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Prospective Observational Study of the Impact of Pulmonary Tuberculosis Post Treatment on the Radiological and Lung Function of Patients

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ABSTRACT

Pulmonary dysfunction following tuberculosis treatment is observed in a substantial proportion of patients, ranging from 40-75%, even after achieving bacteriological cure. The objective of this study was to determine the prevalence of structural and functional pulmonary impairment in patients who have completed supervised institutional treatment for pulmonary tuberculosis. A prospective observational study on 66 newly diagnosed pulmonary tuberculosis patients who had received treatment was conducted in this setting. The participants underwent spirometry and chest X-ray (CXR) examinations at the conclusion of the treatment period. The pulmonary function of the individuals was categorized as either within the normal range or exhibiting abnormalities, specifically characterized as obstructive, restrictive, or a combination of both patterns. The chest radiographs were documented as either normal or abnormal. The researchers employed logistic regression models to investigate the variables linked to abnormal lung function. Functional impairment was present in 38.7% cases, 30.66% had restrictive, 6.4% had mixed and 1.6% had obstructive pattern on spirometry, respectively. Out of the 66 patients having restrictive pattern,89.56% had mild restriction, 9.56% had moderate restriction,. Structural impairment on CXR was present in 82.4% of patients. Despite successful treatment, pulmonary impairment was present in 38.7% of patients and structural changes evident on CXR was present in 82.4% of patients.

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Key Words
Pulmonary impairment obstruction, restriction, pulmonary tuberculosis, lung fibrosis

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INTRODUCTION

Tuberculosis (TB) remains a prominent cause of mortality on a global scale, attributable to its infectious nature. In the period from 2000 to 2017, there has been a notable decrease in tuberculosis-related mortality, amounting to a reduction of 42%[1]. India bears 25% of the worldwide tuberculosis burden. Among the worldwide prevalence of 10.4 million cases, approximately 2.8 million cases were reported in India, resulting in 480,000 tuberculosis-related fatalities. Due to the effective implementation of the revised national tuberculosis program (RNTCP), there has been a significant decline in the annual mortality rate attributed to tuberculosis (TB), with figures dropping from 5.6 million in 2000 to 3.6 million in 2015. The advancement in treatment efficacy has led to a significant increase in the population of individuals who have successfully recovered from tuberculosis. Despite achieving microbiological cure, a significant number of tuberculosis (TB) survivors often encounter pulmonary impairment. The primary objective of a successful treatment program for tuberculosis (TB) is the achievement of bacteriological cure and treatment completion.

Pulmonary tuberculosis is the result of the inhalation of droplet nuclei that contain Mycobacterium tuberculosis bacilli. Cell-mediated immunity plays a crucial role in the host's defense against tubercle bacilli. At the histopathological level, this condition is distinguished by the presence of caseating granuloma, caseation necrosis and the formation of a cavity[2]. In individuals with a fully functioning immune system, the process of gradual healing takes place through fibrosis, resulting in lasting structural alterations in the lungs of those who survive, ultimately leading to sequelae. The pulmonary sequelae may manifest as structural alterations in the parenchyma, such as the presence of persistent cavities, aspergillomas, fibrosis and cicatrization. Structural alterations such as bronchiectasis, emphysema and bronchovascular distortion are observed within the airways and these changes continue to exist even after achieving microbiological cure[3]. According to existing recommendations, it is advised to conduct sputum examination and chest X-ray (CXR) upon completion of treatment. However, there is currently no provision for assessing functional impairment. Numerous studies have demonstrated that a notable portion of individuals undergoing treatment for pulmonary tuberculosis exhibit functional impairment, as evidenced by the presence of chronic obstruction, restriction, or mixed disorders on spirometry. Pulmonary impairment following tuberculosis (TB) or post-tuberculosis lung impairment has been identified as separate clinical conditions[4-6].

MATERIALS AND METHODS

This study is a prospective observational study aimed at assessing the clinical and radiological consequences of treated cases of pulmonary tuberculosis. The study focuses on individuals admitted between January and December 2020, with the objective of gaining insights into different aspects of post-tubercular lung diseases. These aspects include predisposing factors, underlying lung pathology (whether transient, permanent, or likely to recur), the extent of radiological evidence and the impact of co-morbidities. The ultimate goal of this research is to enhance the management of post-tubercular lung diseases. The study's inclusion criteria encompassed patients diagnosed with either smear positive or smear negative pulmonary tuberculosis. These patients were required to have successfully completed a supervised treatment regimen lasting a minimum of 24 weeks and were declared cured or had completed treatment according to the guidelines set forth by the revised national tuberculosis control program (RNTCP). The study excluded individuals who had pre-existing lung diseases such as bronchial asthma, chronic obstructive pulmonary disease (COPD), occupational lung diseases, extrapulmonary tuberculosis, previously treated cases of multidrug-resistant tuberculosis, as well as patients with compromised immune systems including those with HIV infection. Additionally, individuals with any structural deformities of the chest wall or spine, such as kyphosis or scoliosis, were also excluded from the study. The study employed consecutive enrollment of participants. A study proforma was developed and employed for the purpose of gathering the clinical data of patients. This was done subsequent to conducting a comprehensive patient history, performing a physical examination and reviewing relevant case documents. The proforma was completed with all pertinent information, such as the duration between the onset of symptoms and the diagnosis of tuberculosis, the results of sputum smear and culture tests and the time required for sputum conversion. The spirometry and chest radiography findings for each patient were recorded in the proforma.

RESULTS

Baseline characteristics of the study population. A cohort of 66 participants was extended an invitation to partake in the research endeavor. Out of the total sample size of 66 participants, 36 individuals, accounting for 54.3% of the participants, were identified as male. The median duration of symptoms prior to the diagnosis of tuberculosis (TB) was found to be 4 weeks, with an interquartile range (IQR) of 3-8 weeks. The duration of the condition was found to be significantly longer in patients with LFI (median 8, IQR 4-12) compared to patients without any LFI

(median 4, IQR 3-6) (p<0.000). Table 1 displays additional attributes pertaining to the study population.

The incidence of lung function impairment In this study, the observed prevalence of lung function impairment was determined to be 45.4% (95% confidence interval: 39-51%). The prevalence of the restrictive defect was found to be the highest among the ventilator disorders, with 36.1% (97 participants) exhibiting this condition. On the other hand, obstructive and mixed defects were observed in 4.1% (11 subjects) and 5.2% (14 subjects) of the sample, respectively.

Factors associated with decreased lung function The examination of single variables to determine their correlation with lung function impairment revealed that the duration of symptoms, presence of phlegm, experience of dyspnea, presence of a fibrotic pattern and a radiological score greater than 8 were all associated with lung function impairment (Table 2). Following the adjustment for each variable in a multivariate analysis, the variables found to be independent predictors of lung function impairment were fibrosis and duration of symptoms, as indicated in Table 3.

Table 1: Baseline characteristics of participants

Variables	No. (66)	Percentage
Gender	146 (54.3%)	123 (45.7%)
Male	36	54.3%
Female	30	45.7%
Age (mean±SD), years	34.20±9.07 years	
School education		
≤Primary school	7	9.7%
≥Secondary school	59	90.3%
Smoking		
Yes	2	2.2%
Ex-smoker	5	7.8%
No	59	90%
Alcohol consumption		
Yes	12	17.5%
No	54	82.5%
Symptoms at TB diagnosis		
Cough	62	93.7%
Phlegm	34	51.3%
Haemoptysis	18	27.9%
Chest pain	41	62.8%
Dyspnea	22	33.8%
Duration of symptoms, median (IQR)	4 weeks (3-8)	
Body mass index		
Median (IQR)	23.4 (21.6-25.8)	
Underweight	2	3%
Normal	42	63.2%
Overweight	15	22.3%
Obesity	7	11.5%
Lung function impairment		
None	36	54.6%
Obstructive	3	4.1%
Restrictive	24	36.1%
Mixed	3	5.2%

Table 2: Univariate analysis of factors associated with lung function impairment

	Lung function impairment			
Variables	Yes (30)	No (36)	Crude odds ratio (95% CI)	p-value
Sex				
Male	13 (42.5%)	21 (57.5%)	0.77 (0.47-1.25)	0.30
Female	15 (48.8)	18 (51.2%)		
Age, per year increase BMI (kg m^{-2})				
≥30	14 (45.8%)	20 (54.2%)	0.70 (0.41-1.17)	0.68
30	12 (41.9%)	21 (58.1%)		
HIV infection			0.92 (0.49-1.73)	0.80
YES	13 (43.8%)	20 (56.2%)		
NO	14 (45.7%)	20 (54.3%)		
Cough			2.08 (0.71-6.07)	0.17
Yes	14 (46.4%)	19 (53.6%)		
No	9 (29.4%)	25 (70.6%)		
Haemoptysis			1.44 (0.84-2.47)	0.17
Yes	16 (52%)	17 (48%)		
No	13 (42.8%)	21 (57.2%)		
Phlegm				
Yes	16 (52.2%)	17 (47.8%)	1.76 (1.08-2.87)	0.02
No	11 (38.2%)	22 (61.8%)		
Chest pain				
Yes	14 (47.6%)	19 (52.4%)	1.30 (0.79-2.15)	0.29
No	12 (41%)	21 (59%)		
Dyspnea	14 (48.4%)	18 (51.6%)	1.21 (0.73-2.01)	0.45
Yes	13 (43.5%)	20 (56.5)		
No	14 (48.4%)	19 (51.6%)		
Duration of symptoms			1.16 (1.08-1.23)	0.00
Micronodules			1.17 (0.60-2.27)	0.64
Yes	13 (44.3%)	20 (55.7%)		
No	14 (48.2%)	19 (51.8%)		
Lung in ltrates				
Yes	14 (47.3%)	19 (52.7%)	1.16 (0.71-1.87)	0.54
No	13 (43.6%)	20 (56.4%)		
Cavities			1.17 (0.60-2.27)	0.64
Yes	14 (48.2%)	19 (51.8%)		
No	13 (44.3%)	20 (55.7%)		
Fibrotic pattern			4.21 (1.72-10.29)	0.002
Yes	22 (73.3%)	10 (26.7%)		
No	12 (39.5%)	22 (60.5%)		
Site of lesions			1.37 (0.71-2.68)	0.34
Bilateral	15 (50%)	18 (50%)		
Unilateral	13 (42%)	21 (58%)		
Radiological score			2.69 (1.35-5.35)	0.005
>8	18 (59.7%)	15 (40.3%)		
<8	13 (35.4%)	23 (64.6%)		

Table 3: Multivariate analysis of factors associated with lung function impairment

Variables	Adjusted odds ratio (95% CI)	p-value
Phlegm		
Yes	1.57 (0.74-3.33)	0.230
No		
Duration of symptoms (weeks)	1.08 (1.01-1.15)	0.014
Fibrotic pattern		
Yes	3.54 (1.40-8.95)	0.007
No		
Radiological score		
>8	1.75 (0.82-3.74)	0.140
≤8		

DISCUSSIONS

This study, one of the initial investigations on spirometric changes following tuberculosis in sub-Saharan Africa, revealed that 45.4% of individuals with a previous history of treated pulmonary tuberculosis exhibited impairment in lung function. The most prevalent disorder observed was a restrictive pattern. The presence of fibrosis on the chest radiograph and a prolonged duration of symptoms prior to the diagnosis of tuberculosis were identified as factors associated with LFI.

The prevalence of participants exhibiting a low functional index (LFI) in this study aligns with previous research findings, which have reported rates ranging from 32-80%[7,8]. According to the findings of our study, prior research has characterized pulmonary restriction as the prevailing pattern, exhibiting varying proportions[7,4-9]. The reason for this restrictive pattern can be attributed to the degradation of lung parenchyma. In contrast, previous research has indicated that airflow obstruction was identified as the prevailing impairment in several other studies[10-12]. The underlying mechanisms responsible for the development of air ow obstruction subsequent to treatment for pulmonary tuberculosis are currently not well understood and are subject to conjecture. The occurrence of bronchial stenosis has been demonstrated to be caused by external pressure from enlarged peribronchial lymph nodes, as well as by the involvement of tuberculosis within the bronchial walls, leading to extensive destruction of granulation tissue and subsequent fibrosis[13]. Furthermore, akin to the effects of smoke exposure, tuberculosis (TB) has been found to enhance the activity of metalloproteinase enzymes, thereby contributing to the deterioration of lung tissue[14]. Gothi *et al*.[15] conducted a study in India which provided evidence that obliterative bronchiolitis could potentially lead to post-tuberculous air ow obstruction[15].

After conducting an investigation on factors related to latent tuberculosis infection (LFI), this study discovered that there was an independent association between an increase in the duration of time between the appearance of disease symptoms and the diagnosis of tuberculosis (TB) with LFI. Additionally, our study demonstrated that the median duration of symptoms preceding the diagnosis of tuberculosis was significantly longer in patients with latent tuberculosis infection (LFI) compared to those without LFI. The results presented here are consistent with prior studies[16,17]. In our current context, as well as in other countries in Africa where resources are limited, a considerable portion of patients initially engage in self-medication within their homes or seek guidance from traditional healers prior to seeking formal healthcare services. Previous studies have shown that extended periods of time between the identification and treatment of tuberculosis (TB) are linked to unfavorable clinical results[18,19]. The likely reason for the decline in pulmonary function following the completion of tuberculosis (TB) treatment in these individuals is the progression of lung damage and subsequent formation of scar tissue within the lungs[11]. In the conducted study, there was no observed correlation between the severity of the disease as depicted on the chest radiograph and the lung function index (LFI). The findings of this study are in contradiction with prior research that demonstrated a correlation between the radiological extent of tuberculosis on chest radiographs and the impairment of pulmonary function[11,17,20]. The observed discrepancy may be attributed to the omission of investigating the relationship between the duration of symptoms before tuberculosis (TB) diagnosis and the likelihood of experiencing late first intervention (LFI) in the latter studies, whereas our study specifically examined this association. The potential influence of the duration of symptoms on the relationship between the radiological score and the prediction of LFI in this study may have been negative.

The second factor that was found to be associated with LFI in the present study was the presence of a fibrotic pattern on the chest radiograph. This particular lesion is frequently observed as a consequence of pulmonary tuberculosis and it may also manifest in individuals who have experienced prolonged TB symptoms prior to receiving treatment[13]. In the current investigation, a subset of our patients exhibited this particular radiological feature on their initial chest radiograph and a statistically significant correlation was observed between this feature and LFI. The process of lung restriction in this case involves the degradation of lung tissue, resulting in a decrease in lung volume, the formation of scar tissue leading to reduced pulmonary compliance and an elevation in elastic retraction pressure[12,21]. According to prior research findings, there was no significant association found between gender, HIV status, BMI and respiratory symptoms prior to TB diagnosis and LFI[4]. Previous research has demonstrated a positive correlation between advancing age and LFI[11]. The lack of identification of this association may be attributed to

the relatively lower mean age of patients in our study. The prevalence of smoking, which has been recognized as a risk factor for impairment of lung function, was found to be very low in our study. Consequently, we were unable to examine its association with lung function impairment (LFI).

Although, our study makes a valuable contribution to the existing literature on post-tuberculous lung function in sub-Saharan Africa, it is important to acknowledge certain limitations. The omission of sputum culture in this study precluded the exclusion of non-tuberculous mycobacterial disease. Additionally, the inability to measure total lung capacity, which is considered the most reliable diagnostic method for lung restriction, limited our findings. Furthermore, the lack of pre-symptom tuberculosis lung function data for participants prevents us from definitively attributing ventilatory changes to tuberculosis. It is important to acknowledge the potential for recall bias, as participants with more severe TB symptoms may have had a greater ability to recall and report them, while those with normal spirometry may not have noticed or may have forgotten such symptoms. An additional constraint pertains to the absence of a detailed account regarding the temporal sequence of symptoms in the present investigation. The presence of warning symptoms such as cough and haemoptysis, which were not linked to lower respiratory tract infections (LFI), may have served as a potential incentive for the patient to seek medical attention at an earlier stage.

CONCLUSION

In summary, a notable percentage of individuals diagnosed with pulmonary tuberculosis in Cameroon exhibited compromised lung function following the completion of their treatment regimen. The implementation of timely patient visits to healthcare facilities for individuals exhibiting respiratory symptoms, coupled with the provision of training to healthcare personnel for the prompt identification of tuberculosis, has the potential to mitigate the adverse effects of the disease on pulmonary function.

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