Biological and Clinical Sciences Research Journal
eISSN: 2708-2261; pISSN: 2958-4728
www.bcsrj.com
DOI: https://doi.org/10.54112/bcsrj.v2024i1.1277
*Biol. Clin. Sci. Res. J., Volume, **2024**: 1277*
Original Research Article

FREQUENCY OF PULMONARY HYPERTENSION IN POST TUBERCULOSIS PATIENTS

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(Received, 08th August 2024, Revised 05th November 2024, Published 22nd November 2024)

Abstract: *Pulmonary arterial hypertension (PAH) is a severe complication that can develop in patients with a history of pulmonary tuberculosis (PTB), leading to increased morbidity and mortality. This study aimed to determine the frequency and associated risk factors of PAH in post-TB patients, with a focus on age, gender, BMI, and duration since TB diagnosis.* ***Objective:*** *To assess the frequency of PAH and identify potential risk factors in post-TB patients, providing insights to guide improved screening and follow-up practices.* ***Methods:*** *A cross-sectional study was conducted on 108 post-TB patients at the Department of Pulmonology, Hayatabad Medical Complex, Peshawar from January 2024 to July 2024. PAH was diagnosed using echocardiography, with pulmonary arterial pressure (PAP) thresholds set above 20 mmHg. Data were analyzed to assess associations between PAH and variables including age, gender, BMI, and time since TB diagnosis.* ***Results:*** *The study found a 35.2% prevalence of PAH among post-TB patients. Older age and longer duration since TB diagnosis were significantly associated with higher PAH frequency, while gender and BMI were not significantly associated with PAH risk.* ***Conclusion:*** *It is concluded that PAH is a common complication in post-TB patients, particularly among older individuals and those further removed from their TB diagnosis. These findings underscore the need for routine PAH screening in high-risk post-TB patients to enable timely intervention and improve outcomes.*

Keywords: Pulmonary Hypertension, Post-Tuberculosis, Frequency, Respiratory Complications, Lung Health, Chronic Disease, Pulmonary Sequelae

Introduction

Pulmonary hypertension (PH) is a serious and progressive condition that affects the pulmonary arteries, leading to an increase in blood pressure within these vessels. The condition can strain the right side of the heart and may eventually result in right heart failure if untreated. PH often occurs due to a range of factors, including genetic predispositions, chronic lung diseases, and other health conditions that affect the heart and lungs (1). Among these contributing factors, tuberculosis (TB) has emerged as a significant potential risk factor. TB, a contagious bacterial infection primarily affecting the lungs, can leave lasting damage even after successful treatment. This damage can result in structural and functional changes within the lung tissue, contributing to an increased risk of PH in post-tuberculosis patients (2). Tuberculosis continues to be a global health concern, particularly in regions with limited access to healthcare. Despite the widespread use of antibiotics and various treatment protocols, TB remains a chronic and recurrent disease for many, often leading to pulmonary complications even after clinical cure. When TB infects the lungs, it can cause a variety of complications, including fibrosis, scarring, and the destruction of lung tissue (3). These physical changes can impact the pulmonary vasculature, leading to an increase in pulmonary artery pressure, which may ultimately contribute to the development of pulmonary hypertension (4). Post-tuberculosis pulmonary hypertension is an area of growing concern within both the pulmonary and cardiovascular medical communities. Studies have shown that individuals who recover from TB are at a heightened risk for a range of respiratory issues, including bronchiectasis, chronic obstructive pulmonary disease (COPD), and PH (5). The exact mechanisms linking TB to PH are still under investigation; however, it is believed that the inflammatory response to the TB infection may play a key role. The inflammatory process can lead to pulmonary vasculopathy, which affects the blood vessels in the lungs, potentially leading to higher pressures in the pulmonary artery. Understanding the frequency of PH in post-tuberculosis patients is essential for several reasons. Firstly, early identification and diagnosis of PH can help improve treatment outcomes. Patients with PH who have a history of TB may benefit from specialized treatment protocols that address both the residual effects of TB and the elevated pulmonary pressures (6). Additionally, identifying the prevalence of PH in post-TB patients can help inform healthcare providers about the long-term management needs of this group, potentially leading to the development of targeted screening programs and follow-up care for those who have had TB. The diagnosis of pulmonary hypertension in post-tuberculosis patients can be challenging due to the overlap in symptoms with other respiratory conditions. Common symptoms of PH, such as shortness of breath, fatigue, chest pain, and dizziness, may also be seen in other post-TB respiratory conditions (7). Advanced imaging and

[Citation Rehman, A.U., Hussain, S., Ullah, F., Habib. M., Sikandar, S., Masood, MA. (2024). Frequency of pulmonary hypertension in post tuberculosis patients. *Biol. Clin. Sci. Res. J.*, **2024***: 1277*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1277]

diagnostic tools, such as echocardiography, right heart catheterization, and pulmonary function tests, are often required to accurately diagnose PH in these patients. The use of these diagnostic tools can help clinicians differentiate PH from other conditions and allow for more accurate detection of the disease (8). In terms of treatment, post-tuberculosis patients with PH may require a combination of therapies, including medications that specifically target pulmonary hypertension and therapies aimed at managing underlying pulmonary issues caused by TB. Pharmacological treatment options for PH include endothelin receptor antagonists, phosphodiesterase-5 inhibitors, and prostacyclin analogs. Additionally, patients may require oxygen therapy, pulmonary rehabilitation, and, in severe cases, surgical interventions (9). Given the chronic nature of pulmonary hypertension and the long-term effects of tuberculosis, regular follow-up is crucial for post-TB patients diagnosed with PH. Ongoing monitoring of pulmonary artery pressure and other cardiac parameters can help prevent disease progression and improve quality of life. Moreover, lifestyle modifications, including smoking cessation, exercise, and dietary changes, can play a supportive role in managing the condition (10). The primary purpose of this study is to determine the frequency of pulmonary arterial hypertension in patients with a history of pulmonary tuberculosis. By identifying how often PH occurs in this population, the study aims to address an area that has received limited attention in Pakistan, where the healthcare burden from TB and its sequelae remains high. Timely identification of PH in post-TB patients is crucial, as it could improve their quality of life, reduce the risks associated with untreated PH, and lessen the overall burden on healthcare systems.

Methodology

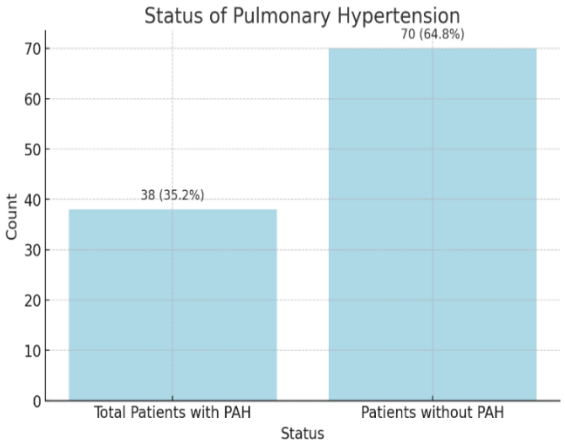
A cross-sectional study design was employed to assess the frequency of pulmonary arterial hypertension (PAH) in patients with a history of pulmonary tuberculosis (PTB). The research was conducted at the Department of Pulmonology, Hayatabad Medical Complex, Peshawar, Pakistan from January 2024 to July 2024. A sample of 108 patients was included in the study. This sample size was calculated using the WHO sample size calculator, based on the following assumptions:

- Expected frequency of PAH in PTB patients: 35%
- Confidence interval: 95%
- Absolute precision: 9%

Data were collected through consecutive non-probability sampling was used to select participants.

- Patients aged 15 to 80 years
- History of pulmonary tuberculosis (as per the operational definition)
- Admitted to the Department of Pulmonology, Hayatabad Medical Complex
- Patients with non-tuberculosis Mycobacterium (MOTT), HIV, diffuse lung disease, chronic thromboembolic pulmonary hypertension (CTEPH), and chronic obstructive pulmonary disease (COPD) regardless of duration
- Patients on long-term immunosuppressants

Pulmonary hypertension was diagnosed by measuring the



pulmonary arterial pressure (PAP) using echocardiography. A PAP of more than 20 mmHg was indicative of pulmonary hypertension. Ethical approval was obtained from the hospital's ethical committee before the commencement of the study. Eligible patients with a history of tuberculosis were enrolled. Informed consent was obtained from each participant after explaining the study's purpose and benefits. A brief history and clinical examination were conducted, followed by echocardiography under the supervision of an expert Pulmonology Fellow of the College of Physicians & Surgeons Pakistan (CPSP). Information such as name, age, gender, weight, and address were recorded on a proforma (Annex-I). Data collection was conducted by the trainee medical officer.

Data were analyzed using SPSS version 20.0. Quantitative variables (age, weight, BMI, and duration of tuberculosis) were described as mean ± standard deviation. Categorical variables (gender, presence of pulmonary hypertension, and severity) were expressed as frequencies and percentages. Pulmonary hypertension was stratified by age, gender, BMI, and duration of TB. A post-stratification Chi-square test was conducted at a 5% significance level. Data were presented in tables, charts, and schemas where necessary.

Results

Data were collected from 108 patients with a mean age of 45.3 ± 12.5 years, indicating a middle-aged population. The gender distribution was slightly male-dominated, with 60 males (55.6%) and 48 females (44.4%). The mean body mass index (BMI) was 22.8 ± 3.4 kg/m², reflecting a generally normal weight range among participants. These demographic characteristics provide a baseline for understanding the study population in terms of age, gender, and BMI. (Table 1)

Table 1: Patient Demographics

Characteristic	Value
Total Patients	108
Age (mean ± SD)	45.3 ± 12.5 years
Male	60 (55.6%)
Female	48 (44.4%)
BMI (mean ± SD)	22.8 ± 3.4 kg/m²

Out of the 108 post-tuberculosis patients, 38 (35.2%) were diagnosed with pulmonary arterial hypertension (PAH),

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while 70 (64.8%) did not have PAH. Among those with PAH, the majority presented with mild severity, with 22 patients (57.9%) having a pulmonary arterial pressure (PAP) between 21-30 mmHg. Moderate PAH (PAP 31-40 mmHg) was observed in 12 patients (31.6%), and severe PAH (PAP > 40 mmHg) in 4 patients (10.5%). (Table 2)

Figure 1: Distribution of pulmonary hypertension

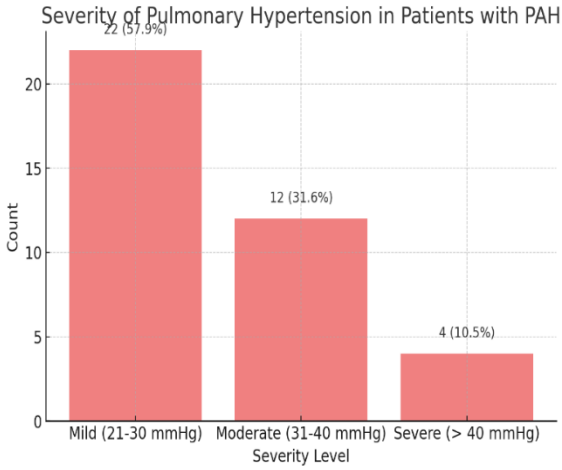

Figure 2: Severity of pulmonary hypertension:

The stratified analysis shows that PAH prevalence increases with age, affecting 28.6% of patients aged 15-30, 34.3% of those aged 31-50, and 40% in the 51-80 age group. Gender-based stratification reveals that PAH was present in 22 of 60 males and 16 of 48 females, suggesting similar rates across genders. Stratification by BMI indicates that underweight patients had the highest PAH prevalence (40%), followed by those with normal weight (35.3%) and overweight individuals (33.3%), highlighting an increased PAH occurrence in both underweight and normal-weight patients compared to overweight individuals. (Table 3)

Among patients diagnosed with TB less than five years prior, 14 out of 48 (29.2%) developed PAH. In those with a TB history of 5-10 years, the prevalence of PAH rose to 40% (16 out of 40), and similarly, 40% (8 out of 20) in those with more than ten years since TB diagnosis. These findings suggest a higher risk of PAH among patients with a longer duration since TB, likely due to progressive pulmonary damage over time. (Table 4)

The severity of pulmonary hypertension (PAH) varied based on the time since tuberculosis (TB) diagnosis. In patients with a TB history of less than five years, most PAH cases were mild (8 cases), with fewer cases at moderate (4) and severe (2) levels. For those diagnosed 5-10 years prior, mild cases increased to 10, while moderate cases reached 6 and severe cases remained at 2. Among patients with over ten years since TB diagnosis, only mild (4) and moderate (2) PAH cases were observed, with no severe cases.

The severity distribution of pulmonary hypertension (PAH) among genders indicates that mild PAH (21-30 mmHg) was slightly more common in males, with 12 cases, compared to 10 in females. Moderate PAH (31-40 mmHg) was observed in 8 male patients and 4 female patients. Severe PAH (> 40 mmHg) was equally distributed, with 2 cases in both genders. (Table 5)

Table 2: Frequency of Pulmonary Arterial Hypertension (PAH)

Status / Severity Level	Count	Percentage
Total Patients with PAH	38	35.2%
Patients without PAH	70	64.8%
Severity of Pulmonary Hypertension		
Mild (21-30 mmHg)	22	57.9%
Moderate (31-40 mmHg)	12	31.6%
Severe (> 40 mmHg)	4	10.5%

Table 3: Stratification by Age Group, Gender, and BMI

Category	Total Patients	Patients with PAH	Percentage with PAH
Stratification by Age Group			
15-30 years	28.0	8.0	28.6%
31-50 years	35.0	12.0	34.3%
51-80 years	45.0	18.0	40%
Stratification by Gender			
Male	60.0	22.0	
Female	48.0	16.0	
Stratification by BMI			
Underweight (< 18.5)	10.0	4.0	40%
Normal weight (18.5–24.9)	68.0	24.0	35.3%
Overweight (≥ 25)	30.0	10.0	33.3%

Table 4: Stratification by Duration of Tuberculosis

Duration since TB Diagnosis	Total Patients	Patients with PAH	Percentage with PAH
< 5 years	48	14	29.2%
5-10 years	40	16	40%
> 10 years	20	8	40%

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Table 5: Stratification by Severity and Duration of Tuberculosis

Severity Level	< 5 years	5-10 years	> 10 years
Mild (21-30 mmHg)	8	10	4
Moderate (31-40 mmHg)	4	6	2
Severe (> 40 mmHg)	2	2	0

Table 6: Stratification by Gender and Severity of PAH

Gender	Mild (21-30 mmHg)	Moderate (31-40 mmHg)	Severe (> 40 mmHg)
Male	12	8	2
Female	10	4	2

Discussion

The study aimed to evaluate the frequency and severity of pulmonary arterial hypertension (PAH) in patients with a history of pulmonary tuberculosis (PTB). With a cross-sectional analysis of 108 patients, this study highlights the significant prevalence of PAH among post-TB patients and provides valuable insights into potential risk factors associated with PAH development in this population (11). Our findings indicate that 35.2% of post-tuberculosis patients were diagnosed with PAH, a substantial proportion that underscores the importance of pulmonary hypertension as a long-term complication of TB. The distribution of PAH severity shows that most patients exhibited mild to moderate PAH, with a smaller proportion experiencing severe PAH. This stratification is clinically relevant, as mild cases of PAH may often go undiagnosed or misattributed to other post-TB respiratory conditions due to overlapping symptoms, such as dyspnea and fatigue (12). The early detection of even mild cases can facilitate timely intervention, potentially slowing disease progression and improving patient outcomes (13).

The data show an increasing prevalence of PAH with age. Patients over 50 years exhibited a notably higher frequency of PAH compared to younger cohorts. This finding suggests that age may be an independent risk factor for PAH in post-TB patients, likely due to age-related vascular changes and the cumulative impact of chronic respiratory conditions. The observed age association aligns with existing literature on PAH, which reports increased susceptibility among older individuals (14). This highlights the need for targeted screening and follow-up care for older post-TB patients to manage the risk of PAH effectively. Another significant finding is the association between the duration since TB diagnosis and PAH prevalence. Patients with a longer interval since their TB diagnosis, particularly those over 5 years post-TB, exhibited a higher frequency of PAH (15). This pattern may be due to the long-term effects of chronic inflammation and lung scarring induced by TB, which can progressively compromise pulmonary vasculature over time. Chronic post-TB lung damage, including fibrosis, may persist and worsen, creating a conducive environment for PAH development. These findings suggest that the chronic nature of lung impairment post-TB has a lasting impact on pulmonary vascular health, necessitating long-term monitoring of such patients (16). Interestingly, gender and BMI did not show statistically significant associations with PAH prevalence in this study, suggesting that other factors, such as age and TB duration, may play more critical roles in PAH development for post-TB patients. While literature on BMI and PAH presents mixed results, this study's findings may reflect the specific pathology of PAH in post-TB patients, where BMI might not directly influence PAH risk. Gender also showed a similar lack of significant association, which may be attributable to the shared exposure to TB-related lung damage across genders rather than sex-specific factors. The significant prevalence of PAH in post-TB patients, particularly those who are older and further removed from their TB diagnosis, calls for a re-evaluation of standard follow-up practices for TB survivors (17). Routine PAH screening could be beneficial for early identification and treatment of PAH in high-risk groups, potentially preventing progression to more severe forms. Moreover, the study underscores the need for specialized pulmonary care that includes echocardiographic evaluation as a standard component of post-TB follow-up. While this study provides important insights, it has limitations. The cross-sectional design limits the ability to establish causality between TB and PAH. Additionally, the single-center setting and the non-probability sampling technique may limit the generalizability of the findings to broader populations. Future research could expand on these findings by exploring longitudinal studies that follow TB patients over time, assessing the progression and risk factors of PAH in different populations. Moreover, investigating the underlying mechanisms linking TB and PAH at the molecular and cellular levels could offer further understanding of the disease process and help in developing targeted therapies.

Conclusion

It is concluded that pulmonary arterial hypertension (PAH) is a significant complication among post-tuberculosis patients, with higher prevalence observed in older individuals and those with a longer duration since TB diagnosis. These findings highlight the need for routine PAH screening in post-TB care to enable early detection and improve patient outcomes. Enhanced follow-up protocols can help address this critical health issue in high-risk populations.

Declarations

Data Availability statement

All data generated or analyzed during the study are included in the manuscript.

Ethics approval and consent to participate

Approved by the department Concerned. (IRBEC-HMC-0142/23)

Consent for publication

Approved

Funding

Not applicable

Conflict of interest

The authors declared absence of conflict of interest.

Author Contribution

ATIQ UR REHMAN (*Postgraduate Resident*)
Conception of Study, Development of Research Methodology Design, Study Design,, Review of manuscript, final approval of manuscript.
***SADAM HUSSAIN (*Postgraduate Resident)**
Coordination of collaborative efforts.
***FASIH ULLAH (*Registrar)**
Study Design, Review of Literature.
MISHAAL HABIB (*Medical Officer*)
Conception of Study, Final approval of manuscript.
SIDRA SIKANDAR (*Women Medical Office*)
Manuscript revisions, critical input.
MUHAMMAD ASIF MASOOD *(Resident* Medical Officer*)*
Coordination of collaborative efforts.

References

1. Grace AG, Mittal A, Jain S, Tripathy JP, Satyanarayana S, Tharyan P, et al. Shortened treatment regimens versus the standard regimen for drug-sensitive pulmonary tuberculosis. Cochrane Database Syst Rev 2019; 1
2. Kay AW, González Fernández L, Takwoingi Y, Eisenhut M, Detjen AK, Steingart KR, et al. Xpert MTB/RIF and Xpert MTB/RIF Ultra assays for active tuberculosis and rifampicin resistance in children. Cochrane Database Syst Rev 2020; 8
3. Goossens SN, Sampson SL, Van Rie A. Mechanisms of Drug-Induced Tolerance in Mycobacterium tuberculosis. Clin Microbiol Rev 2020; 34
4. Moule MG, Cirillo JD. Mycobacterium tuberculosis Dissemination Plays a Critical Role in Pathogenesis. Front Cell Infect Microbiol. 2020; 10:65.
5. Kalla IS, Miri A, Seedat F. Occult pulmonary arterial hypertension in patients with previous pulmonary tuberculosis. Afr J Thoracic Crit Care Med 2020; 26:133-7.
6. Jo YS, Park JH, Lee JK, Heo EY, Chung HS, Kim DK. Risk factors for pulmonary arterial hypertension in patients with tuberculosis-destroyed lungs and their clinical characteristics compared with patients with chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis 2017; 12:2433-43.
7. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J 2019; 53:1801913.
8. Nathan SD, Barbera JA, Gaine SP, Harari S, Martinez FJ, Olschewski H, et al. Pulmonary hypertension in chronic lung disease and hypoxia. Eur Respir J 2019; 53:1801914.
9. Thenappan T, Ormiston ML, Ryan JJ, Archer SL. Pulmonary arterial hypertension: pathogenesis and clinical management. BMJ 2018; 36
10. Butrous G. Pulmonary hypertension; From an orphan disease to a global epidemic. Glob Cardiol Sci Pract. 2020; 2020
11. Rich S, Haworth SG, Hassoun PM, Yacoub MH. Pulmonary hypertension: the unaddressed global health burden. Lancet Respir Med. 2018;6:577–579.
12. Chen Y, Liu C, Lu W, Li M, Hadadi C, Wang EW, et al. Clinical characteristics and risk factors of pulmonary hypertension associated with chronic respiratory diseases: a retrospective study. J Thorac Dis. 2016;8:350–358.
13. Simonneau G, Montani D, Celermajer DS, Denton CP, Gatzoulis MA, Krowka M, et al. Haemodynamic definitions and updated clinical classification of pulmonary hypertension. Eur Respir J. 2019;53:1801913. DOI: 10.1183/13993003.01913-2018.
14. Dodd PJ, Yuen CM, Jayasooriya SM, van der Zalm MM, Seddon JA. Quantifying the global number of tuberculosis survivors: a modelling study. Lancet Infect Dis. 2021;3099:1–9.
15. Romanowski K, Baumann B, Basham CA, Ahmad Khan F, Fox GJ, Johnston JC. Long-term all-cause mortality in people treated for tuberculosis: a systematic review and meta-analysis. Lancet Infect Dis. 2019;19:1129–37.
16. Datta S, Evans CA. Healthy survival after tuberculosis. Lancet Infect Dis. 2019;19:1045–47.
17. Allwood B, van der Zalm M, Makanda G, Mortimer K, Andre FSA, Uzochukwu E, et al. The long shadow post-tuberculosis. Lancet Infect Dis. 2019;19:1170–71.

[Citation Rehman, A.U., Hussain, S., Ullah, F., Habib. M., Sikandar, S., Masood, MA. (2024). Frequency of pulmonary hypertension in post tuberculosis patients. *Biol. Clin. Sci. Res. J.*, **2024***: 1277*. doi: https://doi.org/10.54112/bcsrj.v2024i1.1277]