Longitudinal studies previously reported also showed persistent radiographic changes that were related to decreased pulmonary reserve and chronic respiratory symptoms. Persistent airflow abnormalities and radiological sequelae were observed despite successful treatment for TB, highlighting long-term pulmonary consequences of the disease in a Brazilian cohort study to assess post-TB lung disease [16]. A decrease in fibrosis and infiltrates seen in our study may be a response to the natural progression of healing, but the anatomical damage observed may have contributed to the continuing functional impairment.

The current cohort had significantly reduced exercise capacity at follow-up. At baseline 6MWD was 313.13 ± 104.84 meters, and was not significantly different at 6 months (300.92 ± 140.71 meters; $p = 0.16$). Likewise, the percentage of the expected walking distance stayed low. This is similar to the mean 6MWD value of 294.5 ± 122.7 m documented by Daniels et al. in patients cured of TB, which is significantly less than

the expected normal 6MWD [15]. Meanwhile, another observational study showed mean 6MWD of approximately 333 m in post-TB patients, consistent with the diminished exercise tolerance following completion of TB treatment [17]. This significant decrease in walking distance that was seen throughout our cohort may be attributed to poor gas exchange, muscle deconditioning, and chronic respiratory limitation.

Although there was minor improvement in exercise performance, the dyspnea symptoms showed substantial improvement with time in our study. Subjective symptomatic relief was as indicated by the Modified Borg Scale which was lowered from 4.84 ± 1.17 to 3.96 ± 1.45 ($p < 0.001$). In pulmonary rehabilitation studies, there was an improvement in symptom burden in both post-TB and non-post-TB populations. Structured pulmonary rehabilitation interventions were shown to be significantly effective in a pilot rehabilitation study for reducing dyspnea, FEV1, FVC and 6MWD [18]. In addition, recent metaanalysis revealed that rehabilitation produced a mean gain of 60.04 m in 6MWD in patients with post-tuberculosis lung disease [19]. These results indicate that rehabilitation programs could achieve symptom improvement without full recovery of the physiological function and thus provide a potential benefit in post-TB management.

Results for HRQoL in the current study showed mixed results in each of the domains of the SF-36. Emotional well-being improved significantly from 43.73 ± 12.44 to 46.88 ± 13.12 , while pain scores increased from 35.51 ± 13.14 to 41.36 ± 13.90 ($p < 0.05$). In contrast, increased role limitation resulting from emotional problems worsened from 24.30 ± 30.29 to 18.05 ± 23.04 . Likewise, the scores on the physical and mental HRQoL were lower for the cured TB patients compared to the healthy controls, especially in mental health [15]. Similarly, post-TB sequelae studies have shown that there remains a significant psychosocial disability more than a year following microbiological cure [17]. This is why it is possible that some of our participants experienced both better emotional health as well as a deterioration in their emotional role functioning, which could be a reflection of ongoing social and occupational problems despite slowly improving symptoms.

The trends found in this study were also confirmed in repeated measures ANOVA. Significant declines were identified for FEV1 ($F = 6.356$, $p < 0.001$), FVC ($F = 26.524$, $p < 0.001$), and PEF ($F = 15.892$, $p < 0.001$), with the largest effect size observed for FVC (Partial $\eta^2 = 0.342$). No significant change was seen in 6MWT ($F = 1.746$, $p = 0.16$), but Borg dyspnea scores were improved significantly ($F = 18.856$, $p < 0.001$). Similar longitudinal decline in pulmonary function was reported in previous post-TB studies that assessed long-term chronic airflow limitation and restrictive impairment [16]. These results all add to the need for functional monitoring and multidisciplinary rehabilitation in pulmonary TB patients for the longer duration.

Strengths and Limitations

One of the strengths of this study was that lung function, exercise capacity, radiological results and HRQoL measures were repeatedly assessed over several follow-up periods following completion of TB treatment. Standardized assessment tools such as spirometry, six-minute walk test, Modified Borg Scale, chest radiography and validated SF-36 questionnaire provided a multidimensional assessment of post-TB recovery. Moreover, the study provides much local evidence from a resource-limited environment in which long-term post-TB follow-up data are limited. Some caveats should be noted, however. Findings may not be generalizable to larger populations due to the relatively small sample size and single center design. Tracing up to the end of the study period could also have brought about attrition bias. In addition, the absence of a healthy control group and limited long-term follow-up to 6 months limited the ability to assess functional recovery and chronic respiratory sequelae over the long-term.

Conclusion

The present study showed that in spite of successful microbiological treatment

of pulmonary TB, there are still significant impairment of lung function, exercise capacity, radiological abnormalities and some aspects of health related quality of life that persist. Improvement in functional and physiological parameters was observed in certain parameters during follow-up but marked functional and physiological limitations persisted. The results underscore the need to acknowledge the PBLD as a chronic condition to be monitored in the clinical setting, as well as supported by pulmonary rehabilitation and multi-disciplinary care to enhance functional recovery and the quality of life in TB survivors.

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