Original Research Article

Frequency of impaired lung function in treated tuberculosis patients in tertiary care hospital of Pakistan: a cross sectional study

Comment [WU1]: Say study on----- add year of study as well and better to say frequency and type of ----

ABSTRACT:

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Background: Pulmonary impairment is a common manifestation in previously treated pulmonary tuberculosis (PTB) patients. Approximately 40-60% of patients with history of complete anti-tuberculosis therapy (ATT) developed the obstructive, restrictive or mixed patterns of lung disease.
Objective: To determine the frequency and type of impairment of lung function in previously treated PTB patients.
Methods: A descriptive cross-sectional study was conducted at Ojha Institute of Chest diseases, Dow University of Health Sciences, Karachi during the period of six months from April 2021 to September 2021. One hundred and forty four previously treated PTB patients with age of 18-60 years were selected through consecutive sampling. Spirometry of each patient was performed by trained spirometry technician and lung function was assessed by an experienced pulmonologist. Data was interpreted with SPSS v. 25.0.
Results: Out of 144 previously treated PTB patients, male were 83 (57.6%) and female were 61 (42.4%). Impaired pulmonary function was present in 87 (60.4%) patients, out of which 49 (56.3%) patients had obstructive impairment; 23 (26.4%) patients had restrictive impairment while 15 (17.2%) patients had mix pattern.
Conclusion:. Prevalence rate of impaired pulmonary function was higher in treated PTB patients who have completed ATT. Obstructive pulmonary impairment was the most common pulmonary impairment followed by restrictive and mixed pulmonary impairment.

Keywords: Pulmonary tuberculosis, anti-tuberculosis, obstructive, restrictive, lung.

INTRODUCTION:

Tuberculosis (TB) is a multi-systemic ancient human infectious disease, caused by Mycobacterium tuberculosis, mainly affecting lungs of human body, making pulmonary tuberculosis (PTB) as most common manifestation of TB [1, 2]. Globally, TB is one of the leading cause of mortality from an infectious disease agent specifically including human immunodeficiency virus (HIV) infected population of world [3, 4].

Global tuberculosis report of year 2020 published by World Health Organization (WHO), reports ten million new cases of TB along with 1.2 million and 208000 deaths in HIV negative and positive TB cases respectively in year 2019. Pakistan was listed in top eight countries accountable for two-third of total TB cases with prevalence of 5.7% [5]. According to Pakistan national guidelines of TB, Pakistan is ranked 5th among the highest TB burden countries with an estimation of 562,000 new cases of TB per year [6]. WHO aims to finish the TB by decreasing 90% of TB incidence and 95% of TB mortality till year 2035 [7].

Patients who have recovered from PTB are at risk of developing pulmonary and extrapulmonary sequelae of the PTB throughout their lives, which in turn affects their quality of life [8]. However, PTB treatment with ATT does not prevent the development of pulmonary complications, followed by lung injury and pulmonary sequelae and even disability [9]. High prevalence of obstructive lung disease is seen in treated PTB patients. Some studies in past have shown obstructive defects as the main abnormality in treated TB patients, but recently studies have shown that functional abnormalities of lungs could be obstructive, restrictive. or mixed defects [10-12]. In a study by Mbatchau Ngahane BH, et al. has found the prevalence of lung function impairment as 45.4% (95% CI 39-51) in treated TB patients [11]. In another study reported by Singh B, et al. has shown obstructive, restrictive. or mixed defects seen in Post-tuberculosis patients as 56.25%, 10.42% and 33.33% respectively [12].

As the prevalence of TB is significant in our society, it is important to identify patients with pulmonary function impairment after the completion of PTB treatment with ATT. If we know the pattern of lung impairment in these treated PTB patients which in turn help us in planning further management of these patients so that they become useful citizen of the society. In the past, no such study has been conducted in Sindh; this study will provide the data of Sindh which in turn will help us to design our routine practice guidelines for proper management of impaired lung function in post TB patients in order to reduce the morbidity of these particular patients and improving the quality of life.

METHODOLOGY:

A descriptive cross-sectional study was conducted at Ojha Institute of Chest diseases, Dow University of Health Sciences, Karachi during the period of six months from April 2021 to September 2021.

All treated PTB Patients with (1) age of 18-60 years and (2) completed ATT prior to six months of study were selected through consecutive-sampling. Patients with (1) current use of ATT, (2) history of pleural or pericardial tuberculous effusion, (3) history of obstructive airway disease (including chronic obstructive pulmonary disease (COPD) and bronchial asthma), interstitial lung disease, lung malignancy, congestive cardiac failure, chronic renal failure, chronic liver disease or chest deformity, (4) treated TB patients of Multi-drug resistant (MDR), (5) failed to perform spirometry and (6) not willing to be a part of study were excluded.

Sample size of 144 was calculated with the help of Open EPI software by using confidential interval of 95%, confidential limit of 5% and lowest proportion of pulmonary impairment reported by previous study by Singh B et al. who has shown obstructive. Restrictive, or mixed defects seen in treated tuberculosis patients as 56.25%, 10.42% and 33.33% respectively [10].

Those patients who were previously diagnosed with PTB on the basis of clinical (cough with sputum, fever (> 98.4 °F), blood in sputum, night sweats and shortness of breathing (respiratory rate > 20/minute) and radiological findings (consolidation, cavitation, nodular opacity and military shadows on chest X-ray) and confirmed on laboratory investigations (AFB smear. Gene Xpert, AFB C/S on sputum) were labelled as PTB patients. Those PTB patients who have completed course of ATT were labelled treated PTB patients. Spirometry of each patient was performed by trained spirometry technician and lung function was assessed by an experienced pulmonologist (Table-1). Statistical analysis was performed with

Comment [WU3]: Better to make it short as much as possible. Better to focus on impairment and its types than TB/PTB.. As the same time reduce the paragraphs..

Comment [WU4]: What is the use of saying descriptive? You are not going to describe the state of affairs.. Therefore, better to say a crossectional study design was conducted.....

Comment [WU5]: Add the inclusion criteria in brief as well,
What about HIV-co infected patients??

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Comment [WU8]: Which percentage you used to calculate? Or what methods did you follow? Mention how you selected the samples for the study.. Method of selection should be stated..

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statistical package for social sciences (SPSS) version 25.0. Binary logic regression was used with p value ≤ 0.05 as significant.

Comment [WU10]: If this table is a result, please put it under the result.

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Table 1: Pulmonary Function Test		
Lung Function	**FEV1/FVC**	**FVC**
Normal	80%	80-120%
Abnormal		
Obstructive	< 70%	> 80%
Restrictive	≥ 70%	< 80%
Mixed	< 70%	< 80%
FEV1: Forced expiratory volume in one second; FVC: Forced vital capacity.		

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Comment [WU13]: Please try to separet each paragraph..
The table should come first and then the description follows, that is the usual trend..

RESULTS:

Out of 144 previously treated PTB patients, male were 83 (57.6%) and female were 61 (42.4%). Most of the patients were in age group of 51-60 years 56 (38.9%) patients followed by 41-50 years 51 (35.4%) patients, 31-40 years 24 (16.7%) patients and 18-30 years 13 (9.0%) patients with mean age of 46.92 ± 10.096 years. Most of the PTB patients were from rural area 63 (43.8%) patients and employed 101 (70.1%) patients. Most of the patients were in range of normal BMI 87 (60.4%) patients followed by underweight 28 (19.4%) patients, over-weight 16 (11.1%) patients and obese 13 (9.0%) patients with mean BMI of 25.54 ± 5.77 Kg/m2. 77 (53.5%) patients have positive family history of TB contact. Most of the patients 29 (20.1%) received their last dose of ATT 6-12 and 37-48 months before included in the study with mean duration of 35.90 ± 19.822 months (Table 2).

Impaired pulmonary function was present in 87 (60.4%) patients, out of which 49 (56.3%) patients had obstructive impairment; 23 (26.4%) patients had restrictive impairment while 15 (17.2%) patients had mix pattern (Table 3).
Significant risk factors for impaired lung function were place of living (p=0.001) and occupation (p=0.002), whereas non-significant risk factors were gender (p=0.902), age (p=0.711), family history of TB (p=0.126) and duration of ATT completion (p=0.360).
Binary logistic regression shows that odds of impaired lung function was 0.95 times higher in male PTB patients (95% CI: 0.45-2.02), 1.16 times higher in PTB patients of age < 50 years (95% CI: 0.54-2.48), 3.54 times higher in PTB patients living in rural areas (95% CI: 3.54-1.65), 0.29 times higher in employed PTB patients (95% CI: 0.29-0.13), 1.79 times higher in PTB patients with positive family history of TB (95% CI: 1.79-0.85) and 0.63 times higher in PTB patients who have completed ATT more than one year before the study (95% CI: 0.63-0.23) (Table 4).

Table 2: Demographic and Disease Details of Cured PTB Patients (n=144)

Variables	Frequency	Percentage
Gender		
Male	83	57.6
Female	61	42.4
Age (Years)		
Mean ± SD	46.92 ± 10.096	
18-30	13	9.0
31-40	24	16.7
41-50	51	35.4
51-60	56	38.9
Place of Living		
Rural	63	43.8
Urban	81	56.3
Occupation		
Employed	101	70.1
Unemployed	43	29.9
BMI (Kg/m2)		
Mean ± SD	25.54 ± 5.77	
Normal	87	60.4
Under weight	28	19.4
Over weight	16	11.1

Comment [WU14]: Make it again as I commented in Table-1.
You can make the font size 10..

Obese	13	9.0
Family History of TB		
Yes	77	53.5
No	67	46.5
Duration of ATT Completion (months)		
Mean ± SD	35.90 ± 19.822	
6-12	29	20.1
13-24	19	13.2
25-36	23	16.0
37-48	29	20.1
49-60	21	14.6
> 60	23	16.0

Table 3: Impaired Lung Function In Cured PTB Patients (n=144)

Variables	**Frequency**	**Percentage**
Impaired Lung Function		
Present	87	60.4
Absent	57	39.6
Type of Impaired Lung Function (n=87)		
Obstructive	49	56.3
Restrictive	23	26.4
Mixed	15	17.2

Table 4: Risk Factors For Impaired Lung Function (n=144)

Risk Factor	**OR**	**95% CI**	**P-value**

Comment [WU15]: Tabel 3 and table 4 are merged..

Gender: Male vs Female	0.95	0.45-2.02	0.902
Age: < 50 years vs > 50 years	1.16	0.54-2.48	0.711
Place of Living: Rural vs Urban	3.54	3.54-1.65	0.001
Occupation: Employed vs Unemployed	0.29	0.29-0.13	0.002
Family History: Positive vs Negative	1.79	1.79-0.85	0.126
Duration of ATT Completion: < 1 year vs > 1 year	0.63	0.63-0.23	0.360
P-values were calculated from binary logistic regression. * significant p-values ≤ 0.05			

DISCUSSION:

Patients either suffering from PTB or treated from PTB are at a higher risk of developing pulmonary and extrapulmonary sequelae of the PTB. Impairment of lung function in treated PTB patients is one of the commonly reported complication. A wide variety of studies reported the impaired pulmonary function in 33.3-94.0% of treated PTB patients [10-13]. In this study most of the treated PTB patients 83 (57.6%) were male and 61 (42.4%) were female. Similar high prevalence of male was reported by other authors like; Chushkin MI, et al., male (61.7%) and female (38.3%) [14], Pasipanodya JG, et al., reports the 69% male and 31% female [15], Vecino M, et al., reports the 71% male and 29% female [16] and Manji M, et al., reports the 60.5% male and 39.5% female [17]. All similar studies reflecting that male PTB patients were more affected with disease as compare to female patients because in our society male are predominantly working and spending their time out of home and are at a higher risk of infection.

In current study most affected age group were 51-60 years 56 (38.9%) and 41-50 years 51 (35.4%) patients whereas other affected groups were; 31-40 years 24 (16.7%) patients and less affected age group was 18-30 years having 13 (9.0%) patients. Similar results were reported by Chushkin MI, et al., who reports the most affected age group were 40-49 in 27.6%, 50-59 in 22.9 and other affected age groups were < 40 in 21.5%, 60-69 in 15.0% and ≥ 70 in 3.1% patients [14]. Difference in age group was reported by Manji M, et al., 33.1% in 18-30, 31.9% in 31-40, 19.2% in 41-50, 8.4% in 51-60 and 6.4% in > 60 [17]. Similar studies reflecting that patients having age > 40 years are at higher risk of development of impaired pulmonary function. Patients were suffering from pulmonary impairment due to advanced age and exposure to environmental irritants.

In our research 77 (53.5%) patients report the positive family history of PTB contact. Majority of the patients 81 (56.3%) were from urban area and remaining 63 (43.8%) patients were from rural area. Most of the selected patients were working 101 (70.1%) patients including 65 (45.1%) in field and 36 (25.0%) patients were working in office. Manji M, et al., reports the occupation; agriculture in 3.8%, domestic in 34.1%, industrial in 12.8%, office in 23.8% and 25.5% other [17].

In current study patients treated for PTB were investigated for impaired pulmonary function

Comment [WU16]: Series grammatical corrections is required. There are some fragmented ideas and they should be aligned to give sense. In most of the cases argument are lacking.. that means sound reasoning might be required in some instances..

Comment [WU17]: Add s

Comment [WU18]: Please rewrite it again.

Comment [WU19]: Similar high prevalences of male are reported....

Comment [WU20]: Use present tense for the findings made by other authors...therefore is..

Comment [WU21]: Make et al.italic

Comment [WU22]: This should be explained interms of impairment

Comment [WU23]: The current

Comment [WU24]: Please try to conduct a chi-square test and see the possible association or significant difference among these age groups..

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Comment [WU28]: Focus on the utilization of verb agreements:: singular and plural usages..

by performing spirometry. Lung function was normal in 57 (39.6%) patients, whereas abnormal/impaired in 87 (60.4%) patients. Similar prevalence of impaired pulmonary function was reported by Pasipanodya JG, et al., 59.0% [15] and Vecino M, et al. 57.0% [16]. Manji M, et al., reports the high prevalence of impaired pulmonary function i.e., 74% [17], whereas Chushkin MI, et al., [14] and Fiogbe AA, et al. [18] reports the lower prevalence of impaired pulmonary function 47.6% and 45.0%, respectively than our study. All similar studies showing the higher prevalence of pulmonary impairment in PTB treated patients. The overall prevalence of pulmonary impairment is much alarming in patients treated for PTB. In our patient sample, obstructive impairment (56.3%) was the most common pattern, followed by restrictive (26.4%) and mixed (17.2%) impairment. A similar result for obstructive impairment was reported by Manji M, et al., who observed the obstructive impairment in 56.6%, restrictive in 17.5% and mixed in 25.9% [17]. Chushkin MI, et al., who reports the high prevalence of obstructive in 72.5%, restrictive in 17.6%, mixed in 7.8% and non-specific in 1.9% [14]. Vecino M, et al., reports the lower obstructive prevalence i.e., 38.6%, restrictive in 37.4% and mixed in 24.3% [16]. In all similar studies obstructive impairment was most common followed by restrictive and mixed pattern of pulmonary important.

In conclusion, it was found that patients having history of PTB were at a higher risk of pulmonary function impairment. The eradication of the bacteria does not necessarily translate to the end of the disease. After PTB treatment, 60% of patients evolves to pulmonary impairment mainly obstructive type of impairment. The result shows the importance of pulmonary function testing in patients who have been treated for PTB.

Comment [WU29]: Why you conclude here? You put it below.. therefore, take it to the conclusion part or this one should be rewritten again in a sense that you want to explain.

CONCLUSION:

It was concluded from the study that prevalence rate of impaired pulmonary function was higher in PTB patients who have completed ATT. It was also concluded that obstructive impairment was most common pulmonary impairment followed by restrictive and mixed pulmonary impairment.

Comment [WU30]: What is then your recommendation/s?

xxxx.

Comment [WU31]: Add conflict of interest.. And ethical issue..

REFERENCES:

1. Adigun R, Singh R. Tuberculosis. [Updated 2021 Jul 25]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan.
2. Mbuh TP, Ane-Anyangwe I, Adeline W, Thumamo Pokam BD, Meriki HD, Mbacham WF. Bacteriologically confirmed extra pulmonary tuberculosis and treatment outcome of patients consulted and treated under program conditions in the littoral region of Cameroon. BMC Pulm Med. 2019 Jan 17;19(1):17.
3. MacNeil A, Glaziou P, Sismanidis C, Date A, Maloney S, Floyd K. Global epidemiology of tuberculosis and progress toward meeting global targets—worldwide, 2018. Morb Mortal Wkly Rep. 2020 Mar 20;69(11):281-5.
4. Glaziou P, Floyd K, Raviglione MC. Global epidemiology of tuberculosis. Semin

Respir Crit Care Med. 2018 Jun;39(3):271-85.
5. World Health Organization. Global tuberculosis report 2020. Geneva, Switzerland: World Health Organization; 2020.
6. Pakistan Chest Society. Diagnosis and management of drug-susceptible tuberculosis: a national clinical guideline. Pakistan, Islamabad: Pakistan Chest Society; 2020.
7. Al Abri S, Kasaeva T, Migliori GB, Goletti D, Zenner D, Denholm J, et al. Tools to implement the world health organization end TB strategy: addressing common challenges in high and low endemic countries. Int J Infect Dis. 2020 Mar 1;92:S60-8.
8. Radovic M, Ristic L, Ciric Z, Dinic-Radovic V, Stankovic I, Pejcic Tet al. Changes in respiratory function impairment following the treatment of severe pulmonary tuberculosis–limitations for the underlying COPD detection. Int J Chron Obstruct Pulmon Dis. 2016;11(1):1307-16.
9. Gupte AN, Paradkar M, Selvaraju S, Thiruvengadam K, Shivakumar SVBY, Sekar K, et al. Assessment of lung function in successfully treated tuberculosis reveals high burden of ventilatory defects and COPD. PLoS One. 2019 May 23;14(5):e0217289.
10. Harries AD, Ade S, Burney P, Hoa NB, Schluger NW, Castro JL. Successfully treated but not fit for purpose: paying attention to chronic lung impairment after TB treatment. Int J Tuberc Lung Dis. 2016 Aug 1;20(8):1010-4.
11. Ngahane BH, Nouyep J, Motto MN, Njankouo YM, Wandji A, Endale M, et al. Posttuberculous lung function impairment in a tuberculosis reference clinic in Cameroon. Resp Med. 2016;114:67-71.
12. Singh B, Chaudhary O. Trends of pulmonary impairment in persons with treated pulmonary tuberculosis. Int J Med Res Prof. 2015:1(1):8-11.
13. Ravimohan S, Kornfeld H, Weissman D, Bisson GP. Tuberculosis and lung damage: from epidemiology to pathophysiology. Eur Resp Rev. 2018 Mar 31;27(147):170077.
14. Chushkin MI, Ots ON. Impaired pulmonary function after treatment for tuberculosis: the end of the disease?. J Bras Pneumol. 2017;43(1):38-43.
15. Pasipanodya JG, Miller TL, Vecino M, Munguia G, Garmon R, Bae S, et al. Pulmonary impairment after tuberculosis. Chest. 2007;131(6):1817-24.
16. Vecino M, Jotam G. Pasipanodya, Slocum P, Bae S, Munguia G, et al. Evidence for chronic lung impairment in patients treated for pulmonary tuberculosis. J Infect Public Health. 2011;4(5-6):244-52.
17. Manji M, Shayo G, Mamuya S, Mpembeni R, Jusabani A, Mugusi F. Lung functions among patients with pulmonary tuberculosis in Dar es Salaam - a cross-sectional study. BMC Pul Med. 2016;16:58.
18. Fiogbe AA, Agodokpessi G, Tessier JF, Affolabi D, Zannou DM, Adé G, et al. Prevalence of lung function impairment in cured pulmonary tuberculosis patients in Cotonou, Benin. Int J Tuberc Lung Dis. 2019 Feb 1;23(2):195-202.