

## Original Research Article

## Special Issue: Pulmonary Medicine

**Prevalence and Risk Factors for Pulmonary Artery Hypertension and Cor Pulmonale in Post Tuberculosis Pulmonary Sequelae: A Cross Sectional Study****Dr. Deepak Kumar Thakur<sup>\*1</sup>, Shouvik Chatterjee<sup>2</sup>, Akhilesh Kumar<sup>3</sup> & Pawan Kumar Agrawal<sup>4</sup>**<sup>1,2</sup>Resident, Pulmonary Medicine, Patna Medical College, Patna.<sup>3</sup>Senior Resident, Pulmonary Medicine, Patna Medical College, Patna.<sup>4</sup>HOD, Department of Respiratory Medicine, Patna Medical College, Patna.

## HIGHLIGHTS

1. High prevalence of pulmonary artery hypertension observed.
2. Tuberculosis survivors face increased risk factors.
3. Cor pulmonale linked with TB sequelae
4. Study highlights need for early detection.
5. Management strategies essential for improved outcomes.

## ARTICLE INFO

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## ABSTRACT

**Introduction:** Tuberculosis (TB) remains a global health challenge, particularly in endemic regions like India. While the primary focus has been on reducing TB incidence and mortality, the long-term complications, such as pulmonary hypertension and cor pulmonale, among patients with post-tuberculosis pulmonary sequelae, are often overlooked. These conditions significantly contribute to morbidity and mortality, highlighting the need for targeted interventions. **Objective:** The study aimed to evaluate the prevalence and risk factors associated with pulmonary hypertension and cor pulmonale in patients with post-tuberculosis pulmonary sequelae. **Methods:** This cross-sectional study was conducted at the Department of Respiratory Medicine, Patna Medical College Hospital, from January 2023 to June 2024. A total of 100 patients with a history of pulmonary tuberculosis and evidence of post-tuberculosis pulmonary sequelae on chest X-ray and HRCT were included. Patients with active TB or other causes of pulmonary hypertension were excluded. **Results:** The study found that 56% of patients had pulmonary hypertension, with a 33% prevalence of cor pulmonale. Bilateral lung involvement was associated with a 5.6 times greater risk of pulmonary hypertension compared to unilateral involvement. Male gender and lower BMI were significant risk factors, with underweight patients showing a higher prevalence of pulmonary hypertension. Fibrosis was the most common sequelae, and patients with multiple types of sequelae had a significantly higher risk of developing pulmonary hypertension. **Conclusion:** The high prevalence of pulmonary hypertension and cor pulmonale among patients with post-tuberculosis pulmonary sequelae underscores the need for long-term monitoring and preventive strategies. Integrating these considerations into TB management programs is crucial to reduce morbidity and mortality and improve patient outcomes.

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\* Corresponding author.

Dr. Deepak Kumar Thakur, Resident, Pulmonary Medicine, Patna Medical College, Patna.

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## INTRODUCTION

Tuberculosis (TB) remains a global health challenge, particularly in light of its persistence as a leading cause of mortality despite significant advances in medical treatment and public health strategies. Caused by *Mycobacterium tuberculosis*, TB is primarily an airborne disease that continues to affect millions worldwide. The Global TB Report for 2022 highlighted a notable rebound in the diagnosis and treatment of TB cases, marking a recovery from the severe disruptions caused by the COVID-19 pandemic over the preceding two years[1]. This recovery is crucial as it begins to reverse the adverse impacts of the pandemic on TB-related illness and mortality. Despite this progress, TB persisted as the second leading cause of death from a single infectious agent globally in 2022, trailing only COVID-19 and resulting in nearly double the number of deaths compared to HIV/AIDS[2].

In 2022, a staggering 7.5 million new TB diagnoses were reported globally, underscoring the enduring threat posed by this disease. The Indian TB 2024 Report further shed light on the situation in India, where TB is endemic, reporting 230,000 missed TB cases in 2023[3]. This marked a significant decrease from the 320,000 missed cases the previous year, reflecting ongoing improvements in TB management and patient tracking, particularly through initiatives like the Ni-kshay portal. This government-backed platform has played a pivotal role in enhancing the identification and monitoring of TB patients, contributing to the reduction in missed cases and ensuring that more individuals receive timely treatment[4].

However, even as global and national efforts focus on reducing TB incidence and mortality, a critical yet often overlooked aspect of TB management is the post-treatment phase. Patients who have successfully completed TB treatment, particularly those with pulmonary tuberculosis, frequently suffer from lasting structural and functional lung damage. These conditions, collectively termed post-tuberculosis pulmonary sequelae, can have profound implications on patients' long-term health. Given the high global incidence of TB, the impact of these sequelae is considerable[5]. Yet, despite their significance, current global health initiatives, such as the Sustainable Development Goals and the WHO End TB Strategy, primarily emphasize reducing TB incidence and mortality. These initiatives lack specific guidelines for monitoring patients after they complete treatment to detect and manage these sequelae effectively[6].

Research indicates that more than half of the patients who are microbiologically cured of TB continue to exhibit some form of pulmonary impairment. These post-tuberculosis sequelae manifest as persistent respiratory symptoms, diminished quality of life, frequent exacerbations that often require hospitalization, and severe complications such as hemoptysis (coughing up blood)[7]. Moreover, these sequelae are associated with increased mortality, representing an additional, often unmeasured, burden of TB. Among the myriad conditions associated with TB sequelae, fibrosis with volume loss, bronchiectasis, and cavity formation are the most common.

These conditions are not only prevalent in chronic respiratory diseases but are also indicative of the long-term damage inflicted by chronic infections and inflammatory diseases, including TB[8].

One of the most concerning complications of post-tuberculosis pulmonary sequelae is the development of pulmonary hypertension. The damage to the pulmonary vascular bed caused by TB can lead to increased pulmonary vascular resistance, which, in turn, results in pulmonary hypertension. Chronic hypoxia, a common consequence of impaired lung function, exacerbates this condition by inducing hypoxic vasoconstriction and subsequent vascular remodeling[9]. If left unchecked, prolonged pulmonary hypertension can lead to right ventricular hypertrophy and dysfunction, a condition known as cor pulmonale. This progression highlights the critical need for early detection and intervention to prevent irreversible cardiovascular damage[10].

Despite these significant risks, pulmonary tuberculosis is not commonly recognized as a primary cause of pulmonary hypertension[11]. This oversight is particularly concerning in regions where TB is endemic, such as India, where the prevalence of pulmonary hypertension among patients with TB sequelae is likely substantial. The lack of recognition and subsequent investigation into this association underscores a gap in our understanding of the full spectrum of TB's long-term effects on health[12].

The underappreciated relationship between pulmonary tuberculosis sequelae and the development of pulmonary hypertension[13]. By highlighting this connection, the study advocates for the integration of regular follow-up and monitoring protocols for patients who have completed TB treatment. Such measures are crucial for the early detection of pulmonary hypertension and other long-term complications, which, if managed appropriately, can significantly reduce morbidity and mortality associated with TB[14].

Global efforts to combat TB have made significant strides, especially in the wake of the COVID-19 pandemic, the focus must also expand to include the long-term health of TB survivors[15]. The burden of post-tuberculosis pulmonary sequelae, including the risk of pulmonary hypertension, represents a critical area of concern that requires immediate attention. Strengthening follow-up care and establishing clear guidelines for monitoring these patients can help mitigate the long-term impacts of TB and improve overall patient outcomes[16].

The aim of this study is to evaluate the prevalence and risk factors associated with cor pulmonale and pulmonary artery hypertension in patients with post-tuberculosis pulmonary sequelae. Specifically, the objectives are to determine the prevalence of these conditions in affected individuals, to compare patients with post-tuberculosis pulmonary sequelae who have pulmonary hypertension with those who do not, and to identify the specific risk factors contributing to the development of cor pulmonale in patients suffering from pulmonary hypertension.

**MATERIALS AND METHODS**

The research was conducted at the Department of Respiratory, Medicine, Patna Medical College and Hospital, Patna. with Institutional Ethical Committee approval. This cross-sectional study, conducted from January 2023 to June 2024, involved 100 patients. Participants included those attending the outpatient clinic or admitted as inpatients, selected based on inclusion criteria: age  $\geq 18$  years, history of pulmonary tuberculosis, post-tuberculosis pulmonary sequelae on chest X-ray and HRCT, and no active TB. Exclusion criteria were pregnant women, HIV-positive individuals, unwilling participants, other causes of pulmonary hypertension, lung resection history, lung cancer,

smoking, or major comorbidities.

**RESULTS**

The majority of patients in the study, accounting for 51%, were aged between 18 and 40 years, indicating that TB-related pulmonary complications predominantly affect younger adults. The gender distribution revealed a higher prevalence among males, who made up 63% of the cohort, compared to 37% females. This male predominance may reflect gender-related differences in exposure to risk factors, healthcare access, or the biological response to tuberculosis, highlighting the need for targeted interventions in these demographics.

**Table 1: Comparison of Number of Zones Involved and Core Pulmonale**

	Cor Pulmonale Present	Cor Pulmonale Absent	Total PH Patients
One	0	1	1
Two	02	12	14
Three	18	08	26
Four	07	02	09
Five	01	0	01
Six	05	0	05
	Total-33	Total-23	56

A significant difference was observed in the number of lung zones affected between patients with and without cor pulmonale, with a p-value of less than 0.001. Patients with three or more lung zones involved were at a markedly higher risk, inc-

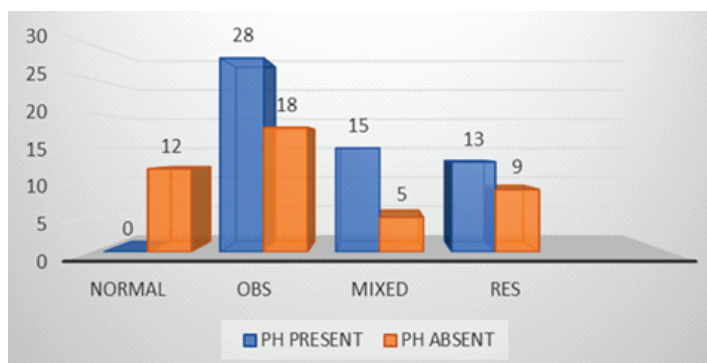
-reasing the likelihood of developing cor pulmonale by 20.15 times, with this association being statistically significant, reflected by a p-value of 0.0239.

**Table 2: Comparison of Laterality in Chest X-Ray and Pulmonary Hypertension**

	PH Present	PH Absent	Total Patients
Bilateral	35	10	45
Unilateral	21	34	55
	Total-56	Total-44	100

Most patients (55%) had unilateral disease, while those with bilateral disease had a significantly higher incidence of pulmonary hypertension, with 77.7% affected compared to 38.1% in unilateral cases. Bilateral involvement was associated

with a 5.6 times greater risk of developing pulmonary hypertension, a statistically significant finding with a p-value of less than 0.001.



**Figure 1: Spirometry Pattern and Pulmonary Hypertension**

Patients with normal spirometry were unlikely to develop pulmonary hypertension or cor pulmonale. However, most patients exhibited abnormalities: 46 with an obstructive pattern, 22 with restriction, and 20 with a mixed pattern. Among these, 60.8% with obstruction, 75% with a mixed Patte-

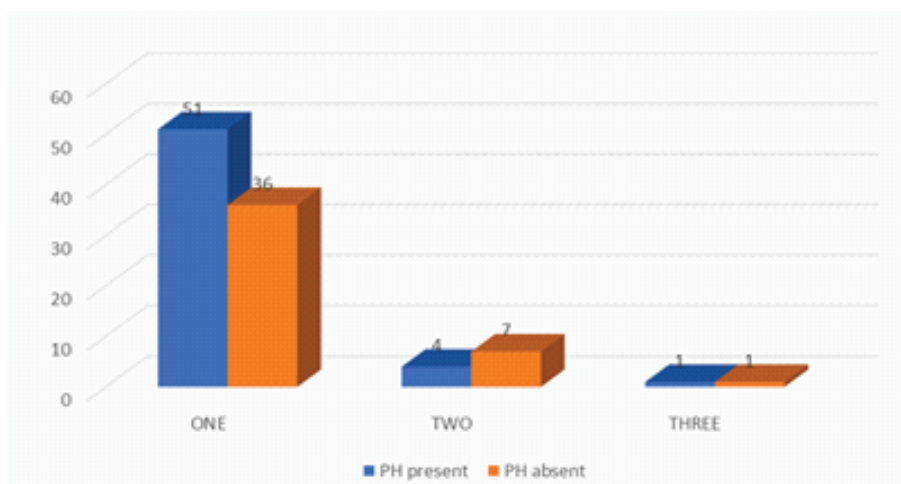
-rn, and 59% with restriction had pulmonary hypertension. Any spirometry abnormality significantly increased the risk of pulmonary hypertension ( $p < 0.001$ , OR 5.55), with an obstructive pattern posing a 17.14 times higher risk ( $p = 0.0006$ ).

**Table 3: Comparison of BMI and Presence of Corpulmonale.**

	Cor Pulmonale Present	Cor Pulmonale Absent	Total Ph Patients
Underweight	15	09	24
Normal	15	07	22
Overweight	02	05	07
Obese	01	02	03
	Total-33	Total-23	56

In our study, BMI ranged from 14 to 33.2, with 37% of patients underweight, 45% of normal weight, 11% overweight, and 7% obese. Underweight patients had a significantly higher risk of developing pulmonary hypertension, with a p-value of less th-

-an 0.001 and an odds ratio of 2.6. Additionally, BMI significantly influenced the severity of pulmonary hypertension ( $p = 0.05$ ) and the risk of developing cor pulmonale ( $p = 0.011$ ).



**Figure 2: Number of Pulmonary Tuberculosis Episodes and Pulmonary Hypertension**

Most patients in the study had a single episode of pulmonary tuberculosis, with only 13% experiencing a relapse. Among those with a relapse, 38.4% developed pulmonary hypertension, while 58.6% of patients with a single episode al-

-so had pulmonary hypertension. However, analysis of variance revealed no significant impact of the number of TB episodes on the risk of pulmonary hypertension ( $p = 0.14$ ). A larger sample size is needed to determine the actual relationship.

**Table 4: Comparison of Drug Sensitivity Pattern and the Presence of Pulmonary Hypertension**

	PH Present	PH Absent	Total
Resistant	7	4	11
Sensitive	49	40	89
Total	56	44	100

No significance between drug sensitivity pattern and pulmona-

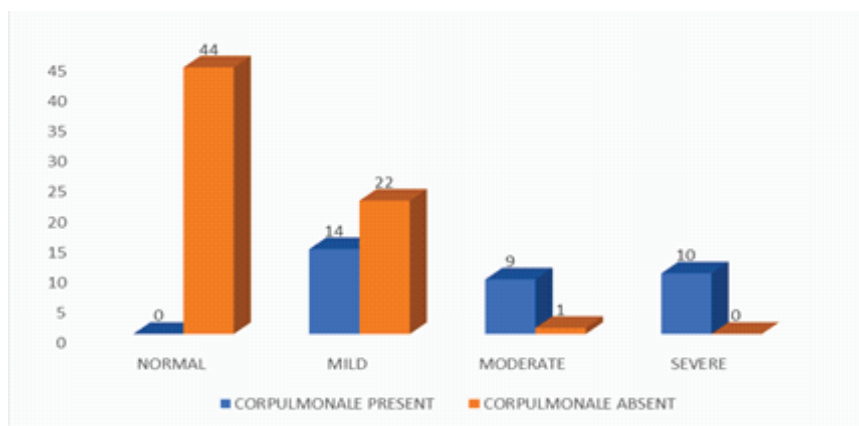
-ry hypertension was seen as  $p = 0.95$ .

**Table 5: Comparison of the Number of Lesion Types and the Presence of Pulmonary Hypertension.**

	PH Present	PH Absent	Total Patients
Multiple	52	27	79
Single	04	17	21
	Total-56	Total-44	100

Among the patients, 79 had multiple types of lesions, while 21 had a single type. Pulmonary hypertension was observed in 65.8% of those with multiple lesions, compared to only 19.04% of patients with a single lesion. The presence of multiple types

of sequelae is statistically significantly associated with a higher risk of developing pulmonary hypertension. The odds ratio is 8, with a p-value of less than 0.001, indicating a strong correlation between multiple lesions and pulmonary hypertension.

**Figure 3: Pulmonary Hypertension Severity and Cor Pulmonale**

Cor pulmonale was present in 14 of 36 patients with mild pulmonary hypertension, 9 of 10 with moderate pulmonary hypertension, and all 10 patients with severe pulmonary hypertension.

## DISCUSSION

In Western literature, pulmonary tuberculosis (TB) is not typically associated with the development of pulmonary hypertension. However, in endemic regions like India, where TB incidence is high and the risk of post-disease complications is significant, it becomes a major contributor to pulmonary hypertension. This condition often exacerbates the morbidity and mortality linked to tuberculosis, a concern that is frequently overlooked. Our study aimed to assess the prevalence and risk factors of pulmonary hypertension and cor pulmonale in patients with post-tuberculosis pulmonary sequelae [17].

Our study found that 56% of patients with post-tuberculosis pulmonary sequelae had pulmonary hypertension, a rate significantly higher than those reported in studies by Mani Tiwari et al. from Europe (24%) and Russia (44.2%), suggesting a greater prevalence in endemic regions. Additionally, we observed a 33% prevalence of cor pulmonale among our patients, which is markedly higher compared to the 11% prevalence reported by Kotresh N et al. This disparity underscores the increased burden of pulmonary complications in regions where tuberculosis is more prevalent, highlighting the need for targeted interventions and monitoring [18,19].

In our study, 58.9% of patients with pulmonary hypertension al-

-so had cor pulmonale, with its prevalence rising alongside the severity of pulmonary hypertension. This finding aligns with the suggestion by Hilde J. M. et al. that reduced pulmonary vascular compliance can lead to right ventricular hypertrophy and remodeling even before significant increases in pulmonary artery pressure are evident. This pathophysiological mechanism may account for the high prevalence of cor pulmonale observed in our cohort. The study highlights the importance of early detection and management of pulmonary hypertension to mitigate the progression to cor pulmonale in affected patients [20].

In contrast to Al. Obaidy et al., who found that older age was associated with a higher prevalence of pulmonary hypertension, our study did not observe a significant link between age and pulmonary hypertension. However, we identified male gender as a significant risk factor, differing from Majid Marjani et al., who reported no such relationship. This discrepancy may be due to the anti-remodeling effects of estrogen and the pro-remodeling effects of androgen on pulmonary vessels, as discussed by Ventetuolo et al [21,22,23].

Body mass index (BMI) was identified as a marginally significant risk factor for pulmonary hypertension in our study, with a p-value of 0.05, consistent with findings by Young Suk Jo et al. Underweight individuals were at higher risk, aligning with C.D. Burger et al.'s observation of lower BMI in patients with pulmonary hypertension due to chronic lung and heart diseases. This association may be linked to increased work of breathing, leading to malnutrition, though the exact mechanism remains unclear [24,25].

Radiological characteristics, particularly the extent of involvement measured by the number of affected zones and sides, were statistically significant in our study. Patients with multiple types of sequelae faced a higher risk of pulmonary hypertension compared to those with a single type, highlighting that the degree of parenchymal damage is a crucial factor in pulmonary hypertension risk. This finding aligns with previous research by Lynch DA et al., emphasizing the importance of comprehensive radiological assessment in evaluating the risk of pulmonary hypertension[26].

Fibrosis was the most common type of sequelae observed, followed by bronchiectasis and cavitary lesions, consistent with findings by M.G. Ali et al., who also reported a higher incidence of fibrosis in post-tuberculosis sequelae. Patients with multiple types of sequelae had a significantly higher risk of developing pulmonary hypertension compared to those with only one type. This highlights the importance of recognizing and managing multiple sequelae to mitigate the risk of pulmonary hypertension[27].

Bilateral involvement was associated with a risk of developing pulmonary hypertension at least five times greater than unilateral involvement, with a significantly higher likelihood of progression to cor pulmonale. Most patients with pulmonary hypertension also presented with dyspnea, underscoring the severe impact on morbidity and mortality in post-tuberculosis sequelae, as supported by findings from Lynch DA et al. This highlights the critical need for long-term monitoring to mitigate the risk of pulmonary hypertension in these patients[26].

## CONCLUSION

The significant prevalence of pulmonary hypertension and cor pulmonale among patients with post-tuberculosis pulmonary sequelae underscores the urgent need for long-term follow-up and preventive strategies in tuberculosis care. Integrating these considerations into national and international tuberculosis management programs is crucial. Preventing pulmonary hypertension and cor pulmonale effectively requires early detection, appropriate treatment, and strict adherence to tuberculosis therapy. Emphasizing these areas can substantially reduce morbidity and mortality. A strong national program, supported by dedicated healthcare professionals, is essential to address this post-treatment burden and improve patient outcomes, ensuring comprehensive care for tuberculosis survivors.

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