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Frequency of Pulmonary Hypertension in Post-Tuberculosis Patients: A Cross-Sectional Analysis

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A B S T R A C T

Background: Tuberculosis (TB) is a chronic infectious disease caused by airborne transmission of aerosolized droplets of Mycobacterium tuberculosis. TB is one of the top ten causes of death and the leading cause from a single infectious agent, causing an estimated 1.2 million deaths annually. Even with successful treatment patients with TB mostly suffer from long-term pulmonary complications.

Objective: To determine the Frequency of Pulmonary Hypertension (PH) in post TB patients.

Methodology: This cross-sectional study was carried out at Pulmonology Ward, Ayub Teaching Hospital, Abbottabad over six months from February 4th, 2022 to August 3rd, 2022. A total of 108 patients were included in the study using consecutive sampling technique. The PH patients included those patients who had mean pulmonary arterial pressure (PAPm) ≥ 25 mmHg at rest estimated by echocardiography. Both male and female patients with age between 16 to 80 years having past history of TB were included.

Results: Mean age of Post TB patients was 52.1(±7.2) years. Among Post TB patients 46.3% were males and 53.7% were female patients. The frequency of PH in post TB patients was 44.4% (p<0.03). The Post TB PH difference in different age groups was significant (p=0.03) but difference in both genders was not significant in patients (p=0.221).

Conclusion: Pulmonary Hypertension is found in a significant number of Post TB patients.

Keywords: Tuberculosis; Pulmonary Hypertension; Frequency

Introduction

Tuberculosis (TB) is a chronic disease causing a huge disease burden all over the world, especially in low-income countries.[1] TB is an important cause death and has caused an estimated 1.6 million deaths in 2021 globally.[2] Despite universal efforts, the overall decrease of TB incidence from 2015 to 2020 was 11% instead of the intended 20%.[3]

TB can cause significant complications even following successful treatment completion. The common long-term pulmonary complications include pulmonary fibrosis, bronchiectasis and chronic obstructive pulmonary disease (COPD). These complications can lead to some further sequelae like the development of pulmonary hypertension (PH) and right heart failure. All these sequelae are responsible for a huge impact on the quality of life of these individuals creating a significant burden on the healthcare system.[4]

Pulmonary hypertension (PH) is a serious condition characterized by elevated pressure in the pulmonary arteries, which can lead to right heart failure and reduced life expectancy. It is often secondary to other conditions, including chronic lung diseases, left heart disease, or thromboembolic events. Pulmonary hypertention (PH) is prevalent in around 1% of the population worldwide, with upto 10 % prevalence in those over 65 years of age.[5] The most common causes of PH include left heart disease (LHD Group 2 PH) and chronic lung disease (CLD Group 3 PH).[6,7] CLD is responsible for around 29% to 42% of all cases of PH.[8] The common lung conditions causing PH include COPD, interstitial lung disease (ILD) and obstructive sleep apnea (OSA).[9] In countries with high TB prevalence post tuberculous lung disease is the third leading cause of group 3 PH, yet this fact is not stated in the recent guidelines.[10,11] PH may contribute to the burden of TB disease in patients with even successful treatment completion.[12-15]

The relationship between tuberculosis and pulmonary hypertension is complex, with several contributing factors leading to an increased risk of PH in post-tuberculosis patients. Post-tuberculosis pulmonary hypertension (post-TB PH) develops due to a combination of factors. Pulmonary TB can lead to lung damage through tissue scarring, fibrosis, and distortion of the airways and pulmonary vasculature. This scarring can increase pulmonary vascular resistance, contributing to elevated pulmonary arterial pressures. Additionally, post-TB patients may experience chronic hypoxia due to decreased lung function, which can further exacerbate pulmonary hypertension. Chronic inflammation caused by active TB can also result in damage to the pulmonary arteries, triggering endothelial dysfunction and increased resistance in the pulmonary circulation. This can lead to a cycle of vascular remodeling, ultimately resulting in pulmonary hypertension.

The frequency of pulmonary hypertension in post-tuberculosis patients is a subject of increasing clinical interest, given the serious nature of PH and its impact on quality of life and survival. Patients with post-TB PH often present with symptoms like weakness and fatigue. These symptoms can overlap with other respiratory conditions, leading to under-diagnosis or misdiagnosis of PH in this population; in addition, patients with post-TB PH may have a higher risk of developing other complications such as right heart failure and chronic pulmonary insufficiency, which underscores the importance of early detection and intervention. Although post TB PH has been investigated in some high TB burden areas, there is very limited local data about the frequency of post TB PH after successful completion of TB treatment.[10,16,17]

We aimed to find out the frequency of PH in patients who presented with past history of TB in our population. As a result, those patients with PH can be identified and treated as early as possible and, in this way, we will endeavor to reduce the cost associated with TB both at national level and globally.

Objective

To determine the Frequency of Pulmonary hypertension in post tuberculosis patients admitted to Pulmonology Department Ayub Teaching Hospital Abbottabad.

Methodology

This Cross-sectional study was conducted at Pulmonology Department of Ayub Teaching Hospital Abbottabad, Pakistan over six months from 4th of February 2022 to 3rd of August 2022. A sample size of 108 was calculated using WHO software for determining sample size, based on these assumptions: The estimated frequency of pulmonary hypertension among post-tuberculosis patients is 35%, the confidence level is set at 95%, and the margin of error is 9%.

Using consecutive non probability sampling technique, both male and female patients with age between 16 to 80 years having past history of TB who presented to Pulmonology Department Ayub Teaching Hospital Abbottabad were included.

Patients with mycobacterium other than tuberculosis (MOTT), HIV, idiopathic interstitial pneumonias, thromboembolic pulmonary hypertension and COPD regardless of duration and patients taking oral corticosteroids or immunosuppressive drugs were excluded.

The Pulmonary hypertension patients included were those patients who had mean pulmonary arterial pressure (PAPm) ≥ 25 mmHg at rest estimated by echocardiography.

The study was started following approval by institutional ethical committee. All cases with past history of

Table 1. Pulmonary hypertension in Post TB patients

Pulmonary Hypertension	Frequency	Percent	P value
Yes	48	44.4	0.03
No	60	55.6	
Total	108	100.0	

tuberculosis admitted in Pulmonology Department of Ayub Teaching Hospital Abbottabad, Pakistan were enrolled in study after obtaining informed written consent from each participant. Patients were assessed by the researcher by obtaining history and getting echocardiographs. The echocardiographs were performed by qualified cardiologists.

Informations including name age, gender, height, weight and address was recorded on a specially designed proforma for research purposes.

Data were analyzed using SPSS version 20.0. Quantitative variables like age, weight, height, BMI and duration since the completion of TB treatment were described as Mean ± SD. Categorical variables like gender, presence of PH and its severity were described as frequencies and percentages. PH was stratified among age, gender, BMI and duration since completion of TB. Post stratification chi square test was used at 5% level of significance. Data were presented in tables and charts.

Results

There was total 108 study participants. Mean (±SD) age of study participants was 52.1(±7.2) years. Among study cases 58 (53.7%) were females (Figure 1). Among the participants 13.9% were in age range 16-40 years, 50% patients were in age range 41-60 years and 36.1% patients were in age range 61- 80 years. Mean(±SD) weight of study participants was 52.6(±5.3) kg.

Pulmonary hypertension was observed in 48 (44.4%) patients (Table 1). Out of total patients 5(4.6%) had mild pulmonary hypertension, 15(13.9%) had moderate pulmonary hypertension and 28(25.9%) had severe pulmonary hypertension. In frequency distribution of age with respect to PH we found that 3(2.8%) patients were in age group 16-40 years, 20(18.5%) patients in age group 41-60 years and 25(23.1%) patients in age group of 61-80 years. This finding is statistically significant at p=0.03 out of total 108 patients (Table 2).

In frequency distribution of gender with respect to PH it was found in 20(18.5%) male patients and 28(25.9%) female patients. This finding is not statistically significant at p=0.221 (Table3).

Discussion

Pulmonary TB can result in extensive destruction of the lungs in a wide majority of cases, which increases morbidity and mortality. The resultant condition is known as post TB lung which is one of the important type of CLD. PH may develop as a result of CLD and is regarded as a significant risk factor for clinically worsening respiratory status. Very few reports are available on post TB PH. Due to that very reason the importance of PH in post TB lung is not much highlighted.

The frequency of PH in Post TB patients varies from center to center. PH is reported in 20%–40% of CLD including post TB patients and is related to the severity of

Table 2. Frequency distribution of age with respect to pulmonary hypertension

Age Group	Pulmonary hypertension		Total	P-value
	Yes	No		
16 – 40	3 (2.8%)	12 (11.1%)	15 (13.9%)	0.03
41 – 60	20 (18.5%)	34 (31.5%)	54 (50.0%)	
61 – 80	25 (23.1%)	14 (13%)	39 (36.1%)	
Total	48 (44.4%)	94 (55.6%)	108 (100%)	

Table 3. Frequency distribution of Gender with respect to pulmonary hypertension.

Gender	Pulmonary hypertension		Total	P-value
	Yes	No		
Male	20 (18.5%)	30 (27.8%)	50 (46.3%)	0.221
Female	28 (25.9%)	30 (27.8%)	58 (53.7)	
Total	48 (44.4%)	60 (55.6%)	108 (100%)	

underlying conditions.[18] The PH rate in our study is 44.4%, which is within the range of meta-analysis stating 42% PH rate for patients who were hospitalised or had symptoms; although it is on a higher side compared to outpatients[19]. Reason of this high incidence of PH was probably due to, high incidence of TB in Pakistan and due to delay in its treatment leading to complications like fibrosis and PH. Investigators have reported about the severity of PH and the associated mortality in various studies. Some authors have demonstrated higher mortality in those with pulmonary artery systolic pressure (PASP) >55 mm Hg as compared to those with lower PASP.[20]

Our Study shows highest percentage of severe PH category, followed by moderate PH. A local study done at Pulmonology ward of a tertiary care hospital in our country comprising 90 patients demonstrated PH in 80 (88.9%) patients. The severity of PH was reported as mild in 40 (44.4%) cases, moderate in 38 (42.2%) cases severe in 2 (2.2%) cases.[21] In our study 4.6% participants had mild pulmonary hypertension, 13.9% had moderate pulmonary hypertension and 25.9% had severe PH. This shows that in our study group mild pulmonary hypertension is less as compared to the above study. Reason for this might be that people in our setup with mild symptoms don't visit hospital because of far mountain areas so our cases of mild PH were less.

In majority of previous studies, the investigators have used the electrocardiography or postmortem examination for the diagnosis of PH and cor pulmonale. Also, majority of patients were given proper chemotherapy for the treatment of TB.[22] Our patients also received modern anti-TB medicines and were successfully treated for TB. We used doppler echocardiography in our study to diagnose PH. Doppler echocardiography is considered the best non-invasive method for the diagnosis of PH.[23] The values of PASP obtained with Doppler echocardiography correlates strongly with those found on right heart catheterization.[24]

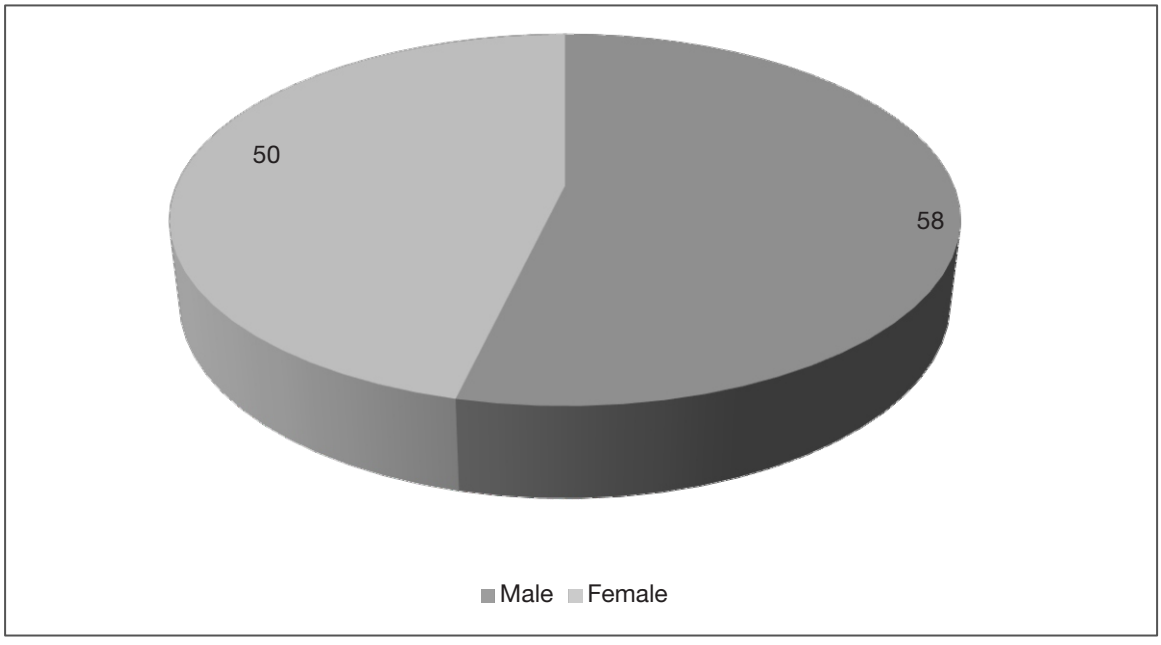

Figure 1. Gender based distribution of study cases

In our study 46.3% male and 53.7% female patients had PH, indicating slightly more prevalence in in females. Although it's not statistically significant and might be because other factors may be involved that need further workup, if they have some protective mechanism. Literature view does not show any such relevance.

In our study majority of patients were elderly (23.1%) while a study done in Karachi reported that young people are more prone to pulmonary hypertension; the difference could be due to the study setting because most of the patients in our study were inpatients.[25] Another study conducted in Korea, stated that the majority of patients of PH due to TB were over 50 years.[26]

The limitation of our study is that most of our patients had advanced disease and the symptoms were severe enough to warrant admission. The effect of this inclusion could be that a substantial number of patients who were asymptomatic or had mild symptoms were not assessed for the presence of PH. A broader study encompassing all TB-treated and under TB treatment patients both at outpatient clinics and in hospitalized patients should be done to find out the actual magnitude of PH after PTB treatment.

Conclusion

TB has an important causal association with PH and the history of PTB, therefore, should be sought in all cases of PH, especially in the developing countries where TB is more common. Elderly patients who have a history of tuberculosis should be screened for pulmonary hypertension. This association between TB and PH needs further investigation.

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