PREVALENCE AND RISK FACTORS FOR PULMONARY ARTERY HYPERTENSION AND CORPULMONALE IN POST TUBERCULOSIS PULMONARY SEQUELAE

DISSERTATION SUBMITTED TO THE TAMILNADU

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In partial fulfilment of the requirements for the degree of

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(TUBERCULOSIS AND RESPIRATORY MEDICINE)

DEPARTMENT OF RESPIRATORY MEDICINE

TIRUNELVELI MEDICAL COLLEGE HOSPITAL

TIRUNELVELI – 627011

MAY-2020

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Date :
Place: TIRUNELVELI

Dr.E.MATHAN, M.D.
SENIOR ASSISTANT PROFESSOR,
DEPARTMENT OF RESPIRATORY MEDICINE,
TIRUNELVELI MEDICAL COLLEGE,
TIRUNELVELI.

DECLARATION BY THE CANDIDATE

I solemnly declare that this dissertation titled "**PREVALENCE AND RISK FACTORS FOR PULMONARY ARTERY HYPERTENSION AND CORPULMONALE IN POST TUBERCULOSIS PULMONARY SEQUELAE"** submitted by me for the degree of M.D., is the record work carried out by me during the period of 2017-2020 under the guidance of **Dr.E.MATHAN, M.D**, Senior Assistant Professor, Department of Respiratory Medicine, Tirunelveli Medical College, Tirunelveli. The dissertation is submitted to The Tamilnadu Dr. M.G.R. Medical University, Chennai, towards the partial fulfilment of requirements for the award of M.D.(Branch XVII) Tuberculosis and Respiratory Medicine examination to be held in May 2020.

Place: Tirunelveli
Date

Dr. GAYATHRI S RAJEEV,
Department of Respiratory Medicine,
Tirunelveli Medical College,
Tirunelveli

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TIRUNELVELI, STATE OF TAMILNADU, SOUTH INDIA PIN 627011
91-462-25/2/93-EXT; 91-462-25/2944; 91-462-25/9785; 91-462-25/2611-16
online@tvmc.ac.in, tirec@tvmc.ac.in; www.tvmc.ac.in

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PRINCIPAL INVESTIGATOR: Dr.GAYATHRI.S.RAJEEV, MBBS.,
DESIGNATION OF PRINCIPAL INVESTIGATOR: PG STUDENT
DEPARTMENT & INSTITUTION: TIRUNELVELI MEDICAL COLLEGE, TIRUNELVELI

Dear Dr.GAYATHRI.S.RAJEEV, MBBS, The Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during The IEC meeting held on 27.10.2017.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☐
2.	Study Protocol	☐
3.	Department Research Committee Approval	☐
4.	Patient Information Document and Consent Form in English and Vernacular Language	☐
5.	Investigator's Brochure	☐
6.	Proposed Methods for Patient Accrual Proposed	☐
7.	Curriculum Vitae of The Principal Investigator	☐
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☐
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☐
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor The study
6. At The time of PI's retirement/leaving the institute, The study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in The original project. (Page no. Clause no. etc.)
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Registrar, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

Dr.J.SureshDurai, MD
Member Secretary, TIREC
Tirunelveli Medical College, Tirunelveli – 627011
State of Tamilnadu, South India

CERTIFICATE – II

This is to certify that this dissertation work title **"PREVALENCE AND RISK FACTORS FOR PULMONARY ARTERY HYPERTENSION AND CORPULMONALE IN POST TUBERCULOSIS PULMONARY SEQUELAE"** of the candidate **Dr. GAYATHRI S RAJEEV** with registration Number **201727201** for the award of **M.D.,** Degree in the branch of **TUBERCULOSIS AND RESPIRATORY MEDICINE (XVII).** I personally verified the urkund.com website for the purpose of plagiarism check. I found that the uploaded thesis file contains from introduction to conclusion page and result shows **5% percentage** of plagiarism in the dissertation.

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CONTENT

ABBREVIATIONS

AFB	: Acid fast bacilli
BMI	: Body mass index
CO	: Cardiac output
COPD	: Chronic obstructive pulmonary disease
CPFE	: Combined pulmonary fibrosis and emphysema
CT	: Computed tomography
DLCO	: Diffusing capacity of lung for carbon monoxide
ECG	: Electrocardiogram
ECM	: Extra cellular matrix
FAC	: Fractional area change
FEV1	: Forced expiratory volume in 1 second
FVC	: Forced vital capacity
HIF-1	: Hypoxia inducible factor 1
HIV	: Human immunodeficiency virus
IFNγ	: Interferon gamma
IL	: Interleukins
IPF	: Idiopathic pulmonary fibrosis

IVC : Inferior vena cava

LV : Left ventricle

MDR TB : Multi-drug resistant tuberculosis

mPAP : Mean pulmonary artery pressure

MPA : Main pulmonary artery

PAH : Pulmonary arterial hypertension

PaO2 : Partial pressure of oxygen in artery

PAWP : Pulmonary artery wedge pressure

PH : Pulmonary hypertension

PTB : Pulmonary tuberculosis

PVR : Pulmonary vascular resistance

RAD : Right axis deviation

RAE : Right atrial enlargement

RAP : Right atrial pressure

RV : Right ventricle

RVH : Right ventricular hypertrophy

RVMPI : Right ventricle myocardial performance index

RVSP : Right ventricle systolic pressure

SaO2 : Oxygen saturation in artery

sPAP : Systolic pulmonary artery pressure

TAPSE : Tricuspid annular plane systolic excursion

TASV/ S’ : Tricuspid annular systolic velocity

TB : Tuberculosis

TGFβ : Transforming growth factor beta

Th1 : T helper cell type 1

Th2 : T helper cell type 2

TNFα : Tumor necrosis factor alpha

TRV/v : Tricuspid regurgitation velocity

VEGF : Vascular endothelial growth factor

WHO : World health organization

INTRODUCTION

Tuberculosis is an air borne infectious disease caused by Mycobacterium tuberculosis. It ranks as one of the leading causes of death worldwide. Global incidence of TB is 9.6million annually, out of which one fourth is from India. More than 40% population in India are infected with the mycobacterium. It causes death of 2.2 lakhs people per year. [(1)]

Pulmonary tuberculosis patients are frequently left with structural and functional sequelae due to irreversible lung damage. These are called post tuberculosis pulmonary sequelae. As the global incidence of Tuberculosis is high, the problem of sequelae could be substantial. But current global policies like Sustainable development goals and WHO end TB strategy focus on reducing incidence and mortality of TB. There is no recommendations regarding follow up of TB patients after completing treatment to look for sequelae. [(2)]

In more than half of the microbiologically cured TB patients,pulmonary impairment was identified [(3)]. Sequelae can result in recurrent respiratory symptom, decreased quality of life, frequent exacerbations requiring hospitalization, many complications like hemoptysis etc. and increased mortality. It adds to the unmeasured burden of TB [(4)].

Sequelae can cause destruction of pulmonary vascular bed resulting in increased pulmonary vascular resistance and pulmonary hypertension. Chronic hypoxia also has role, due to hypoxic vasoconstriction resulting in vascular remodeling. Long standing

pulmonary hypertension can result in right ventricular hypertrophy and dysfunction, called cor pulmonale[5]. But, pulmonary tuberculosis is not mentioned as a cause of pulmonary hypertension. India being an endemic country, prevalence of pulmonary hypertension in TB sequelae patients might be high and it needs to be studied[6].

In this study, we aim to emphasize that pulmonary tuberculosis sequelae is one of the major causes of pulmonary hypertension and thus, the need for follow up and monitoring of treated tuberculosis patients to prevent morbidity and mortality associated with this complication.

AIMS AND OBJECTIVES

AIM

To assess the prevalence and risk factors for pulmonary artery hypertension and corpulmonale in post tuberculosis pulmonary sequelae.

OBJECTIVES

- To assess the prevalence of pulmonary artery hypertension and corpulmonale in patients with post tuberculosis pulmonary sequelae.
- To compare post tuberculosis pulmonary sequelae patients with, and without pulmonary hypertension and assess the risk factors.
- To assess the risk factors for corpulmonale in patients with pulmonary hypertension.

REVIEW OF LITERATURE

Tuberculosis is a chronic infection that is caused by Mycobacterium tuberculosis. It is associated with widespread morbidity and mortality. Despite microbiological cure, there may be residual anatomical and functional changes. These persistent radiological lesions are called post tuberculosis sequelae. It can be pulmonary or extra pulmonary. Pulmonary sequelae can result in long term symptoms and disabilities, effecting quality of life.[7]

Due to parenchymal destruction and resulting hypoxia, pulmonary sequelae have high chance of causing pulmonary hypertension and corpulmonale.

EPIDEMIOLOGY

Tuberculosis is in the top 10 leading causes of death and the leading cause by a single infectious agent worldwide. Globally, TB incidence is 10 million cases of which 5.58lakh are rifampicin resistant (3.5% of new and 18% of previously treated patients).

India is one of the 30 high burden TB countries. India has the highest incidence of both drug sensitive and MDR TB and the second highest incidence of HIV and TB co-infection. Incidence of TB in India is 27.4lakh (27% of global incidence) and MDR-TB is 1.35lakh (24% of global incidence). [1]

There are several initiatives to decrease the incidence, morbidity and mortality associated with tuberculosis like ‘End TB strategy’, ‘Sustainable development goals’, ‘national strategic plan for tuberculosis elimination’ etc. Various indicators are used to assess the programs which include mainly case detection rate, treatment coverage and treatment success rate. There are no recommendations regarding assessing the patient post treatment for persistent radiological manifestations. Thus, these sequelae remain a major cause of unmeasured morbidity and mortality due to TB.

J Ravendran et al had showed that 67.1% patients had persistent symptoms post tuberculosis. Various studies showed incidence of post pulmonary tuberculosis sequelae in a range of 50%-90% [3].

POST PULMONARY TUBERCULOSIS SEQUELAE

Pulmonary tuberculosis can result in a variety of complications and sequlae which can be widely divided as

• Parenchymal	1. Cicatrisation or fibrosis 2. Thin walled cavity 3. Aspergilloma 4. Emphysema or bullae 5. Bronchogenic carcinoma 6. Calcification 7. Tuberculoma

• Airway	1. Bronchiectasis 2. Tracheobronchial stenosis 3. Broncholithiasis
• Pleural	1. Chronic empyema 2. Fibrothorax 3. Pneumothorax 4. Bronchopleural fistula
• Vascular	1. Arteritis and thrombosis 2. Bronchial artery dilation 3. Rasmussen aneurysm
• Mediastinal	1. Esophagobronchial fistula 2. Esophagomediastinal fistula 3. Fibrosingmediastinitis
• Chest wall	1. Chondritis and osteomyelitis 2. Empyema necessititans

Table 1: Classification of post tuberculosis pulmonary sequelae [8]

Among them the most common are

- Fibrosis with volume loss
- Bronchiectasis
- Cavity
- Fibrothorax and Pleural thickening

- Bullae
- Aspergilloma
- Calcification. [8]

FIBROSIS

Fibrosis is the most commonly encountered post pulmonary tuberculosis sequelae. 40% of patient with history of pulmonary tuberculosis has evidence of fibrosis in radiography. Fibrous tissue replaces granulation tissue during healing in tuberculosis [9].

In chest X-ray, it consists of fibrotic parenchymal bands and nodules mostly in upper lobe. It is associated with features of volume loss like retraction of hilum, elevated ipsilateral diaphragm, narrowing of intercostal spaces, shift of mediastinum to same side and hyperinflation of normal lobes (Figure 1). Extensive involvement can result in complete destruction and fibrosis of an entire lung [10] (Figure 2).

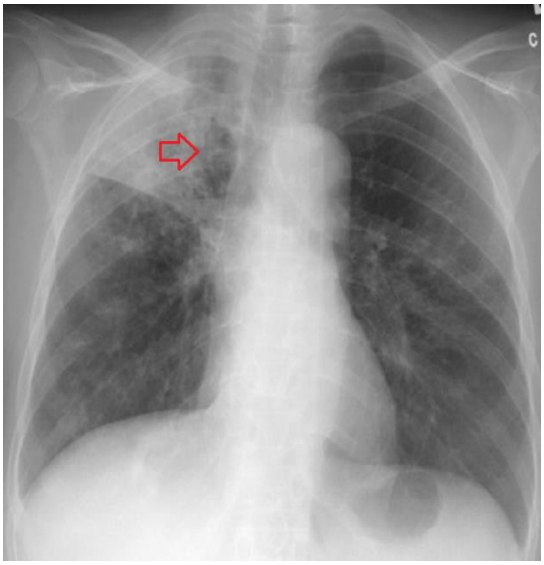


Figure 1: Fibrosis right upper zone

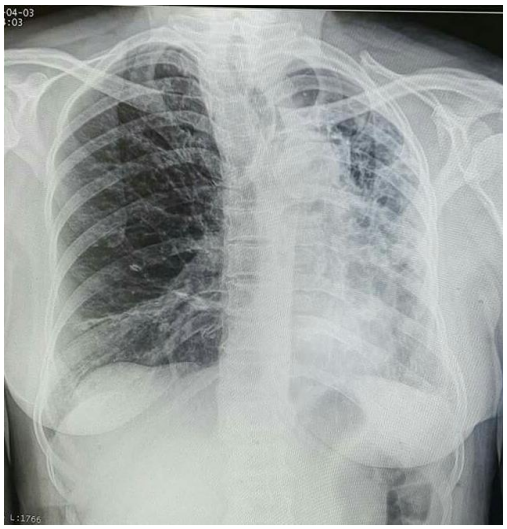


Figure2: Extensive fibrosis of left hemithorax

BRONCHIECTASIS

Bronchiectasis is abnormal irreversible dilation and thickening of bronchi. Systematic review shows 40% of post pulmonary tuberculosis patient develop bronchiectasis. Previous tuberculosis is the most frequent cause of bronchiectasis (35.5%) in tuberculosis endemic countries like India [(11)].

Post tuberculosis Bronchiectasis occurs as a result of:

- Inflammation and destruction of the bronchial wall leading to its weakening and dilation.
- Obstruction by hilar lymphadenitis, Bronchial stenosis and broncholith results in retention of secretion and recurrent bacterial infection leading to destruction and dilation.
- Secondary to parenchymal fibrosis- tractional bronchiectasis [(12)].

It is mostly seen in upper lobe. Due to effective drainage by gravity, it is a dry type- Bronchiectasis sicca. In chest X-Ray dilated bronchi are seen as irregular oval or tubular air filled structures. Thickened bronchial wall is seen as parallel lines called ‘tram track’. In cross sectional view, they form ring shadows. [13](Figure 3)

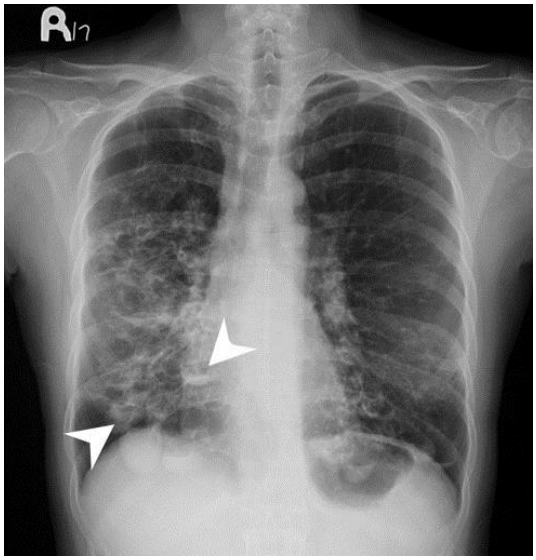


Figure 3: Bronchiectasis right lower zone

CAVITY

Occasionally, after tuberculosis chemotherapy residual thin walled cavity may remain as air filled cystic space. This is called open negative syndrome. Epithelisation of inner wall of cavity occurs, preventing these cavities from collapse and fibrosis [14]. These cavities can lead to secondary infection, fungal colonization, pneumothorax etc.

They represent the presence of liquefactive necrosis during active disease. Liquefactive necrosis favors bacterial growth and is associated with high bacillary load and thus extensive damage to lung parenchyma [15].

In Chest X-ray, it is an air filled space with smooth wall of thickness varying from 1cm to less than 1mm making it difficult to distinguish from cyst [7]. (Figure 4)

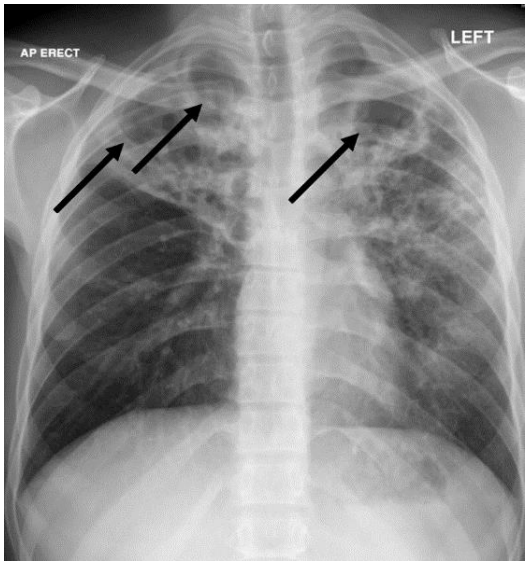


Figure 4: Cavity bilateral upper zone

FIBROTHORAX AND PLEURAL THICKENING

Tuberculosis cause intense inflammation of adjacent pleura that results in deposition of fibrous tissue in visceral pleura during healing. It may be localized or diffuse. The diffuse pleural thickening, known as fibrothorax, prevents the underlying lung from expanding causing trapped lung, resulting in restrictive ventilatory defect.

Localized thickening may be asymptomatic or may result in persistent pleuritic chest pain. It may undergo calcification [16].

Chest X-ray shows unilateral diffuse pleural thickening that may be calcified with shift of mediastinum to same side. (Figure 5 and 6)

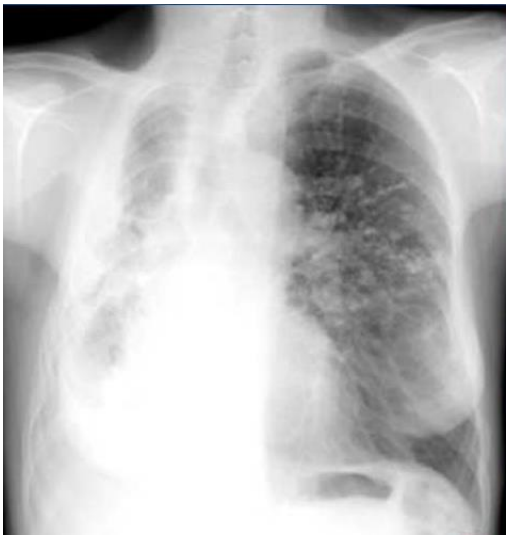


Figure 5: Fibrothorax of right hemithorax

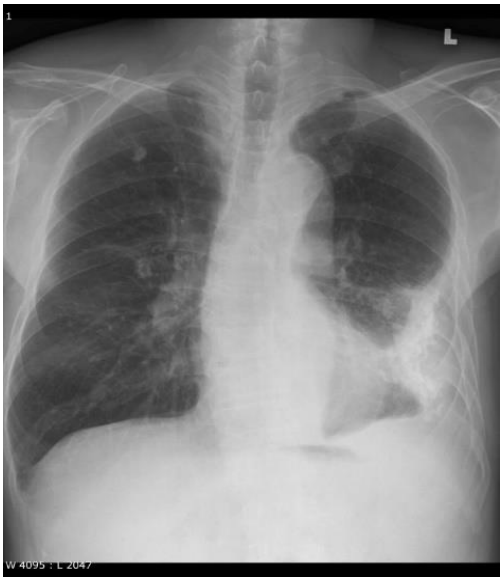


Figure 6: Pleural thickening with calcification left lower zone

BULLAE

Bullae are air filled spaces in the lung parenchyma measuring >1cm. Its wall is thin (<1mm) and made of compressed adjacent lung parenchyma. It is formed by destruction, dilation and confluence of air spaces distal to terminal bronchiole [17]. In Chest X-ray they appear as areas of increased radiolucency with sharp incomplete thin radio-opaque wall. Lung vasculature is not visible inside it [18]. (Figure 7)

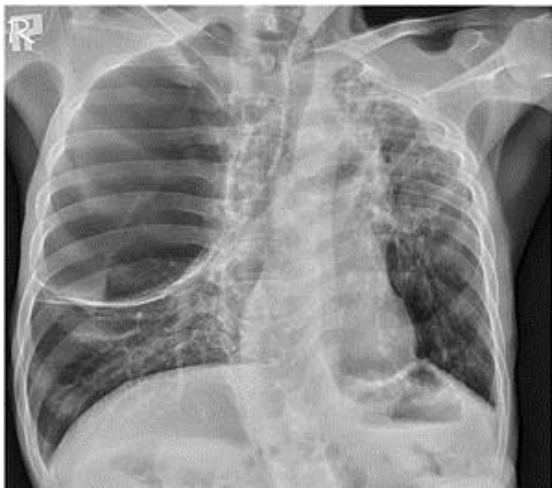


Figure 7: Giant bullae right side

ASPERGILLOMA

Mycetoma or fungal ball is a mass of fungal hyphal material that colonizes and grows in lung cavities. Since, Aspergillus fumigatus is the most frequent agent, it is commonly called aspergilloma. It occurs in cavities associated with many diseases, of which tuberculosis is the most common [19].In healed tuberculosis cavity, 25% had serum Aspergillus precipitin positive and 11% had radiological evidence of aspergilloma[20].

In Chest X-ray it appear as round mobile mass surrounded by a crescentic air shadow in a lung cavity called ‘air-crescent sign’ [21]. (Figure 8)

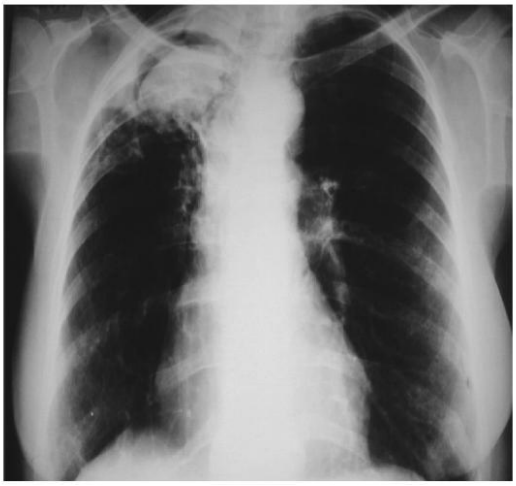


Figure 8: Aspergilloma right upper zone

CALCIFICATION

Pulmonary tuberculosis lesions often heal by calcification. It can be macroscopic or microscopic. In Chest X-ray, it appears as discrete radio opaque shadows in post parenchymal disease (Figure 9) and sheet like calcification in post pleural disease [22].

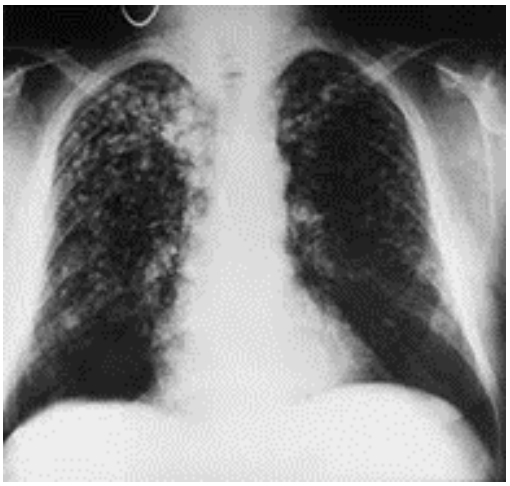


Figure 9: Calcification bilateral

PATHOGENESIS OF SEQUELAE

Various immunopathogenetic mechanisms leading to lung remodeling in pulmonary tuberculosis have been explained. Remodelingis defined asanatomical and structural changes that are not easily reversible[23]. An appropriate host response to Mycobacterium tuberculosis involves a coordinated granuloma formation, containing the infection, followed by its dissolution and maintenance of normal lung architecture. Sometimes an inappropriate response leads to liquefactive necrosis, increased fibroblast activity leading to fibrosis and altered lung architecture [24].

Mycobacterium tuberculosis bacilli are engulfed by alveolar macrophage. They initiate Th1 mediated cell mediated immunity. The released IFNγ causes macrophage apoptosis killing the bacilli along with it. TNFα together with TGFβ maintains the integrity of granuloma by forming encapsulating fibrous wall [25]. The fibrotic activity is kept under control by IFNγ. Macrophages also secrete various proteases which cleave the extracellular matrix and help its removal leaving minimal scarring [26].

In some individuals, there will be progressive disease with liquefactive necrosis. Though it's exact reason is not known, various mechanisms have been explained.

- Necrosis than apoptosis

In the presence of INFγ, macrophages are positive for proapoptotic proteins [27]. The apoptosis leads to killing of the intracellular mycobacterium too. The debris induces less inflammatory reaction and is readily cleared.

Some virulent Mycobacterium inhibits apoptosis by their mannose capped lipoarabinomanan[28]. This leads to necrosis of cells. These necrosis materials are not readily cleared eliciting intense inflammatory reaction. They also serve as culture media for extracellular growth of Mycobacterium.

- Mycobacterial toxins

Mycobacterium has various virulent factors like endopeptidase, polyketide toxic factor which directly induces necrosis [29].

- Th2 cytokines

Certain virulent Mycobacterial strain has certain lipid antigens which induces a Th2 response in addition to Th1 response[30]. The resulting cytokines like IL-4 and IL-13 increases the pathological effect of TNFα, resulting in unchecked protease enzyme secretion leading to distortion of lung architecture[31].

They are profibrotic. They increase TGFβexpression, activate fibroblast and inhibit their apoptosis. Increased TNFαactivity also leads to fibrosis [32].

- Koch phenomenon

Exaggerated immune response are noted in various studies after exposure to Mycobacterial antigen in a previously tuberculosis infected animal. They also demonstrated role of TNFαin its mechanism. This may also explain the inappropriate immune response leading to lung remodeling [33].

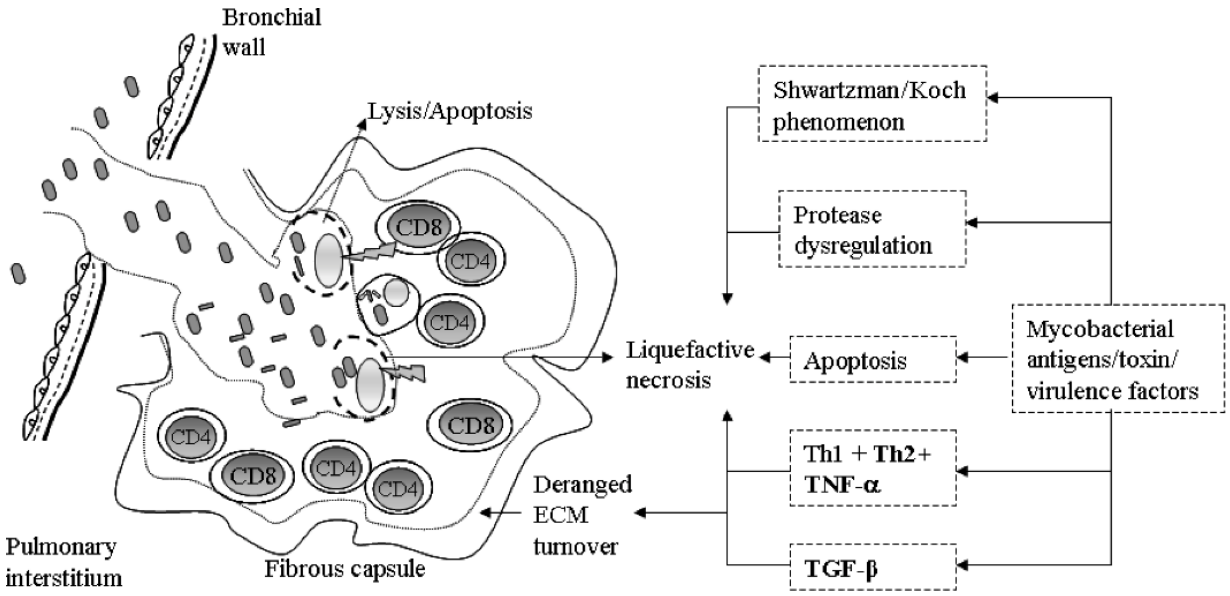


Figure 10: Pathogenesis of post pulmonary tuberculosis sequelae

PULMONARY HYPERTENSION

Pulmonary hypertension is an increase of mean pulmonary arterial pressure ⩾25 mmHg at rest when assessed by right heart catheterization. Normal value ranges between 14±3 mmHg [(34)].

Classification

Comprehensive clinical classification of pulmonary hypertension[(35)] (updated from Simonneau et al.[(36)]) is based on shared similarities in pathophysiology, clinical presentation, hemodynamic features and therapeutic strategies.

1. Pulmonary arterial hypertension

1.1 Idiopathic

1.2 Heritable

1.2.1 BMPR2 mutation

1.2.2 Other mutations

1.3 Drugs and toxins induced

1.4 Associated with:

1.4.1 Connective tissue disease

1.4.2 Human immunodeficiency virus (HIV) infection

1.4.3 Portal hypertension

1.4.4 Congenital heart disease

1.4.5 Schistosomiasis

1'. Pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis

1'.1 Idiopathic

1'.2 Heritable

1'.2.1 EIF2AK4 mutation

1'.2.2 Other mutations

1'.3 Drugs, toxins and radiation induced

1'.4 Associated with:

1'.4.1 Connective tissue disease

1'.4.2 HIV infection

1". Persistent pulmonary hypertension of the newborn
2. Pulmonary hypertension due to left heart disease 2.1 Left ventricular systolic dysfunction 2.2 Left ventricular diastolic dysfunction 2.3 Valvular disease 2.4 Congenital/acquired left heart inflow/outflow tract obstruction and congenital cardiomyopathies 2.5 Congenital/acquired pulmonary veins stenosis
3. Pulmonary hypertension due to lung diseases and/or hypoxia 3.1 Chronic obstructive pulmonary disease 3.2 Interstitial lung disease 3.3 Other pulmonary diseases with mixed restrictive andobstructive pattern 3.4 Sleep-disordered breathing 3.5 Alveolar hypoventilation disorders 3.6 Chronic exposure to high altitude 3.7 Developmental lung diseases
4. Chronic thromboembolic pulmonary hypertension and other pulmonary artery obstructions 4.1 Chronic thromboembolic pulmonary hypertension 4.2 Other pulmonary artery obstructions 4.2.1 Angiosarcoma

4.2.2 Other intravascular tumours 4.2.3 Arteritis 4.2.4 Congenital pulmonary arteries stenosis 4.2.5 Parasites
5. Pulmonary hypertension with unclear and/or multifactorial mechanisms 5.1 Haematological disorders: chronic haemolyticanaemia, myeloproliferative disorders, splenectomy 5.2 Systemic disorders: sarcoidosis, pulmonary histiocytosis, lymphangioleiomyomatosis, neurofibromatosis 5.3 Metabolic disorders: glycogen storage disease, Gaucher disease, thyroid disorders 5.4 Others: pulmonary tumoral thrombotic microangiopathy, fibrosingmediastinitis, chronic renal failure (with/without dialysis), segmental pulmonary hypertension

TABLE 2: Classification of pulmonary hypertension

In practice, patients with group 2 and group 3 pulmonary hypertension represent an important part. Various studies have shown that group 2 pulmonary hypertension associated with left heart disease is most common. Epidemiological study on incidence on group 3 pulmonary hypertension is not widely available [(35)].

PULMONARY HYPERTENSION DUE TO LUNG DISEASE (GROUP 3)

It encompasses a group of pre-capillary pulmonary hypertension resulting from chronic lung disease, where mean pulmonary artery pressure ≥25mmHg and pulmonary capillary wedge pressure <15mmHg [(35)].

The most common causes are categorized as [(37)]

- chronic obstructive pulmonary disease (COPD),
- idiopathic pulmonary fibrosis and diffuse pulmonary lung disease(IPF) and
- Combined pulmonary fibrosis and emphysema and other cause (CPFE)

Hemodynamic classification is [(37)]

- COPD/IPF/CPFE without PH. :mPAP< 25mmHg
- COPD/IPF/CPFE with PH. :mPAP>/=25mmHg
- COPD/IPF/CPFE with severe PH. :mPAP>/=35 mm Hg or mPAP>/=25mmHg with low cardiac output <2.0 l/min/m2

Post pulmonary tuberculosis sequelae as a cause of pulmonary hypertension has been mentioned in only limited literatures. In a review series about corpulmonale, the causes were classified as obstructive lung diseases, restrictive lung diseases and respiratory insufficiency of central origin. In it, sequelae of pulmonary tuberculosis was mentioned under restrictive lung diseases [(38)]. But given the high burden of Tuberculosis in India and the resultant chronic lung disease, the need to address post pulmonary tuberculosis sequelae as a cause of pulmonary hypertension is vital.

Pathogenesis of pulmonary hypertension in post pulmonary tuberculosis sequelae.

Pulmonary hypertension in chronic lung disease is due to increased pulmonary vascular resistance. The etiological factors are many, in which the most common causes attributable to post pulmonary tuberculosis sequelae are[39]

- Alveolar hypoxia
- Destruction and obliteration of the pulmonary vascular bed.
- Inflammation

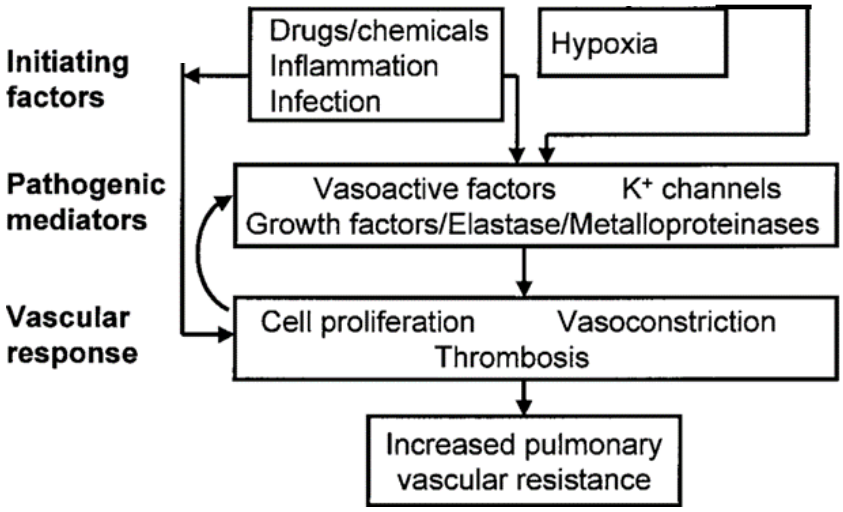


Figure 11: pathogenesis of pulmonary hypertension

1) ALVEOLAR HYPOXIA

Physiological response of pulmonary vasculature to hypoxia is vasoconstriction. This shunts blood away from poorly ventilated lung maintaining the optimal ventilation

perfusion matching [40]. Chronic hypoxia causes sustained vasoconstriction which leads to vascular remodeling and increased pulmonary vascular resistance.

It is caused by various mechanisms:

1. **Ion channels**

Hypoxia down regulates expression of voltage gated potassium channel in pulmonary vascular smooth muscle cells. This results in depolarization and activation of voltage gated calcium channels causing increased calcium influx into cytoplasm from extracellular space. Calcium binds to calmodulin and activates myosin light chain kinase. Myosin light chain is phosphorylated and cross bridging occurs between actin and myosin chains resulting in smooth muscle contraction and vasoconstriction [41].

The key mediator is Hypoxia inducible factor 1(HIF 1), a transcription factor which binds to hypoxia response element and down regulate the potassium channel gene [42].

2. **Vasoactive mediators**

Endothelin 1 are found increased in patients with hypoxia and has correlation with severity. The exact mechanism behind it is unknown. Inflammation induced endothelial damage may be a cause. They are potent vasoconstrictors and also cause smooth muscle hypertrophy and hyperplasia [43]. Vascular endothelial growth factor (VEGF) expression is also induced by hypoxia [44].

They act via Rho/Rho kinase pathway to increase sensitivity of smooth muscle to calcium [45].

3. Neurohormones

There is increased sympathetic activity in individuals with chronic hypoxia. This is due to reflux increase in catecholamines due to systemic vasodilation due to hypoxia [46].

4. Hyperviscosity of blood

Hypoxia induces polycythemia, leading to hyper viscosity of blood, increased risk of thrombus formation and pulmonary hypertension [47].

REMODELING

Remodeling in pulmonary vessels occur due to chronic hypoxia and sustained vasoconstriction. They cause proliferation and extension of smooth muscle cells to arterioles leading to its muscularisation, compromising its dispensability [48]. There is proliferation and fibrosis of adventitia and intima, causing obliteration of pulmonary vessel [49]. All in turn result in further increase in pulmonary vascular resistance. Plexiform lesions are not usually seen in pulmonary hypertension induced by chronic lung disease [50].

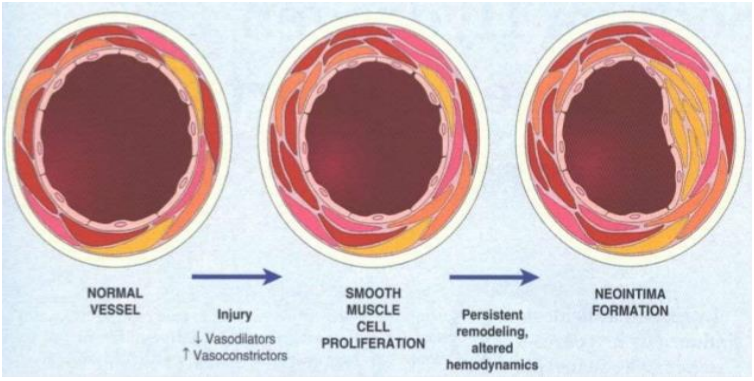


Figure 12: pulmonary vascular remodeling

2) REDUCTION IN VASCULAR BED

Pulmonary vascular bed is either destroyed or obliterated by parenchymal abnormalities, associated inflammation, perivascular fibrosis, vasculitis and/or thrombotic angiopathy. This results in decreased cross sectional area of pulmonary vessels increasing pulmonary vascular resistance [51].

3) INFLAMMATION

Many inflammatory mediators are over-expressed in pulmonary hypertension patients like thromboxane A2, tumor necrosis factor-α, platelet-derived growth factor, transforming growth factor-β, and fibroblast growth factor. They are shown to be responsible for intimal proliferation [52].

CORPULMONALE

Corpulmonale is also known as pulmonary heart disease. It can be defined as altered right ventricle structure and/or function in the context of chronic lung disease and is triggered by the onset of pulmonary hypertension[53]. The term is used when the pulmonary hypertension is caused by acute/chronic disease affecting structure and/or function of lung. The pulmonary hypertension leads to right heart enlargement, eventually leading to right heart failure [38].

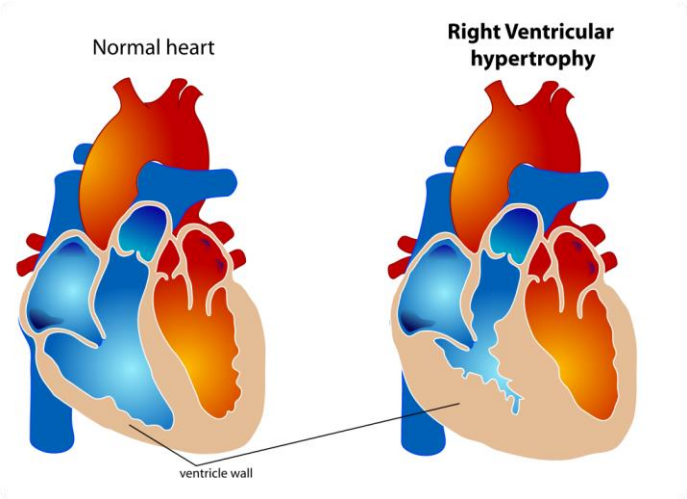


Figure 13: Corpulmonale- changes in right ventricle

In normal heart, right ventricle is thin walled and compliant compared to left ventricle. Right ventricle appearscrescent shaped in cross sectionand triangular when viewed sideways. Under normal condition, septum is concave towards left ventricle [(54)].

Right ventricular function is determined mainly by its contractility, preload and after load[(55)]. After load of right ventricle is the resistance in pulmonary vasculature, which are low resistant, high compliant system. Thus, compared to left ventricle, after load is less for right ventricle, but show heightened sensitivity tochange inafter load[(56)]. Preload represents the load before contraction. Right ventricle is believed to be more compliant than left ventricle, demonstrated in sarcomere length-pressure curve relationship [(57)]. Thus, Right ventricle is shown to tolerate volume overload more than pressure overload [(58)].

In patients with lung disease with pulmonary hypertension, gradual increase in pulmonary vascular resistance and after load, causes right ventricular hypertrophy. Right ventricle also enlarges to spherical shape to improve stroke work. The increased muscle mass and heart rate causes increased myocardial oxygen consumption and decreased myocardial perfusion. This affects functioning of right ventricle. Dilation also causes tricuspid regurgitation, worsening the load on right side. The interventricular septum is pushed towards left affecting left ventricular function [59].

Several studies have shown that, right ventricular function is maintained to near normal range by these compensatory mechanisms. Decompensation occurs when there is a trigger like worsening hypoxia, hypercapnia, acidosis or secondary infection [60].

PULMONARY HYPERTENSION- CLINICAL FEATURES AND DIAGNOSIS

CLINICAL FEATURES

Symptoms and signs of pulmonary hypertension are nonspecific, occur in severe cases and overlaps with underlying pulmonary or cardiac disease. These often results in a delay in its diagnosis.

Symptoms

Dyspnea on exertion is the most common symptom, occurring in up to 84% of cases [61]. Other early symptoms are chest discomfort, easy fatigability, palpitation etc. Angina like chest pain results from increased right ventricle workload and myocardial

ischemia. Syncope or light headedness during exercise is seen in later stages due to decreased cardiac output and cerebral blood flow. It is an ominous symptom.

Right ventricle dysfunction leads to swelling of lower extremities, abdominal distention, right hypochondrial pain etc. [62]

I	Patients without limitation of physical activity. Ordinary physical activity does not cause undue dyspnea or fatigue, chest pain or near syncope.
II	Patients with slight limitation of physical activity. Comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
III	Patients with marked limitation of physical activity. Comfortable at rest. Less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
IV	Patients with inability to carry out any physical activity without symptoms. Signs of right heart failure. Dypsnea and/or fatigue may be present at rest. Discomfort increased by any physical activity.

Figure 14: Functional classification of Pulmonary hypertension (WHO) [63]

Signs

High pulmonary pressure and resulting turbulent flow leads to accentuated pulmonic component of S2, early systolic click and mid-systolic ejection murmur. Severe PAH leads to tricuspid regurgitation causing holosystolic murmur in tricuspid area, increased jugular ‘v’ wave, pulsatile liver and hepatojugular reflex.

Right ventricular hypertrophy and increased pressure leads to left parasternal heave, right ventricular S4 and elevated jugular ‘a’ wave.Right ventricular failure results in right ventricular S3, distention of jugular veins, hepatomegaly, ascites and peripheral edema [64].

DIAGNOSIS

Chest radiography

Shows enlarged main and hilar pulmonary artery with pruning or attenuation of peripheral vasculature. Size of right interlobar artery >15mm in women and >16mm in men, measured from its lateral aspect to medial portion near bronchus intermedius. On left side, size >18mm, measured from orifice of left upper lobe bronchus to posterior aspect of vessel in lateral view is considered significant.

Right atrial enlargement is seen as lateral enlargement of right heart border. Right ventricle enlargement shows cardiomegaly with apex shifted outward and upward. In lateral view obliteration of retrosternal airspace is seen [65]. (Fig 13)

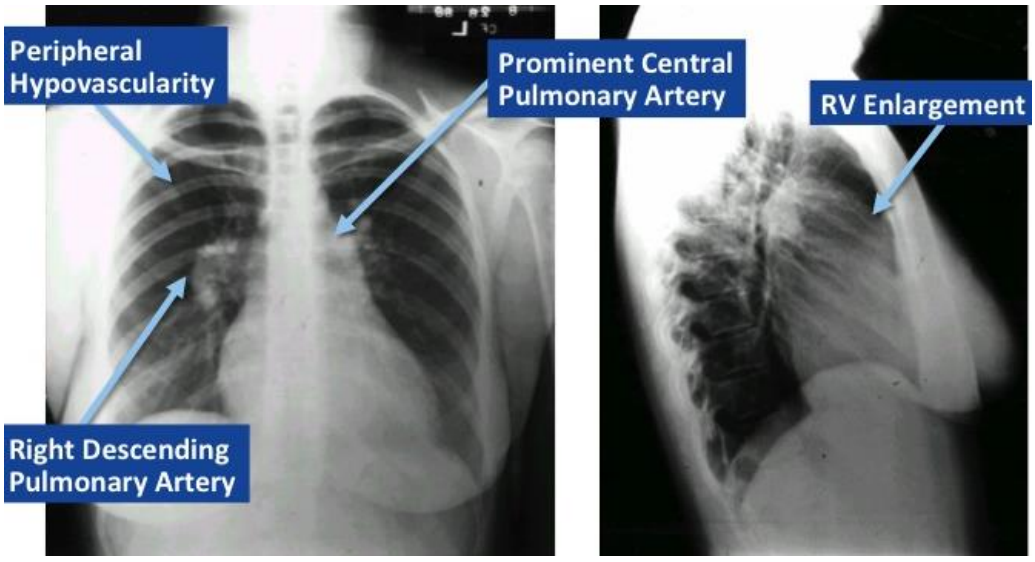
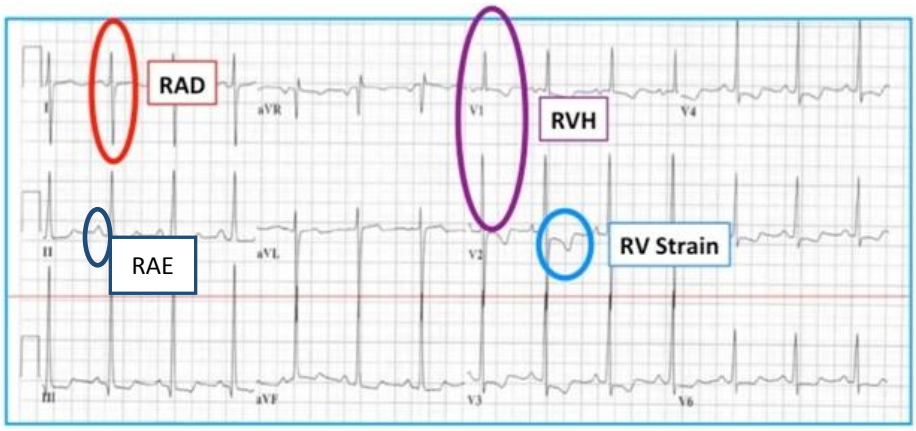


Figure 15: Chest X-ray in pulmonary hypertension

Electrocardiogram

ECG is nonspecific in diagnosing PAH (Fig 14). The common findings are:

- Right atrial enlargement (RAE) : Peaked P wave in Lead II with amplitude > 0.25mV, Lead V1 or V2 having prominent initial positivity of P wave and shift of P wave axis to >+75degree towards right.[66]
- Right ventricular hypertrophy (RVH): results in abnormal tall R wave in anterior and right leads and abnormal small r and deep S wave in posterior and left leads. Diagnostic criteria include R/S ratio in V1 >1, tall R wave in V1 >0.6mV, deep S in V5>1.0mV etc. Pressure overload also results in strain pattern. It is most commonly associated with Right axis deviation.[67]
- Right axis deviation (RAD): cardiac electric axis shifts rightward to +90 degrees to +180 degree. Lead I is negative and lead aVF is positive.[68]



PAH, pulmonary arterial hypertension; RAD, right axis deviation; RVH, right ventricular hypertrophy; RV, right ventricle. RAE, Right atrial enlargement

Figure 16: ECG in pulmonary hypertension

Echocardiography

When pulmonary hypertension is suspected, Echocardiography should always be done. It helps in diagnosing PH and its effect on heart. It identifies patients with high probability of pulmonary hypertension for further evaluation.

Assessment of Pulmonary hypertension

In echocardiography, Systolic pulmonary artery pressure (sPAP) is commonly used to assess pulmonary artery pressure.

sPAP is equal to Right ventricular systolic pressure (RVSP) in the absence of a gradient across pulmonic valve i.e., absence of right ventricular outlet tract obstruction. RVSP can be measured using Bernoulli's equation [(69)]:

$$RVSP/sPAP = 4v2 + RAP$$

v = peak Tricuspid regurgitation jet velocity

RAP = Right atrial pressure

Normal resting sPAP<35mmHg. According to the recommendation of American College of Cardiology Foundation and American Heart Association experts, further evaluation for pulmonary hypertension should be done if RVSP/sPAP> 40 mm Hg[(70)].

Mean pulmonary artery pressure (mPAP) can be approximately derived from sPAP by the formula [(71)]

$$mPAP = 0.61*sPAP + 2$$

Grading of pulmonary hypertension [71]

GRADE	mPAP (mmHg)	sPAP (mmHg)
NORMAL	<20	<30
NORMAL WITH RISK	21-24	30-40
MILD	25-40	40 to 60
MODERATE	41-55	60-90
SEVERE	>55	>90

Table 3: Grading of PH in adult

Tricuspid regurgitation velocity

It can be assessed by parasternal or apical 4 chamber views by continuous wave doppler. The Doppler beam is aligned parallel to the direction of Tricuspid regurgitant flow and velocity, measured during inspiration. v<2.8-2.9m/s corresponds sPAP<36mmHg, if Right atrial pressure is normal [72]. (Fig 15)

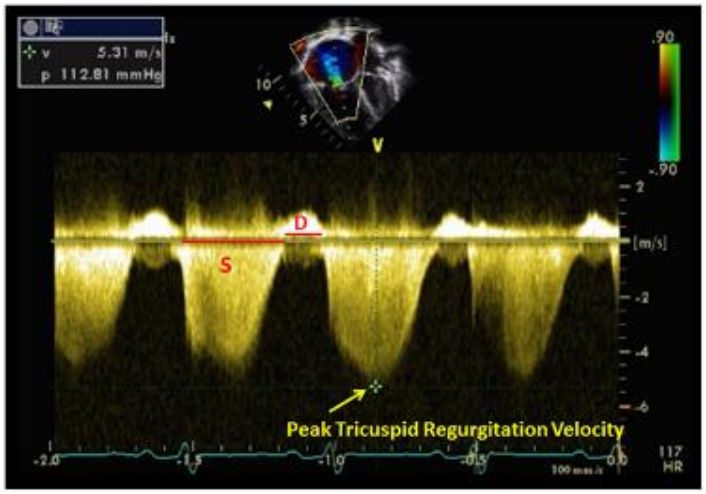


Figure 17: Tricuspid regurgitation velocity

Right atrial pressure:

It is measured by combining two parameters: Inferior vena cava (IVC) dilation and its collapsibility during inspiration. The increase in right atrial pressure is transmitted to IVC resulting in its dilation and reduced collapsibility [73].

IVC is viewed along its long axis in subcostal view and diameter measured just proximal to joining of hepatic vein in end expiration. Patient is asked to take a sniff and change in diameter is assessed. The assessment is as below [74]

IVC Diameter(mm)	IVC Collapsibility	Right atrial pressure
</=2.1mm	>50%	Low (0-5mmHg)
</=2.1mm	<50%	Indeterminate (5-10mmHg)
>2.1mm	>50%	
>2.1mm	<50%	High (10-20mmHg)

Table 4: Right atrial pressure estimated by IVC diameter and collapsibility

Assessment of right ventricular function

Right ventricular assessment usually includes assessment of:

- RV dimensions
- RV systolic function
- RV diastolic function[72]

RV dimensions

Pressure/volume overload will cause dilation of right ventricle. Body surface area indexed end-diastolic right ventricular diameter and right ventricle/left ventricle end diastolic diameter ratio are predictors of adverse clinical events and survival in chronic pulmonary patients [75].

Usually, right ventricle is approximately two third the size of left ventricle. It is likely to be significantly enlarged, if it appears larger than the left ventricle. As RV enlarge and wall thickens, inter ventricular septum progressively flattens and losses its convexity with respect to right ventricle. This leads to left ventricle progressively assuming a D-shaped cavity. [76].

RV size in 2D echocardiography is measured at end diastole in a 4-chamber view from the apical window. It can be quantified using:

1. Basal RV diameter

   Maximum transverse diameter in the lower one third of RV inflow. >41mm is abnormal.

2. Mid cavity RV diameter

   Transverse diameter in the middle one third of RV inflow. >35mm is abnormal.

3. Longitudinal RV diameter

   Measured from plane of tricuspid annulus to the RV apex

4. RV outflow diameter

   Linear measurements of RV outflow tract, proximal and distal

5. RV end diastolic area (Figure 18)

   RV endo-cardial border is traced at end diastole from the lateral tricuspid annulus along the free wall to the apex and back to medial tricuspid annulus, along the interventricular septum. Mean value is 18cm2 with upper reference value 24cm2[77].

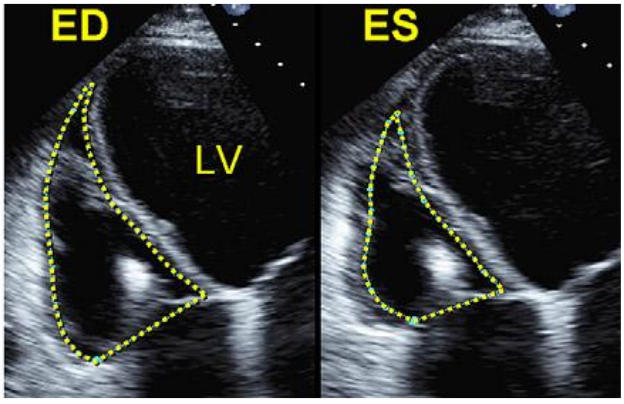


Figure 18: RV end diastolic(ED) and end systolic(ES) area.

RV systolic function

Various parameters are used for global and regional RV function assessment. Few of them are recommended for routine use, due to their easiness in measuring and availability of standard reference value. They are the following parameters:

1. RV MPI – right ventricular myocardial performance index

   It is also known as Tei index. It measures global RV function. It is ratio of isovolumic time and ejection time. It is used for diagnosing and serial monitoring of right ventricular function. The upper limit is more than 0.43 [78].

2. TAPSE – Tricuspid annular plane systolic excursion

   Also called tricuspid annular motion, it measures RV longitudinal function. It measures, along the longitudinal plane, the distance of excursion of RV annular segment in systole. RV dysfunction is highly suggestive, if TAPSE <17 mm [(79)].

3. TASV / RV S' – Tricuspid annular systolic velocity

   It measures longitudinal velocity of excursion of annular segment. RV systolic dysfunction is indicated if TASV < 9.5cm/s [(80)].

4. FAC – fractional area change

   It is defined as the percentage of change in diameter of right ventricle between end-diastole and end-systole. It is (end-diastolic area – end-systolic area)/ end-diastolic area x 100. <35% indicate right ventricular dysfunction [(81)].

Many other parameters have been defined. But due to lack of proper recommendations, defined normal values etc., they are not routinely used.

Right heart catheterization

Right heart catheteristion should be done to confirm the diagnosis of pulmonary hypertension. Direct measurement of mean pulmonary artery pressure (mPAP) and pulmonary artery wedge pressure (PAWP) can be done. Cardiac output (CO) is measured by thermodilution or Fick's principle. Pulmonary vascular resistance (PVR) is measured as PVR = (mPAP-PAWP)/CO. It is also used for testing pulmonary vasoreactivity testing for planning treatment strategies. [(82)]

In patients with Group 3 PH, mPAP is more than 25mmHg, PAWP is more than 15mmHg and PVR is more than 3 wood units. The findings are same for Group 1 PH, but can be distinguished by clinical, radiological and pulmonary function test correlation. [83]

Recommendation of right heart catheterization in Group 3 PH is when lung transplantation is planned or when inconclusive echocardiographic finding in patients with high suspicion. Usage to assist in differential diagnosis and support treatment decisions is weakly recommended. Vasoreactivity testing is not recommended in group 3 PH. [35]

Other diagnostic tests

To confirm group 3 PH

- Chest radiograph and high resolution CT chest
- Pulmonary function test
- DLCO
- Arterial blood gas analysis
- Sleep studies

To rule out other causes

- Ventilation perfusion scan
- Pulmonary angiography
- Abdominal ultrasound
- Serological test for HIV, connective tissue disorders etc.

MANAGEMENT OF GROUP 3 PULMONARY HYPERTENSION

Optimal treatment of the underlying lung disease is the main stay of treatment. The other therapeutic strategies in these patients include:

GENERAL MEASURES

Lifestyle modification

Smoking cessation is very important considering the additional direct effect of it on pulmonary vessels. [84]

Exercise training programs as patients without physical activity undergo deconditioning and are prone for worsening of symptoms. Supervised physical rehabilitation can be done by an expert. [85]

Weight reduction, sodium and fluid restriction, avoiding over exertion and high altitude are some other points.

Pregnancy and birth control

Patients with severe PH should avoid pregnancy. Oral contraceptive pills containing estrogen should be avoided due to risk of thrombosis. [86]

Immunization

These patients are susceptible to infection. So vaccination against influenza and pneumococci should be done. [87]

Psychosocial support

OXYGEN THERAPY

Long term oxygen therapy is shown to reduce the progression of pulmonary hypertension, though the condition rarely returns to normal. The structural abnormalities of pulmonary vessels are irreversible, but longer the duration of oxygen therapy more reduction in pulmonary pressure and more stabilized the disease process without progression. [88]

Indications of long term oxygen therapy is [89]

- PaO_2<55 mmHg or SaO_2< 88% (room air)
- PaO_2 56–59 mmHg or SaO_2 89%–90%, with (one or more)

1. Pulmonary hypertension
2. Evidence of corpulmonale or edema due to heart failure
3. Elevated hematocrit (>56%)

SUPPORTIVE THERAPY

Diuretic

By reducing volume overload, it decreases symptom, congestion and peripheral edema. By decreasing pre load, RV function is improved. [90]

Oral anticoagulants

It can be given to patients with increased risk of thrombosis or emboli. There is no data regarding use of anticoagulation in other patients. [91]

PH-SPECIFIC THERAPIES

They are currently not recommended for use in patients with pulmonary hypertension with lung disease. They are given only for patients with evidence of concomitant group 1 PAH or Group 4 chronic thromboembolic PH.

The major adverse effect with it is reversal of hypoxic pulmonary vasoconstriction due to their vasodilatory effect. This leads to perfusion of poorly ventilated lung units causing ventilation-perfusion mismatching and worsening hypoxia. [92]

SURGICAL THERAPIES

Lung transplantation

Lung transplantation is an important treatment option, for patients who are refractory to medical therapy. The indications are [93]

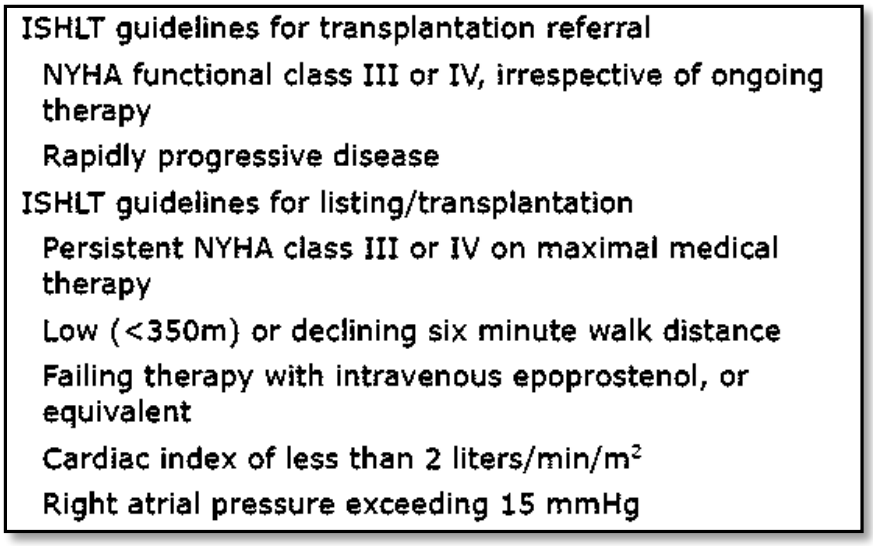


Figure 19: indication of lung transplantation. (ISHTL-international society for heart and lung transplantation, NYHA- New York heart association)

SPIROMETRIC ABNORMALITIES IN TUBERCULOSIS SEQUELAE

Tuberculosis sequelae are associated with both obstruction and restrictive pattern in spirometry. Obstructive pattern is due to obliteration and distortion of airways by cavitation, endobronchial spread of infection and bronchiectasis. Restriction is mainly by fibrotic changes in lung parenchyma and pleural thickening limiting lung expansion. [94]

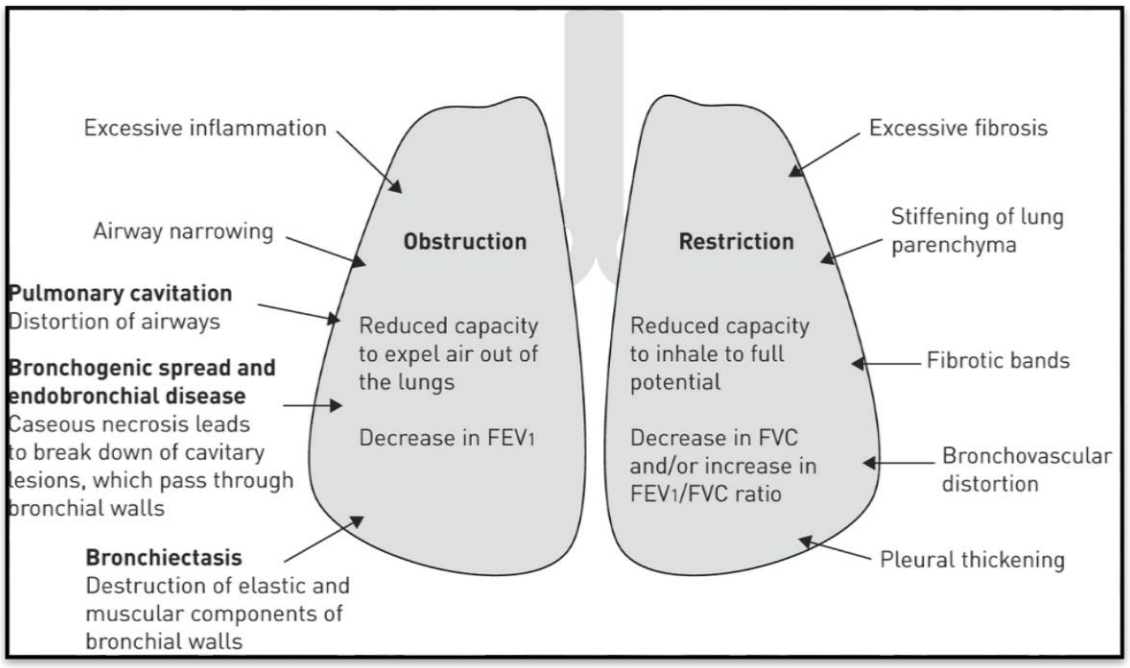


Figure 20: Spirometric abnormalities in tuberculosis sequelae

MATERIALS AND METHODOLOGY

The study was carried out in patients visiting the Department of Respiratory Medicine, Tirunelveli Medical College Hospital, Tirunelveli. The study is approved by the Institutional Ethical Committee of the Tirunelveli Medical College.

STUDY DESIGN

Cross-sectional study

STUDY PERIOD

One and half years, from January 2018 - June 2019.

SAMPLE SIZE : 100

STUDY POPULATION

The patients attending the outpatient clinic or getting admitted as inpatient in the Department of Respiratory Medicine were included. Patients for the study was selected based on inclusion and exclusion criteria.

INCLUSION CRITERIA

1. Age >18 years
2. Patient who can give consent.
3. Patients with history of pulmonary tuberculosis.
4. Patients with features of post tuberculosis pulmonary sequelae in chest X-ray.
5. Patients without evidence of active pulmonary tuberculosis at present.

EXCLUSION CRITERIA

1. Pregnant women
2. Patients living with HIV
3. Patient not willing to participate in study.
4. Other known causes of pulmonary artery hypertension like left heart disease, thrombo-embolism, high altitude dweller etc.
5. History of lung resection and lung malignancy.

RESEARCH VARIABLES

INDEPENDENT VARIABLES	
• Age	• Gender
• Body mass index	• Smoking
• Diabetes	• Spirometry pattern
History of pulmonary tuberculosis	Features in chest X-ray
• Number of episodes	• Number of zones
• Time since first episode	• Bilateral/unilateral
• Treatment outcome	• Type of sequelae
• Drug sensitivity	• Single/multiple sequelae
DEPENDENT VARIABLES	
• Pulmonary hypertension	• Corpulmonale

Table 5: Research variables

METHODOLOGY

After obtaining informed written consent from the patient, demographic and anthropometric values were collected. History regarding his/her occupation, residence area, present symptoms, smoking history, co-morbidities and medication were taken. Previous pulmonary tuberculosis history was taken in detail. Patient was clinically examined and vitals recorded.

Sputum AFB was done to exclude active disease. Chest X-ray was taken and analysed for the type of sequelae and extend of involvement. Spirometry was done and the pattern recorded. ECG was taken.

Transthoracic 2D echocardiography (conventional and tissue Doppler analysis) was done in lateral decubitus position from parasternal view, apical four chamber view and the subcostal view. All of the measurements were performed in accordance with the American Society of Echocardiography/ European Association of Echocardiography recommendation.

After collecting all data, Incidence of pulmonary hypertension and corpulmonale in patients with post pulmonary tuberculosis sequelae were noted. The independent variables as a risk factor were statistically analyzed using SPSS software. For discrete variables, Chi square test/Fisher's exact test were used for testing significance. For continuous variables one way ANOVA test/Students t test were used. Null hypothesis were rejected and significant association established when $p<0.05$.

BMI

BMI was calculated as weight(kg)/height^2(m^2). Classification based on BMI was done according to WHO ASIA classification:

NUTRITION STATUS	**BMI(kg/m^2)**
UNDERWEIGHT	<18.5
NORMAL	18.5-22.9
OVERWEIGHT	23-24.9
OBESE I	25-29.9
OBESE II	>30

Table 6: BMI classification

SMOKING HISTORY

History of duration and amount of smoking were collected. Smoking index was calculated as:

Number of cigarette/beedi smoked per day * Duration of smoking in years.

HISTORY OF PULMONARY TUBERCULOSIS

Detailed history of previous pulmonary tuberculosis episodes were taken. Time since first episode and number of episodes of PTB were collected. Data regarding sensitivity to first line drugs and treatment outcome, whether cured, completed or lost to follow up, in previous episodes were recorded.

Treatment outcome is defined based on Technical and operational guidelines for tuberculosis control in India:

CURED : Microbiologically confirmed TB patients at the beginning of treatment who was smear or culture negative at the end of the complete treatment

COMPLETED : A TB patient who completed treatment without evidence of failure or clinical deterioration but with no record to show that the smear or culture results of biological specimen in the last month of treatment was negative, either because test was not done or because result is unavailable.

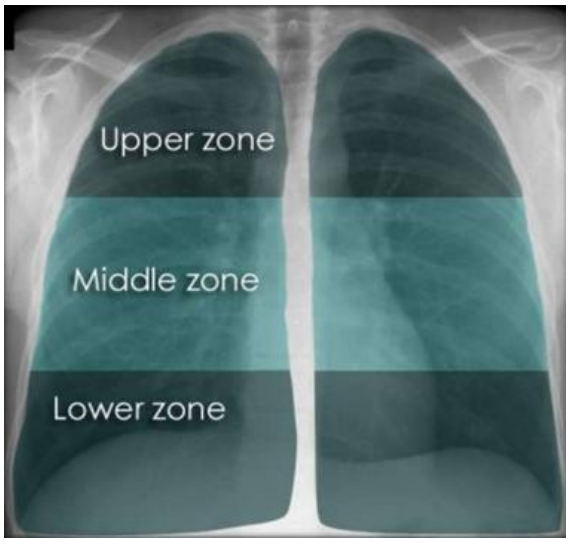
LOST TO FOLLOW UP : A TB patient whose treatment was interrupted for 1 consecutive month or more. They are also called defaulters.

CHEST X-RAY INVOLVEMENT

Chest X-ray report was analyzed for type of post pulmonary tuberculosis sequelae pattern and whether they occur alone or in combination with other patterns. The sequelae included are:

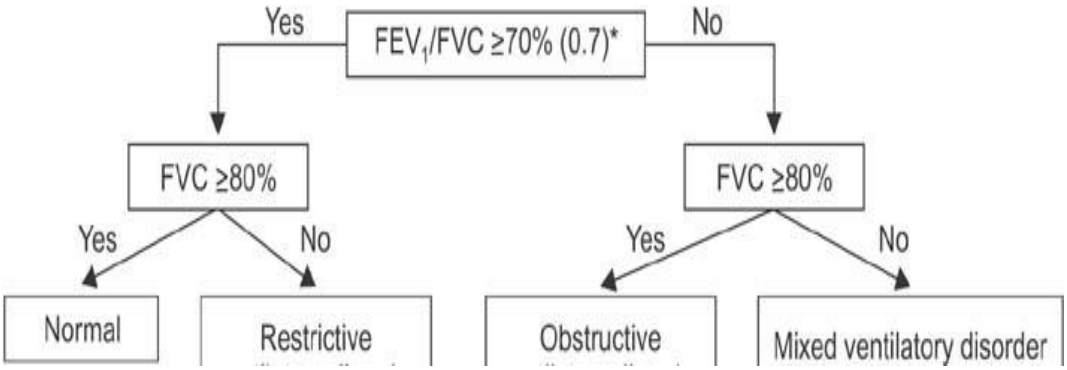
1. Fibrosis
2. Bronchiectasis
3. Cavity
4. Bullae
5. Aspergilloma
6. Calcification/pleural thickening

Extent of involvement is defined by number of zones and sides (unilateral/bilateral) involved. The lung field was divided into 6 zones, 3 on each side. It was divided by two straight lines drawn from 2nd and 4th costal cartilage.



SPIROMETRY

Spirometry was done using Desktop flow sensing spirometer. Patients were classified as normal, obstructive, restrictive or mixed pattern according to their FEV1/FVC, percentage of predicted FVC and FEV1 values as:



ECHOCARDIOGRAPHY

Systolic pulmonary artery pressure was obtained from tricuspid regurgitation velocity, measured from parasternal view by continuous wave Doppler. Pulmonary hypertension was graded as mild, moderate and severe.

Right ventricular dimensions were measured from apical view. Right ventricular function is assessed by measuring end diastolic dimensions, Tricuspid annular plane systolic excursion (TAPSE), Tricuspid annular systolic velocity (TASV) and myocardial performance index (RVMPI).

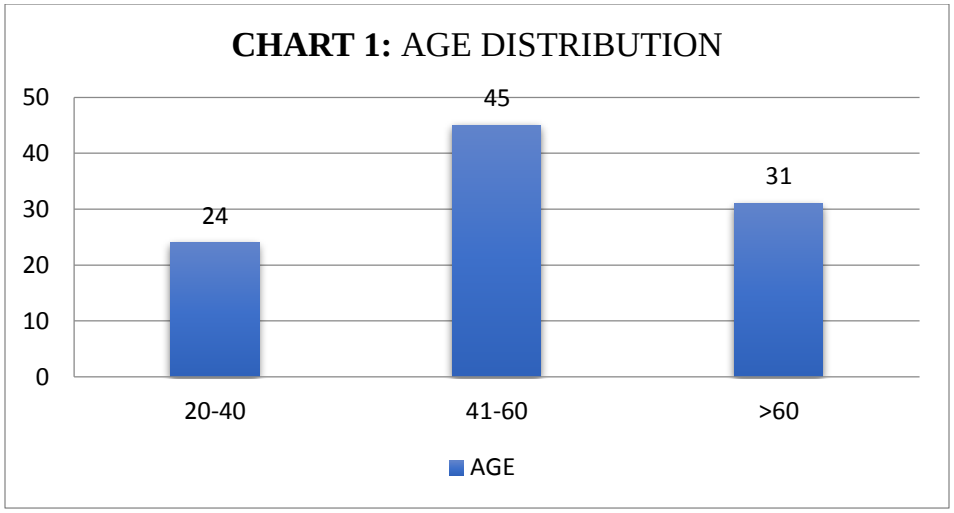
CONSENT

A detailed written consent in local language was obtained from all the participants after clearly explaining the purpose of the study and harm and benefit associated with it.

RESULTS AND ANALYSIS

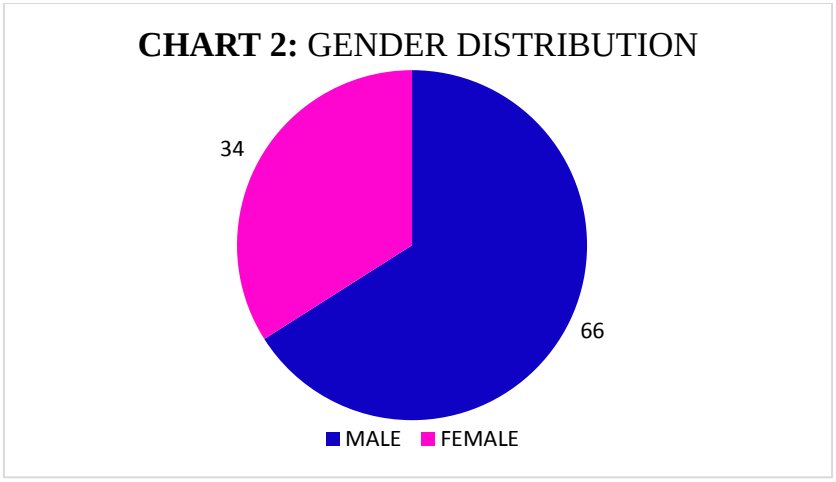
The study population consisted of 100 patients, who had history of pulmonary tuberculosis and radiological evidence of pulmonary sequelae.

AGE DISTRIBUTION



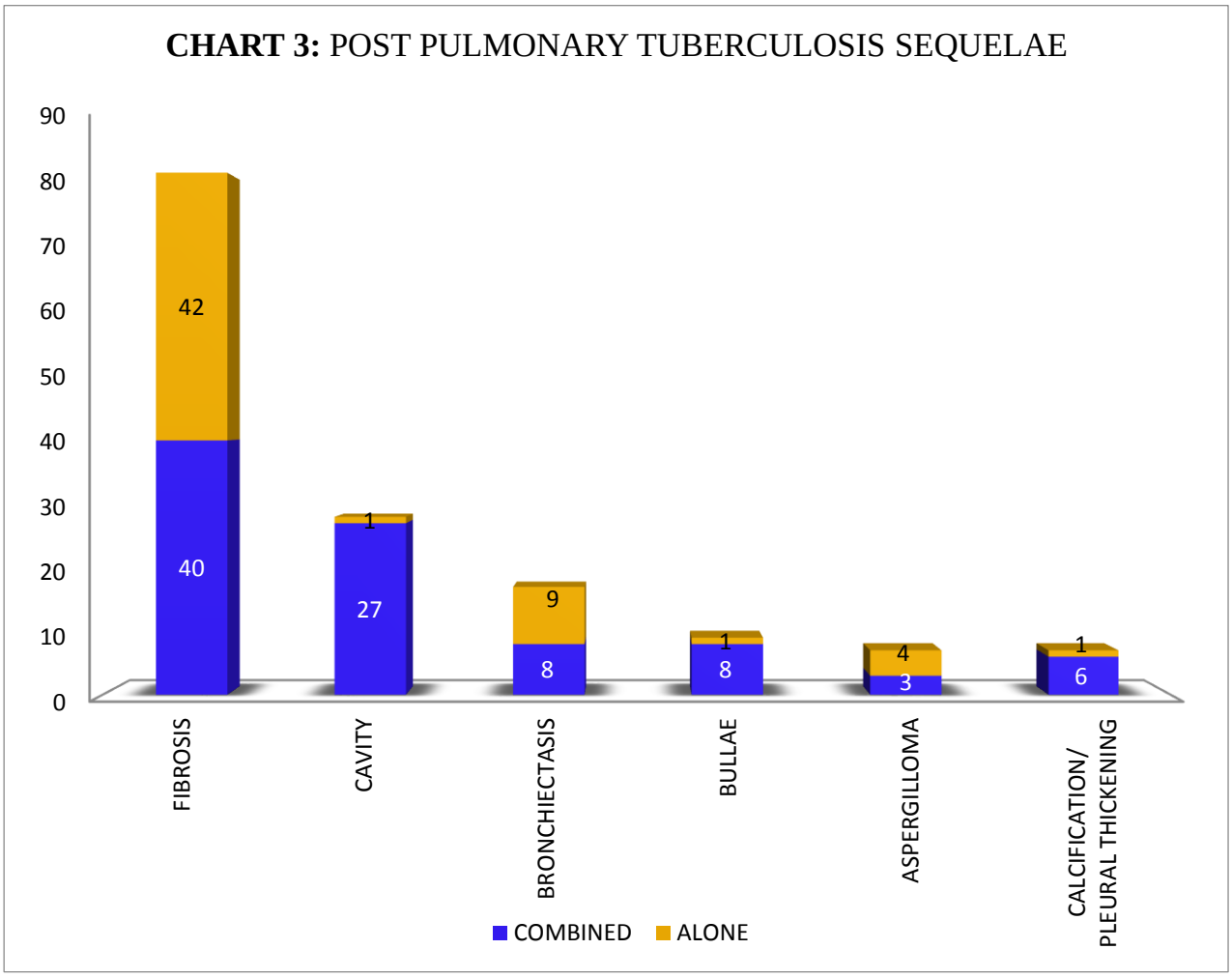
Majority of the patients (45%) were in the age group 41-60years.

GENDER DISTRIBUTION



Majority of the patients were male. 66% were male and 34% were female.

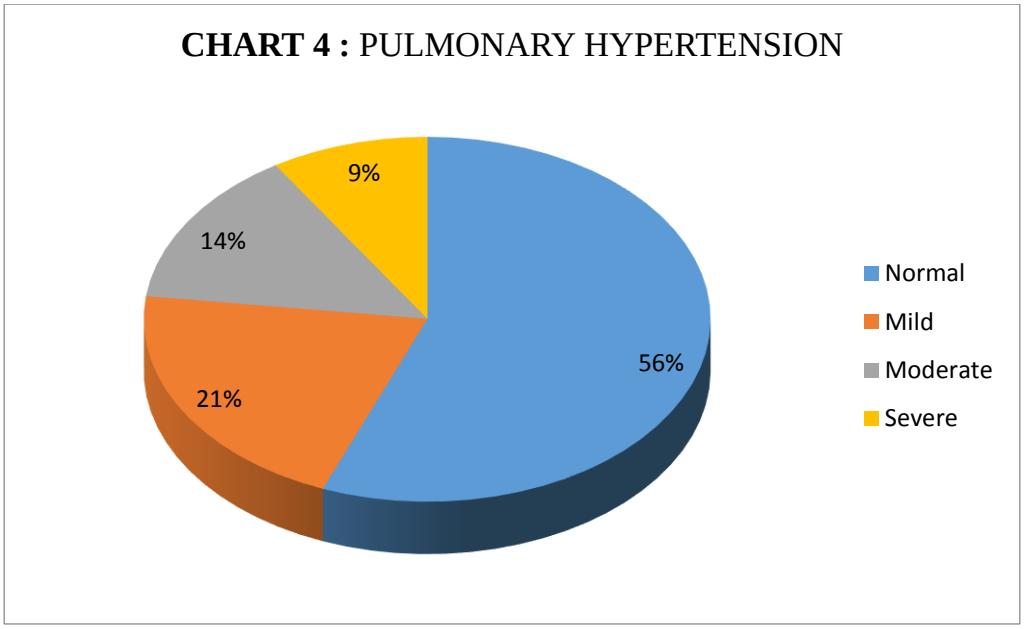
POST PULMONARY TUBERCULOSIS SEQUELAE PATTERN



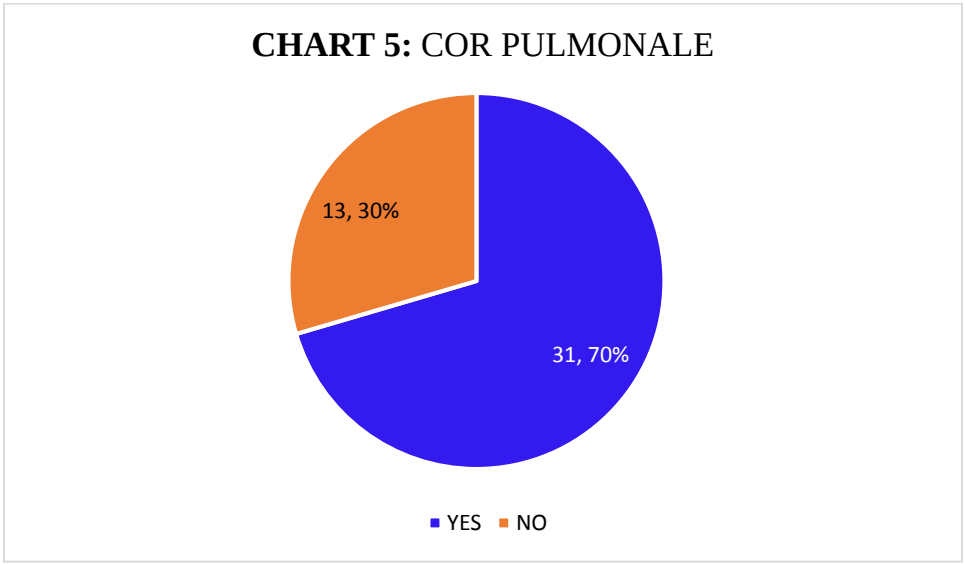
The most common post pulmonary tuberculosis sequelae pattern was fibrosis. 82% of the patient had fibrosis in Chest X-Ray, alone or combined with other patterns. The next common were cavity (28%) and bronchiectasis (17%). Other patterns were relatively less with bullae 9%, aspergilloma 7% and calcification/pleural thickening 7%.

Out of the total cases, 42% of the cases had more than one type of sequelae. Remaining 58% had only a single type.

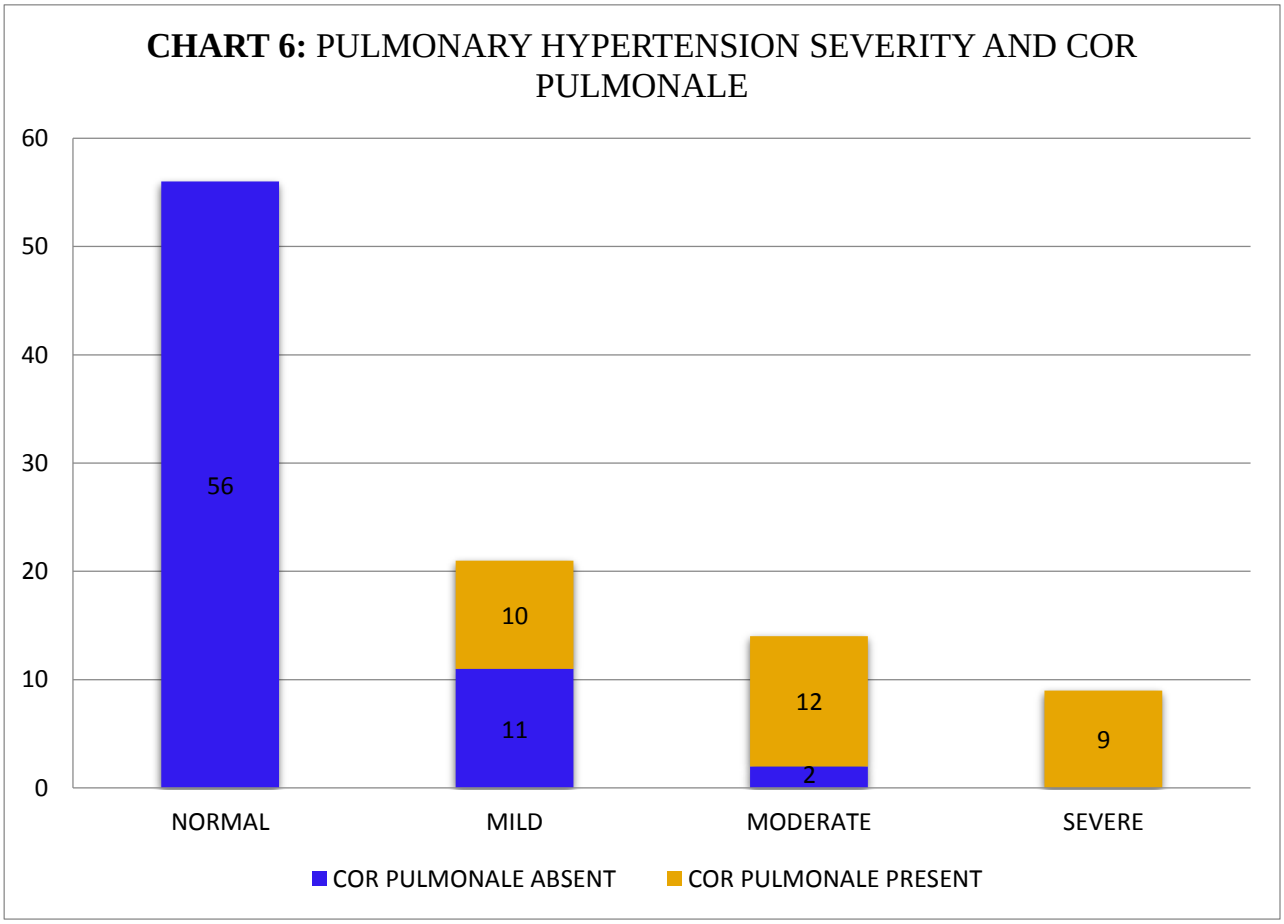
PULMONARY HYPERTENSION AND COR PULMONALE



44 out of 100 patients had evidence of pulmonary hypertension in echocardiography. Among them 21 had mild, 14 had moderate and 9 had severe pulmonary hypertension. In echocardiography of 100 patients, sPAP ranged from 10-106 mmHg with an average of 41.13 mmHg. Average TRV was 2.88m/s.



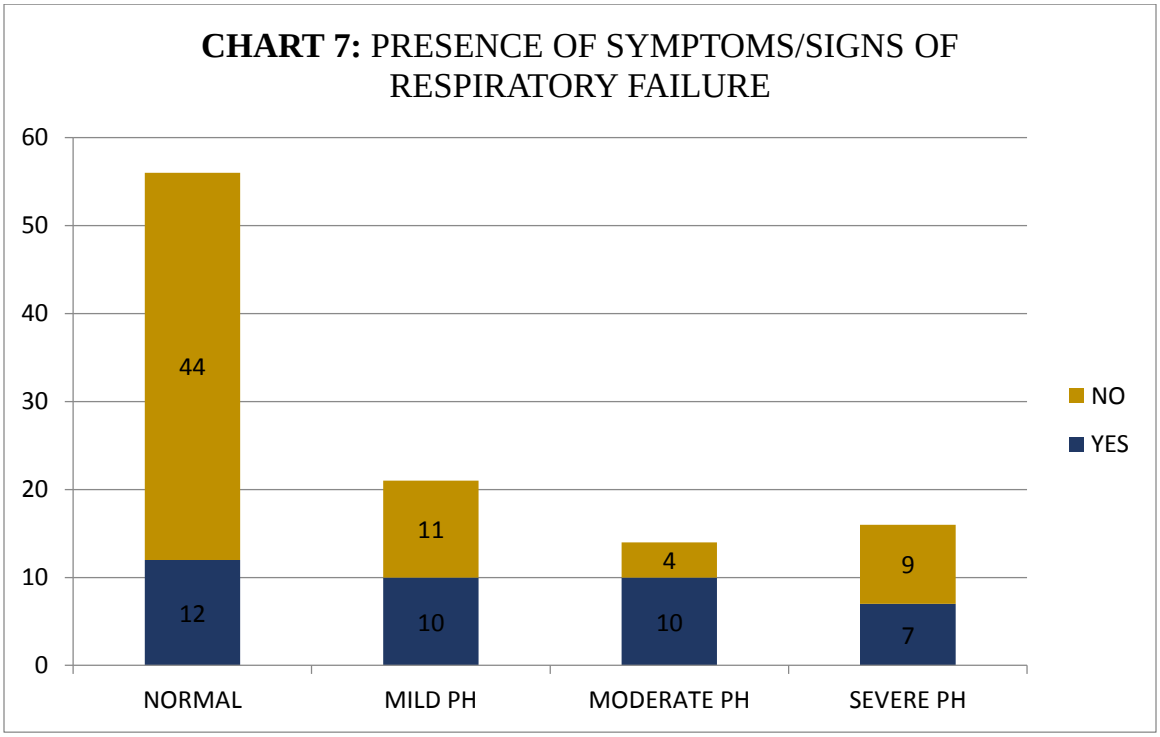
Among pulmonary hypertensive patients, 70.5% had evidence of corpulmonale in echocardiography. Corpulmonale was present in 10 out of 21 patients with mild, 12 out of 14 patients with moderate and all 9 patients with severe pulmonary hypertension. Echocardiography of 100 patients showed average right ventricular end diastolic dimension 13.9cm^2, TAPSE 2cm, TASV 15 cm/s and RVMPI 0.26.



RESPIRATORY FAILURE AND PULMONARY HYPERTENSION

Out of 100 patients, symptoms and signs of respiratory failure was present in 39 patients. 27 of them (69.2%) had evidence of pulmonary hypertension.

61.4% of patients with pulmonary hypertension and 67.7% of patients with corpulmonale had symptoms or signs of respiratory failure. 47.6% of patients with mild, 71.4% of patients with moderate and 77.8% of patients with severe pulmonary hypertension had symptoms and signs of respiratory failure.



Patients have significant risk for respiratory failure in the presence of pulmonary hypertension with $p<0.001$ and odds ratio 5.8.

AGE AS A RISK FACTOR

Youngest patient was 23 years and eldest 82 years old. The average was 52.34.

An analysis of variance showed that the effect of age on risk for pulmonary hypertension was not significant with $p=0.165$.

GENDER AS A RISK FACTOR

51.5%(n=34) of males and 29.4%(n=10) of females had pulmonary hypertension.

	PH PRESENT	**PH ABSENT**	**TOTAL**
MALE	34	32	66
FEMALE	10	24	34
TOTAL	44	56	100

Table 7: Comparison of gender and pulmonary hypertension

Analyzing male gender as a risk factor of pulmonary hypertension, we got p value=0.0349 with odds ratio 2.55. Thus males have statistically significant risk in developing pulmonary hypertension, 2.55 times more than females.

	COR PULMONALE PRESENT	**COR PULMONALE ABSENT**	**TOTAL**
MALE	26	8	34
FEMALE	5	5	10
TOTAL	31	13	44

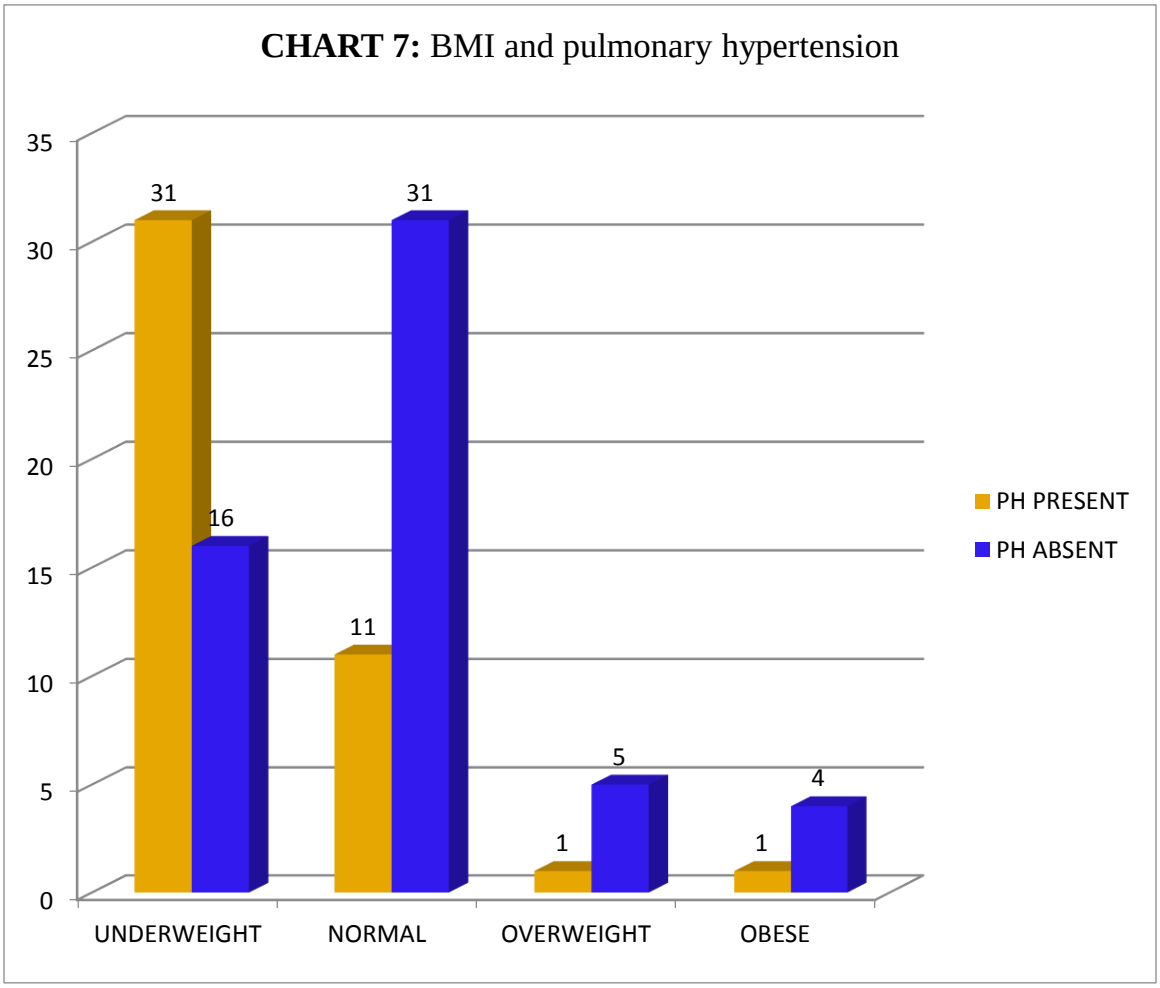
Table 8: Comparison of gender and corpulmonale

The p value was 0.11 for gender as a risk factor for pulmonary hypertension patients progressing to corpulmonaleand thus there was no statistical significance.

BODY MASS INDEX AS A RISK FACTOR

BMI in our study ranged from 10.5-27 with an average of 18.64. 47% of them were underweight and 42% normal weight.

CHART 7: BMI and pulmonary hypertension



Underweight patients had statistically significant risk for developing pulmonary hypertension than other patients with $p<0.001$ with odds ratio 6.49. An analysis of variance showed that, the effect of BMI was statistically significant for severity of pulmonary hypertension with $p=0.05$ and corpulmonale with $p=0.011$.

	Corpulmonale present	Corpulmonale absent	TOTAL
UNDERWEIGHT	22	9	31
NORMAL	8	3	11
OVERWEIGHT	1	0	1
OBESE	0	1	1
TOTAL	31	13	44

Table 9: Comparison of BMI and corpulmonale

SMOKING AS A RISK FACTOR

Smokers and non-smokers were almost equal in number. Smoking index was in a range of 20-2240 with an average of 710.1

	PH PRESENT	PH ABSENT	TOTAL
SMOKER	27	22	49
NON-SMOKER	17	34	51
TOTAL	44	56	100

Table 10: Comparison of smoking and pulmonary hypertension

Smoking habit had statistically significant risk for pulmonary hypertension with p=0.028 and odds ratio 2.45. An analysis of variance showed that the effect of smoking index on severity of pulmonary hypertension was close to being significant with p=0.058.

	Corpulmonale present	Corpulmonale absent	TOTAL
SMOKER	22	5	27
NON-SMOKER	9	8	17
TOTAL	31	13	44

Table 11: Comparison of smoking and corpulmonale

Smoking as a risk factor for pulmonary hypertension progressing to corpulmonale was statistically significant with p=0.043 and odds ratio 3.91.There was a significantdifference in smoking index between patients with and without corpulmonale with p=0.001.

DIABETES AS A RISK FACTOR

Only 13 out of 100 patients had diabetes mellitus. Of them 3 i.e., 23% had evidence of pulmonary hypertension.

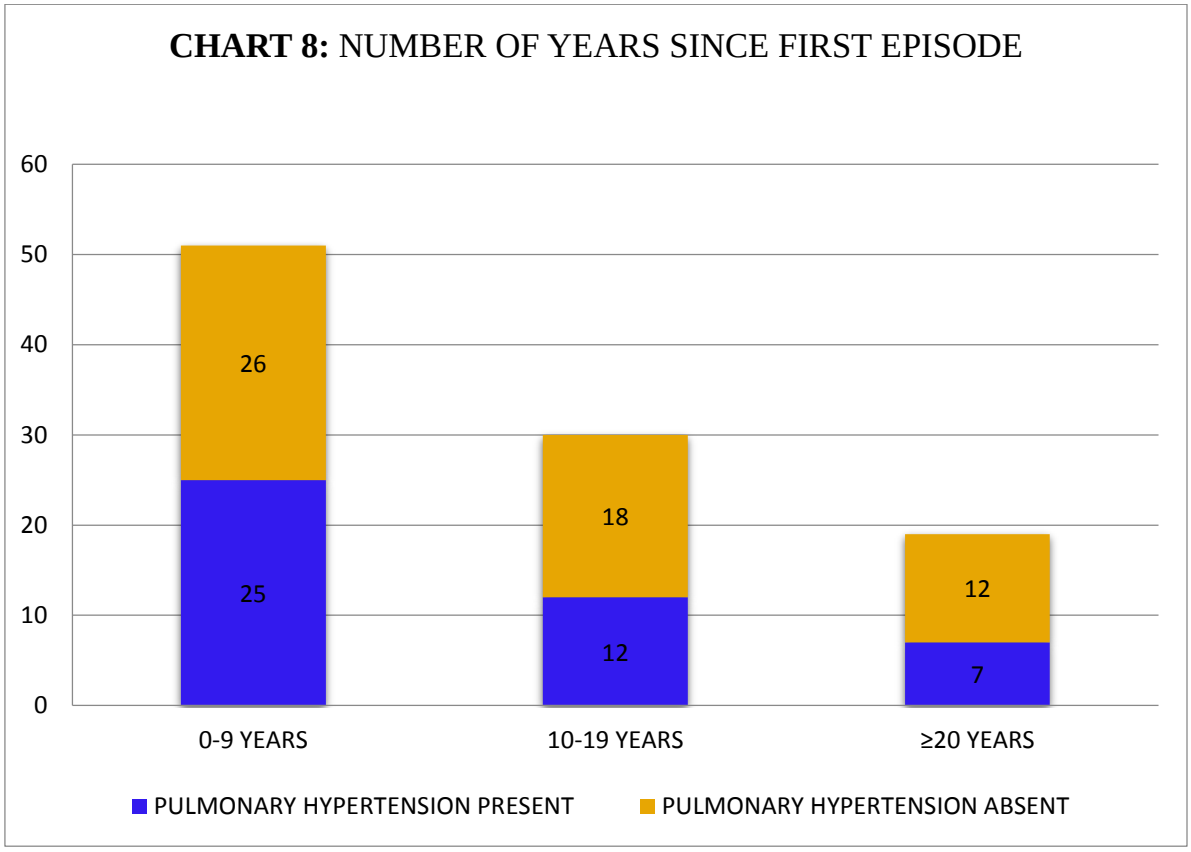
	PH PRESENT	PH ABSENT	TOTAL
DIABETES	3	10	13
NO DIABETES	41	46	87
TOTAL	44	56	100

Table 12: Comparison of diabetes and pulmonary hypertension

There was no statistical significance for diabetes as a risk factor with p=0.1.

DURATION FROM FIRST EPISODE OF PULMONARY TUBERCULOSIS AS A RISK FACTOR

Average duration from first episode of pulmonary tuberculosis in a patient was 10.65 years. The range was 1-40 years. Majority had history of pulmonary tuberculosis in the past 9 years.

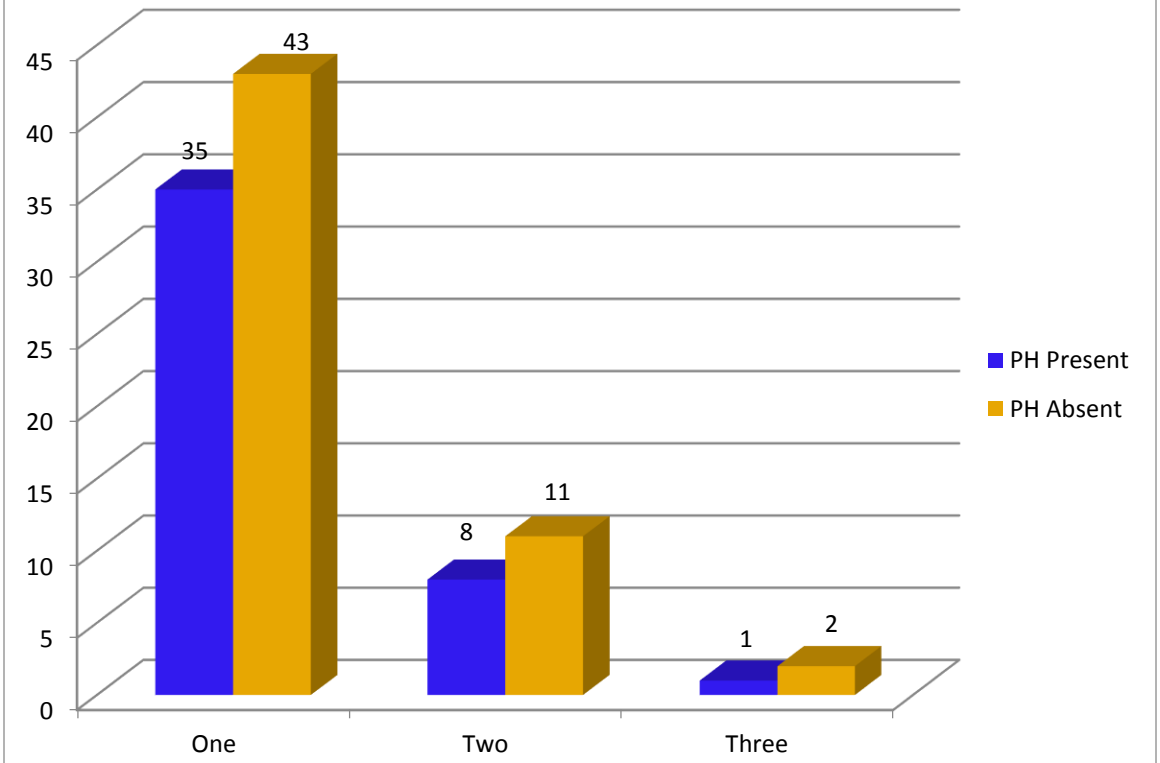


An analysis of variance showed no statistical significance for the effect of duration from first episode of pulmonary tuberculosis on risk for pulmonary hypertension with p=0.49.

NUMBER OF EPISODES OF PULMONARY TUBERCULOSIS AS A RISK FACTOR

Average number of episodes for a patient was 1.25. Majority of the patients had a single history of pulmonary tuberculosis. Only 22% had a history of relapse, of which 9 (40.9%) had pulmonary hypertension. 44.8% of patients with single episode also had pulmonary hypertension.

CHART 9 : Number of episodes of pulmonary tuberculosis and pulmonary hypertension



An analysis of variance showed no statistical significance for effect of number of episodes of pulmonary tuberculosis on risk for pulmonary hypertension with p=0.14.

TREATMENT OUTCOME OF PULMONARY TUBERCULOSIS AS A RISK FACTOR

Out of total patients, 44 patients had defaulted their treatment before completion. Out of 56 patients completed treatment, only 4 had recorded evidence to categorizethem as cured.

	PH PRESENT	**PH ABSENT**	**TOTAL**
Defaulted	25	19	44
Completed/ cured	19	37	56
TOTAL	44	56	100

Table 13: Comparison of treatment outcome and pulmonary hypertension

Treatment defaulted patients had statistically significant risk for developing pulmonary hypertension with p=0.022 and odds ratio 2.56.

	COR PULMONALE PRESENT	**COR PULMONALE ABSENT**	**TOTAL**
Defaulted	18	7	25
Completed/ cured	13	6	19
TOTAL	31	13	44

Table 14: Comparison of treatment outcome and pulmonary hypertension

No statistical significance was found between treatment outcome and corpulmonale with p=0.79

DRUG SENSITIVITY AS A RISK FACTOR

	PH PRESENT	PH ABSENT	TOTAL
RESISTANT	3	4	7
SENSITIVE	41	52	93
TOTAL	44	56	100

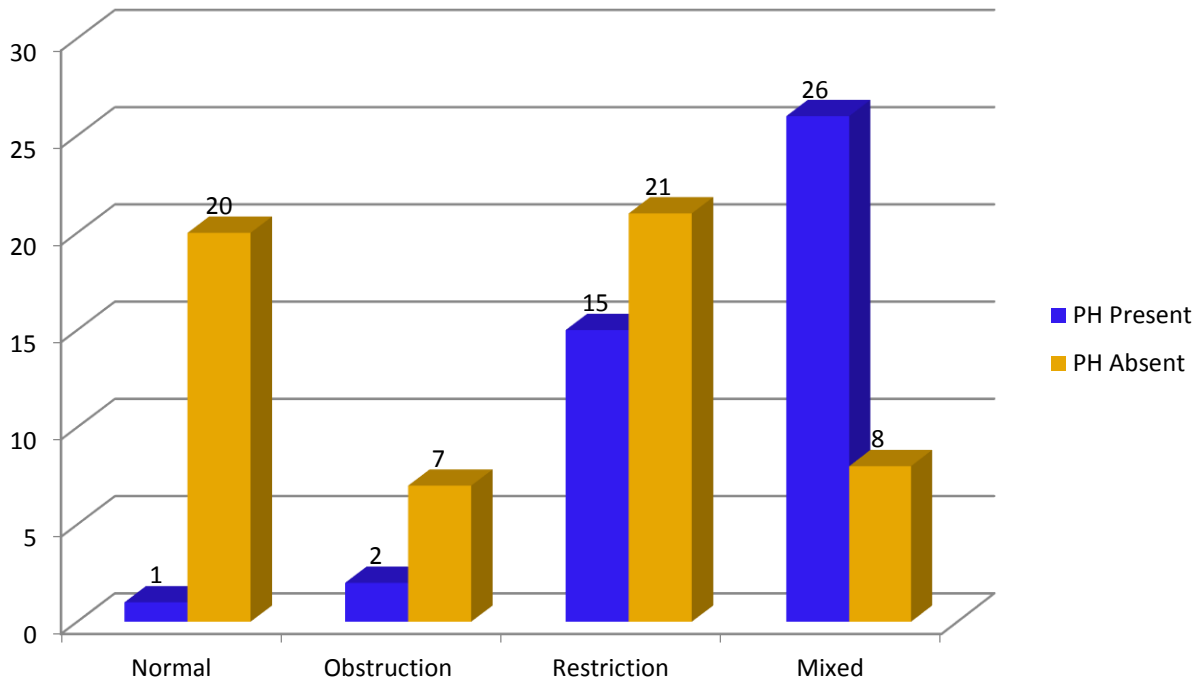
Table 15: Comparison of drug sensitivity pattern and pulmonary hypertension

No significance between drug sensitivity pattern and pulmonary hypertension was seen as p=0.95.

SPIROMETRY PATTERN AS A RISK FACTOR

Average FEV1/FVC was 70.2% with FVC: 60.5% and FEV1: 54.7% of predicted.

Chart 10 : Spirometry pattern and pulmonary hypertension



Majority of the patients had either restriction (n=36) or mixed pattern (n=34) in Spirometry. Remaining 21 had normal and 9 had obstructive pattern. 76.5% of patients with mixed patterns, 57.7% of patients with restriction and 22.2% patients with obstruction in spirometry had evidence of pulmonary hypertension, while it was present in only 4.8% of patients with normal Spirometry.

Any abnormalities in Spirometry, had statistically significant risk for pulmonary hypertension than normal with $p<0.001$ and odds ratio 23.89. In that mixed pattern has 17.14 times significant risk than either pattern with $p=0.0006$

	COR PULMONALE PRESENT	**COR PULMONALE ABSENT**	**TOTAL**
NORMAL	0	1	1
OBSTRUCTION	2	0	2
RESTRICTION	5	10	15
MIXED	24	2	26
TOTAL	31	13	44

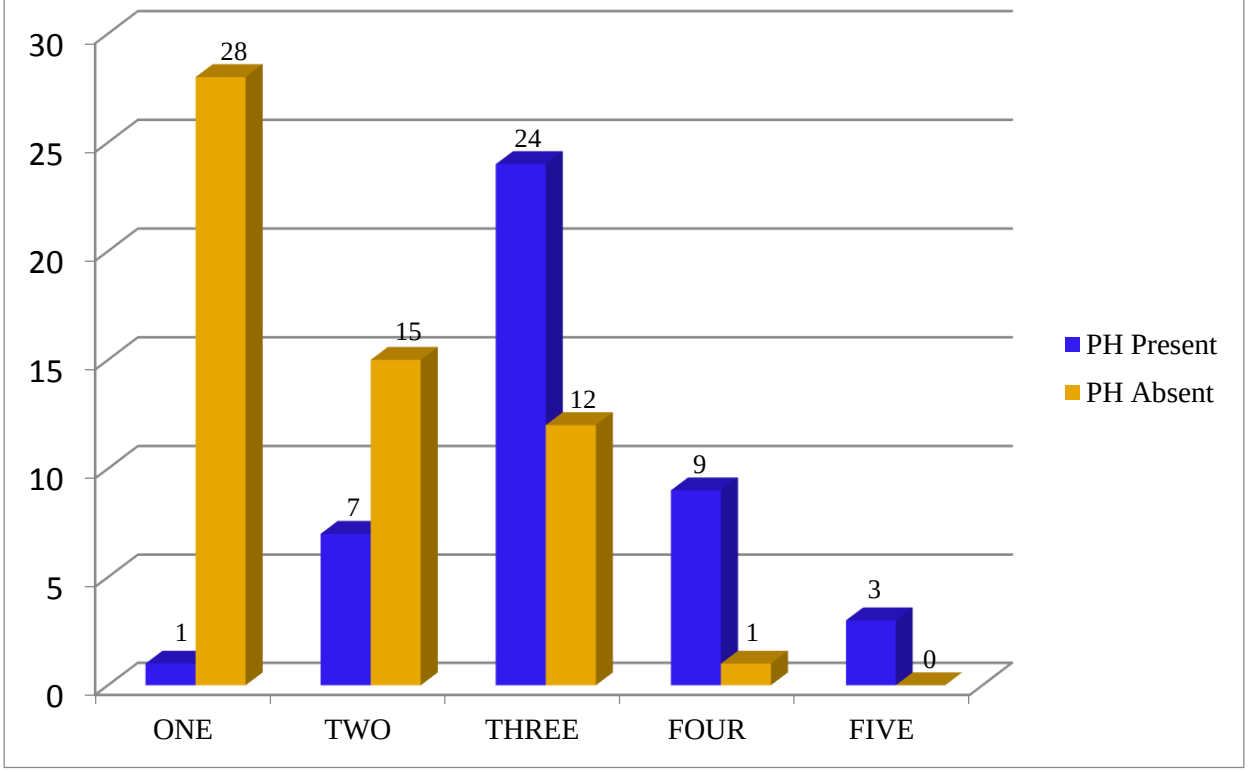
Table 16: Comparison of spirometry pattern and corpulmonale

There was no statistical significance between abnormal and normal pattern in developing corpulmonale with $p=0.29$. But mixed pattern had significant risk than either pattern with odds ratio17.14 and $p=0.003$

NUMBER OF CHEST X-RAY ZONES INVOLVED AS A RISK FACTOR

Average number of zones involved in chest X-ray was 2.36. Majority of them had involvement of 3 zones. As number of zones increased, proportion of patients with pulmonary hypertension also increases. Only 15.7% of patients with number of zones <3 had pulmonary hypertension, while 73.5% of patients with ≥3 zones had it.

Chart 11 : Number of zones involved and pulmonary hypertension



An analysis of variance showed that the effect of number of zones involved in chest X-Ray on severity of pulmonary hypertension was statistically significant with $p<0.001$. The risk is 14.88 with $p<0.001$ when ≥3 zones are involved. It increase to 20.63 with $p<0.001$ when ≥4 zones are involved.

	Corpulmonale present	Corpulmonale absent	TOTAL
ONE	0	1	1
TWO	3	4	7
THREE	16	8	24
FOUR	9	0	9
FIVE	3	0	3
TOTAL	31	13	44

Table 17: Comparison of number of zones involved and corpulmonale

There was a significant difference in number of zones involved between patients with and without corpulmonale with $p<0.001$. Involvement of ≥3 zones had 5.83 times risk with $p=0.0239$.

BILATERAL INVOLVEMENT IN CHEST X-RAY AS A RISK FACTOR

Majority of the patient had unilateral disease (62%). 71.1% of patients with bilateral disease had pulmonary hypertension, while only 27.4% of patients with unilateral disease had it.

	PH PRESENT	PH ABSENT	TOTAL
BILATERAL	27	11	38
UNILATERAL	17	45	62
TOTAL	44	56	100

Table 18: Comparison of laterality in chest X-ray and pulmonary hypertension

Bilateral involvement has 6.49 times risk than unilateral involvemet in developing pulmonary hypertension with $p<0.001$.

	COR PULMONALE PRESENT	**COR PULMONALE ABSENT**	**TOTAL**
BILATERAL	22	5	27
UNILATERAL	9	8	17
TOTAL	31	13	44

Table 19: Comparison of laterality in chest X-ray and corpulmonale

Risk of progression to corpulmonale was statistically significant for bilateral disease with $p=0.043$ and odds ratio 3.91.

NUMBER OF TYPES OF SEQUELAE AS A RISK FACTOR

58 patients had single type of lesion, while 42 had multiple types of lesion. 69.05% of patients with multiple types of lesion had pulmonary hypertension, while only 25.9% of patients with single lesion had it.

	PH PRESENT	**PH ABSENT**	**TOTAL**
MULTIPLE	29	13	42
SINGLE	15	43	58
TOTAL	44	56	100

Table 20: Comparison of number of types of sequelae and pulmonary hypertension

Presence of multiple type of sequelae in a patient has statistically significant risk for pulmonary hypertension than a single type with $p<0.001$ and odds ratio 6.39.

	Corpulmonale present	**Corpulmonale absent**	**TOTAL**
MULTIPLE	21	8	29
SINGLE	10	5	15
TOTAL	31	13	44

Table 21: Comparison of number of types of sequelae and corpulmonale

No significance for risk of corpulmonale in patients with multiple type of sequelae with $p=0.69$.

TYPE OF SEQUELAE AS A RISK FACTOR

Fibrosis

82 patients had fibrosis, out of which 42 had fibrosis alone and 40 had fibrosis combined with other lesions. 48.8% of them had pulmonary hypertension.

FIBROSIS	**PH PRESENT**	**PH ABSENT**	**TOTAL**
PRESENT	40	42	82
ABSENT	4	14	18
TOTAL	44	56	100

Table22: Comparison of fibrosis and pulmonary hypertension

Fibrosis as a type of sequelae has statistically significant risk for pulmonary hypertension with p=0.039 and odds ratio 3.33.

FIBROSIS	COR PULMONALE PRESENT	COR PULMONALE ABSENT	TOTAL
PRESENT	27	13	40
ABSENT	4	0	4
TOTAL	31	13	44

Table 23: Comparison of fibrosis and corpulmonale

Risk for corpulmonale in fibrosis had no statistical significance with p=0.3.

Bronchiectasis

17 patients had bronchiectasis, out of which 9 had bronchiectasis alone and 8 had bronchiectasis combined with other lesions. 47.1% had pulmonary hypertension.

BRONCHIECTASIS	PH PRESENT	PH ABSENT	TOTAL
PRESENT	8	9	17
ABSENT	36	47	83
TOTAL	44	56	100

Table 24: Comparison between bronchiectasis and pulmonary hypertension

There was no statistically significant relationship between bronchiectasis and pulmonary hypertension with p=0.78

Cavity

28 patients had cavity, out of which only 1 had cavity alone and 27 had cavity combined with other lesions. 71.4% of them had pulmonary hypertension.

CAVITY	PH PRESENT	PH ABSENT	TOTAL
PRESENT	20	8	28
ABSENT	24	48	72
TOTAL	44	56	100

Table 25: Comparison of cavity and pulmonary hypertension

Cavity had a statistically significant risk for pulmonary hypertension with p=0.0006 and odds ratio 5.

CAVITY	COR PULMONALE PRESENT	COR PULMONALE ABSENT	TOTAL
PRESENT	14	6	20
ABSENT	17	7	24
TOTAL	31	13	44

Table 26: Comparison of cavity and corpulmonale

There was no statistically significant risk between cavity and corpulmonale with p=0.95.

Bullae

9 patients had bullae, out of which 1 had bullae alone and 8 had bullae combined with other lesions. 88.9% of them had pulmonary hypertension.

BULLAE	PH PRESENT	PH ABSENT	TOTAL
PRESENT	8	1	9
ABSENT	36	55	91
TOTAL	44	56	100

Table 27: Comparison of bullae and pulmonary hypertension

Bullae as a risk factor for pulmonary hypertension was statistically significant with p=0.0045 and odds ratio 12.22.

BULLAE	COR PULMONALE PRESENT	COR PULMONALE ABSENT	TOTAL
PRESENT	7	1	8
ABSENT	24	12	36
TOTAL	31	13	44

Table 28: Comparison of bullae and corpulmonale

Risk for corpulmonale in bullae had no statistical significance with p=0.24.

Aspergilloma

7 patients had aspergilloma, out of which 4 had aspergilloma alone and 3 had aspergilloma combined with other lesions. 14.3% of them had pulmonary hypertension.

ASPERGILLOMA	PH PRESENT	PH ABSENT	TOTAL
PRESNT	1	6	7
ABSENT	43	50	93
TOTAL	44	56	100

Table 29: Comparison between aspergilloma and pulmonary hypertension

There was no statistically significant relationship between aspergilloma and pulmonary hypertension with p=0.1.

Calcification/pleural thickening

7 patients had calcification/pleural thickening, out of which only 1 had it alone and 6 combined with other lesions.

Calcification/pleural thickening	PH PRESENT	PH ABSENT	TOTAL
PRESENT	3	4	7
ABSENT	41	52	93
TOTAL	44	56	100

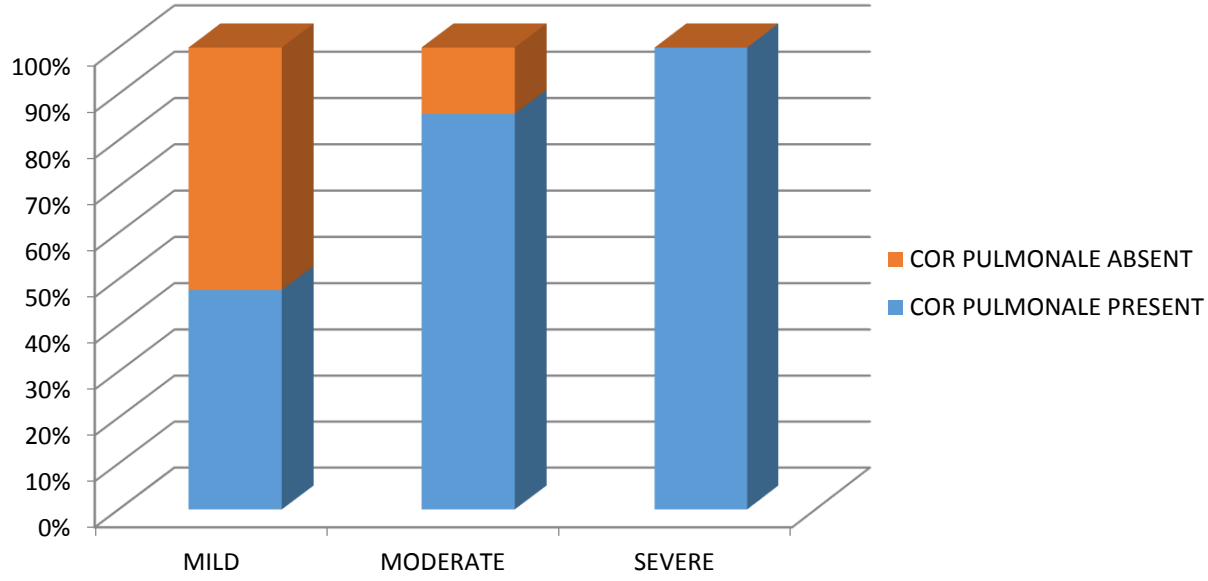
Table 30: Comparison of calcification/pleural thickening and pulmonary hypertension

Risk for pulmonary hypertension in calcification/pleural thickening had no statistical significance with p=0.95.

SEVERITY OF PULMONARY HYPERTENSION AND COR PULMONALE

47.6% of patients with mild, 85.7% of patients with moderate and 100% of patients with severe pulmonary hypertension had evidence of corpulmonale in echocardiography.

Chart 12: Severity of pulmonary hypertension and cor pulmonale



There is statistically significant relationship between severity of pulmonary hypertension and corpulmonale with $p<0.001$. With increasing severity of pulmonary hypertension, there is a significant rise in the risk of development of corpulmonale.

DISCUSSION

Pulmonary tuberculosis is not cited as a cause of pulmonary hypertension in western literatures. But in endemic countries like India, with high TB incidence and risk of sequelae after disease, it is a major cause of pulmonary hypertension [95]. This further increases the morbidity and mortality due to tuberculosis, which is often overlooked. In our study we analyzed the prevalence and risk factors for pulmonary hypertension and corpulmonale in post tuberculosis pulmonary sequelae.

Prevalence of pulmonary hypertension in post tuberculosis pulmonary sequelae patients in our study is 44%. Mani Tiwari et al. from Europe showed a prevalence rate of 24% [96], while Ivanov AK et al. from Russia showed a prevalence rate of 44.2% consistent with our study [97]. This indicates that prevalence is high in endemic countries. The prevalence of corpulmonale was 31% in our study. Kotresh N et al. showed a prevalence of 11%.[5]

Out of the patients with pulmonary hypertension 70.5% had corpulmonale and the prevalence increased with severe grading of pulmonary hypertension. Hilde J M et al. showed that due to decreased pulmonary vascular compliance, even before significant elevation of pulmonary artery pressure, right ventricular hypertrophy and remodeling is seen in patients with chronic lung disease. Thus corpulmonale may be present in patients at the early stage of pulmonary vascular changes itself [98]. The same pathogenesis may be the cause of high prevalence of corpulmonale in our study also.

While analyzing various risk factors for pulmonary hypertension, age had no significance. This is in contrast to Al. Obaidy et al. where mean age of patients with pulmonary hypertension was significantly higher than patients without pulmonary hypertension [99].

In our study, male gender had significant risk for developing pulmonary hypertension. This was in contradiction to Majid Marjani et al. which showed no significant relation [100]. Thiscould possibly be explained by anti remodeling effect of estrogen and pro remodeling effect of androgen on pulmonary vessels as explained in Ventetuoloet al [101]. This may also be due to smoking habit seen more in men in India.

Body mass index as a risk factor has marginal significance with p=0.05, which is similar to finding of Young Suk Jo et al [102]. Underweight individuals had significant risk than others. This is consistent with finding of C D Burger et al. which showed lower BMI in patients with pulmonary hypertension due to chronic lung disease and heart disease. The reason is not known. It may be due to the increased work of breathing resulting in malnourishment [103].

Smoking had a significant effect on development of pulmonary hypertension. This can be explained by the finding of N Weissmann et al. which showed that tobacco smoke increase pulmonary artery pressure by causing inflammation and direct damage of vessels leading to pulmonary vascular remodeling. This is mainly due to reactive oxygen species in tobacco smoke. In addition to this, it also has indirect effect due to increased

parenchymal damage [104]. Diabetes had no effect on risk for pulmonary hypertension consistent with study of Young Suk Jo et al [102].

In pulmonary tuberculosis history, time since first episode of pulmonary tuberculosis, number of episodes of pulmonary tuberculosis or drug sensitivity pattern did not have any significant association with risk of developing pulmonary hypertension. This is consistent with study of Young Suk Jo et al[102]. But patients with history of defaulting treatment had a significant risk for developing pulmonary hypertension. Eun Young Hoe et al. showed that at end of treatment, average extent of residual radiographic lesion was 10.5%. This is higher in TB treatment defaulters. It may further progress to cavitation and extensiveparenchymal damage [105]. This can explain our finding.

In radiological characteristics, extent of involvement measured by number of zones and sides involved was statistically significant. Patients with more than one type of sequelae had significant risk than patients with single type. Thus extent of parenchymal damage has a major role in risk for pulmonary hypertension. Lynch DA et al. showed that extent of parenchymal damage in radiology was an independent predictor for pulmonary hypertension in idiopathic pulmonary fibrosis. This may be due to more decrease in pulmonary vascular bed cross-sectional area because of more fibrosis resulting in increased pulmonary vascular resistance [106]. This can be used to explain our finding also.

In type of sequelae, majority of the patients had fibrosis, followed by cavity and bronchiectasis. M G Ali et al. also showed an increased incidence of fibrosis in post tuberculosis pulmonary sequelae [107].

In assessing type of sequelae as a risk factor, Fibrosis, cavity and bullae had significant risk for developing to pulmonary hypertension. L Farkas et al. in a study about IPF has shown that fibrotic areas release various mediators causing pulmonary vascular remodeling and thrombosis, increasing pulmonary vascular resistance. In addition to other mechanisms, fibrosis also causes mechanical obliteration of vessels. Plexiform lesions are also more common in fibrosis [108]. The same pathogenesis may be the cause of significant risk for pulmonary hypertension in fibrosis in our study also.

Increased risk in cavity may be due to increased bacterial load during primary disease, as cavity is associated with liquefactive necrosis favoring bacterial growth as told in G Aderaye et al. This result in increased parenchymal destruction due to more pathogenand resultant increased host immune response [109].

Risk in bullae may be due to the more area of destruction and decreased pulmonary vascular cross-sectional area. This may also be due to the fact that, they presented combined with other lesions in our study, except for one.

Bronchiectasis had no statistical significance in the risk for developing pulmonary hypertension. This is consistent with the finding in Yong Suk Jo et al [102]. But A Devaraj et al showed that due to hypoxia and destruction of vascular bed, pulmonary hypertension

is expected in bronchiectasis. Few studies have shown that nearly one third of the patients with bronchiectasis develop pulmonary hypertension [110].

No statistical significance seen in aspergilloma and calcification/pleural thickening may be due to relatively lesser zones involved and less extensive destruction of lung parenchyma and pulmonary vasculature.

In spirometry, abnormal patterns had more risk than normal and mixed pattern had more risk than either pattern alone. Di Naso F C et al. showed that sequelae are due to bronchial and parenchymal abnormality. Pulmonary TB can involve airway leading to decrease in its caliber and increase inairway resistance resulting in obstructive pattern. By the mechanism of fibrosis it also causes a restrictive pattern[111]. Andre F S et al. showed that odds ratio for obstructive pattern was 3.33 and restrictive pattern 2.02 in spirometry in a patient with TB history than a patient without [112]. This can be used to explain our finding that a mixed pattern indicate a more extensive disease and thus increased chance of developing pulmonary hypertension.

We also analyzed the risk factors for corpulmonale in patients with pulmonary hypertension. Only smoking and extent of involvement in chest X-ray showed a significant association with corpulmonale. Rubin LJ et al. showed that early lung damage itself can raise pulmonary vascular resistance enough to cause corpulmonale[113]. This may explain our finding as further increase in extent of lung damage increases the risk of corpulmonale.

Majority of the patients with pulmonary hypertension had symptoms or signs of respiratory failure. This emphasize that pulmonary hypertension is indeed a cause of increased morbidity and mortality in patients with post pulmonary tuberculosis sequelae. Thus long term monitoring of patients with post pulmonary tuberculosis is mandatory to prevent development of pulmonary hypertension.

SUMMARY

The present study was conducted to assess the prevalence and risk factors of pulmonary hypertension and corpulmonale in post tuberculosis pulmonary sequelae as it represents the unmeasured parameter of TB burden.

Prevalence of pulmonary hypertension in our study was 44 per 100 patients with post tuberculosis pulmonary seuelae, which is clinically significant. Corpulmonale was present in 31 per 100 patients with sequelae, i.e., 70.5% of patients with pulmonary hypertension. Majority of them had symptoms or signs of respiratory failure.

While assessing risk factors for pulmonary hypertension, male gender, underweight and smoking had a significant risk. Smoking as a risk factor calls for smoking cessation as a preventive step against development of pulmonary hypertension.

In tuberculosis history, only treatment defaulters had significant risk. This indicates that strict adherence to anti tuberculosis treatment, not only cure the active disease, but gives long term benefits to the patients by preventing pulmonary hypertension in future, irrespective of relapse rate or drug sensitivity pattern.

Extensive involvement in chest X-ray and Spirometric abnormalities had a significant risk for pulmonary hypertension. These can be reduced by early diagnosis and treatment of active tuberculosis disease. Among sequelae fibrosis, cavity and bullae had significant risk.

While assessing risk factors for pulmonary hypertension progressing to corpulmonale, severity of pulmonary hypertension had significant risk. Other parameters which had significance were smoking and extension of involvement in chest X-ray. This implies that right ventricular failure is inevitable once pulmonary hypertension has developed.

CONCLUSION

The high prevalence of pulmonary hypertension and corpulmonale in post tuberculosis pulmonary sequelaeemphasizes the need for recommendations regarding long term follow up of treated tuberculosis patients and interventions to prevent them progress to pulmonary hypertension. This should be included in national and international tuberculosis programs.

Early detection, treatment with adequate regimen and ensuring compliance with treatment of pulmonary tuberculosis plays the major role in prevention of pulmonary hypertension and corpulmonale and morbidity and mortality associated with it, in the future. A strong national program and dedicated health workers can achieve this and reduce this post treatment burden due to tuberculosis.

LIMITATION

- Sample size was small.
- Post pulmonary tuberculosis sequelae pattern were assessed using chest X-ray. CT chest was not taken to assess the exact morphology.
- Other common lung diseases causing pulmonary hypertension like COPD, bronchial asthma were not excluded due to overlap of clinical, radiological and functional parameters.
- Hereditary, genetic and autoimmune causes of pulmonary hypertension were not ruled out.

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PROFORMA

Name : **Case id**

Age: Sex: M/F Weight: Height: BMI:

Occupation: Residing in high altitude: Yes/No

Admission/OP :

HISTORY

1) Breathlessness
   a. Duration : b. Grade :
   c. Associated factors:
2) Chest pain
   a. Duration : b. Association factor:
3) Swelling of leg
   a. Duration :
4) Any other symptom:

Previous pulmonary tuberculosis history:

1) Time since 1st diagnosis of PTB:
2) Number of times diagnosed as PTB :
3) Details of each (cured/completed/failure/default/resistance)

Past history:

1) Known case of diabetes : Yes/No
2) Known case of HIV/AIDS : Yes/No
3) Known case of any cardiac disease:
4) Known case of any other disease :

Smoking history :

If yes, smoking index :

History of any drug intake: Yes/No

If yes, drug and duration :

EXAMINATION

Comfortable/dyspneic at rest:

Pallor: Icterus: Cyanosis: Clubbing:

Pedal edema: Raised JVP:

SpO2 at RA: PR: BP: RR:

SYSTEMIC EXAMINATION:

RS:	CVS:
	P/A:

INVESTIGATIONS

SPUTUM AFB :

CHEST X-RAY

1) Type of pulmonary sequelae

2) No. of zones:
3) Features of pulmonary artery hypertension/corpulmonale

SPIROMETRY:

ECG :

ECHOCARDIOGRAPHY :

1) Pulmonary artery hypertension:
    a. Size of MPA
    b. Tricuspid regurgitation velocity:
    c. sPAP:
    d. Severity : mild/moderate/severe

2) Right ventricular function
    a. Dimension : end- diastolic
    b. TAPSE
    c. TASV
    d. Rv MPI
    e. Interventricular septum

5) Left ventricular function
    a. Systolic
        Ejection fraction
    b. Diastolic

6) Chambers

7) Valves

IMPRESSION :

நோயாளிகளுக்கு அறிவிப்பு மற்றும் ஒப்புதல் படிவம்
(மருத்துவ ஆய்வில் பங்கேற்பதற்கு)

ஆய்வு செய்யப்படும் தலைப்பு:
பங்கு பெறுவரின் பெயர்:
பங்கு பெறுவரின் வயது:

		பங்கு பெறுவர் இதனை ✓ குறிக்கவும்
1.	நான் மேலே குறிப்பிட்டுள்ள மருத்துவ ஆய்வின் விவரங்களை படித்து புரிந்து கொண்டேன். என்னுடைய சந்தேகங்களை கேட்கவும், அதற்கான தகுந்த விளக்கங்களை பெறவும் வாய்ப்பளிக்கப்பட்டுள்ளது என அறிந்து கொண்டேன்.	☐
2.	நான் இவ்வாய்வில் தன்னிச்சையாக தான் பங்கேற்கிறேன். எந்த காரணத்தினாலோ எந்த கட்டத்திலும், எந்த சட்ட சிக்கலுக்கும் உட்படாமல் நான் இவ்வாய்வில் இருந்து விலகி கொள்ளலாம் என்றும் அறிந்து கொண்டேன்.	☐
3.	இந்த ஆய்வு சம்பந்தமாகவோ, இதை சார்ந்து மேலும் ஆய்வு மேற்காள்ளும் போதும் இந்த ஆய்வில் பங்குபெறும் மருத்துவர் என்னுடைய மருத்துவ அறிக்கைகளை பார்ப்பதற்கு என் அனுமதி தேவையில்லை என அறிந்து கொள்கிறேன். நான் ஆய்வில் இருந்து விலகிக் கொண்டாலும் இது பொருந்தும் என அறிகிறேன்.	☐
4.	இந்த ஆய்வின் மூலம் கிடைக்கும் தகவலையோ, முடிவையோ பயன்படுத்திக் கொள்ள மறுக்க மாட்டேன்.	☐
5.	இந்த ஆய்வில் பங்கு கொள்ள ஒப்புக் கொள்கிறேன் எனக்கு கொடுக்கப்பட்டஅறிவுரைகளின் படி நடந்து கொள்வதுடன், ஆய்வை மேற்கொள்ளும் மருத்துவ அணிக்கு உண்மையுடன் இருப்பேன் என்று உறுதியளிக்கிறேன். என் உடல் நலம் பாதிக்கப்பட்டாலோ, அல்லது எதிர்பாராத, வழக்கத்திற்கு மாறான நோய்குறி தென்பட்டாலோ உடனே இதை மருத்துவ அணியிடம் தெரிவிப்பேன் என உறுதி அளிக்றேன்.	☐

பங்கேற்பவரின் கையொப்பம் / ..... இடம் .....
கட்டைவிரல் ரேகை
பங்கேற்பவரின் பெயர் மற்றும் விலாசம் .....
ஆய்வாளரின் கையொப்பம் /..... இடம் .....
ஆய்வாளரின் பெயர் .....
மையம் .....
கல்வியறிவு இல்லாதவற்கு (கைரேகை வைத்தவர்களுக்கு) இது அவசியம் தேவை
சாட்சியின் கையொப்பம் /..... இடம் .....
பெயர் மற்றும் விலாசம் ....

Sl no	Name	Age	Sex	Bmi	Diabetes	Smoking index	PULMONARY TUBERCULOSIS HISTORY				Respiratory distress	RADIOLOGICAL FINDING			PFT				ECHOCARDIOGRAPHY								
							Time since 1st	No of Times	Sensitive/ Resistant	Outcome		Zones	Side	Lesion	FVC (% Pred)	FEV1(% Pred)	FEV1/FVC (%)	Result	Size of mpa	TRV	Spap	Severity	End diastolic dimension	Tapse	Tasv	Rvmpi	Iv septum bulge	Rv dysfunction
1	Ramasubbu	35	M	17	N	N	5	1	Resistant	Complete	Y	3	Unilateral	F	57.8	68.2	95.9	Restriction	3.4	3.1	37	Mild	23	1.5	8	0.34	N	Y
2	Esakiyammal	50	F	19.5	N	N	7	1	Sensitive	Complete	N	1	Unilateral	B	80.2	102	82.1	Normal	2.1	1.6	14	Normal	11.6	1.8	13	0.28	N	N
3	Kaniyammal	55	F	10.5	N	N	5	2	Sensitive	Complete	N	1	Unilateral	F	35	30	72.9	Restriction	1.2	2.1	22	Normal	11.2	1.7	12	0.29	N	N
4	Lakshmi	58	F	23.7	N	N	40	2	Sensitive	Complete	N	2	Unilateral	F P	39	26	54.9	Mixed	2.7	1.9	15	Normal	17.9	1.9	16	0.3	N	N
5	Anbuselvi	26	F	18.1	N	N	7	1	Sensitive	Default	Y	3	Unilateral	F	58	63.7	95.7	Restriction	3.6	3.4	50	Mild	17.8	2.2	15	0.29	N	N
6	Paulraj	82	M	22	Y	840	20	1	Sensitive	Complete	N	1	Unilateral	A	57.1	80.5	63.1	Restriction	2.4	2.1	21	Normal	14.3	1.8	15	0.24	N	N
7	Maharajan	48	M	14.4	N	588	30	1	Sensitive	Complete	Y	3	Unilateral	F C	41.1	68.9	132	Restriction	3.7	4	68	Moderate	28	1.4	8	0.41	Y	Y
8	Boothathan	68	M	18.3	N	840	15	2	Sensitive	Default	Y	3	Bilateral	F	26.5	22.4	62.3	Mixed	3.5	4.8	98	Severe	38	1.3	7	0.58	Y	Y
9	Pandaram	75	M	18.3	N	700	10	1	Sensitive	Complete	N	3	Bilateral	F C	43.5	42.5	70.8	Mixed	3.5	3.7	61	Moderate	22	1.6	9	0.33	Y	Y
10	Arumugam	54	F	19.3	N	N	10	1	Sensitive	Complete	N	2	Bilateral	F	68	66.8	77.1	Restriction	2	1.9	20	Normal	11.2	2.3	16	0.29	N	N
11	Patturaj	57	M	21	N	900	7	1	Sensitive	Default	Y	4	Bilateral	F C	42.1	24.5	44.5	Mixed	3.5	5	106	Severe	22.2	1.3	7	0.44	Y	Y
12	Shahul hameed	55	M	13.7	N	675	10	1	Sensitive	Default	Y	5	Bilateral	F B A	52.9	61.9	89.7	Restriction	3.4	3.3	47	Mild	21.7	1.6	9	0.36	Y	Y
13	Ramesh	37	M	22	Y	200	3	1	Sensitive	Default	N	1	Unilateral	F A	81.8	80.6	79.8	Normal	1.5	1.2	10	Normal	8.6	2	14	0.26	N	N
14	Lakshmanan	73	M	23	N	1050	5	1	Sensitive	Default	Y	3	Unilateral	F	39.2	26.4	51	Mixed	3.5	3.9	65	Moderate	29.2	1.3	9	0.47	Y	Y
15	Veyilvandhan	73	M	26	N	812	15	1	Sensitive	Default	N	1	Unilateral	F	83.3	47.6	40.1	Obstruction	2.2	1.7	16	Normal	12.4	1.8	16	0.23	N	N
16	Shanmugathai	50	F	21	N	N	15	2	Sensitive	Default	N	3	Unilateral	F C	89.3	45.4	40.8	Obstruction	3.4	3.4	51	Mild	23.2	1.6	9.8	0.33	N	Y
17	Avudaiyammal	65	F	20	N	N	30	1	Sensitive	Default	N	4	Bilateral	F P	39.9	31.5	60.2	Mixed	3.6	4.7	92	Severe	28	1.1	8	0.48	Y	Y
18	Murugan	49	M	17	N	20	14	2	Sensitive	Complete	N	1	Unilateral	F	80.1	82.3	79.1	Normal	2.1	1.4	12	Normal	13.4	2.1	14	0.26	N	N
19	Murugesan	45	M	20	N	480	6	1	Sensitive	Cured	N	3	Unilateral	F C P	48.9	45.9	73.3	Restriction	3.4	3.2	44	Mild	17.3	1.9	13	0.25	N	N
20	Nallamaran	73	M	26	N	1000	30	1	Sensitive	Complete	N	1	Unilateral	F	81.1	67.1	59.5	Obstruction	1.9	2.4	27	Normal	12.8	1.7	13	0.27	N	N
21	Madathy	52	F	27	N	N	25	1	Sensitive	Cured	Y	1	Unilateral	F	53.1	53.2	79.3	Restriction	2.9	2.1	21	Normal	16.4	1.9	18	0.24	N	N
22	Shanmugavadivu	75	F	11.4	N	N	35	1	Sensitive	Complete	N	2	Unilateral	F	26	29	83.5	Restriction	2.1	2.5	28	Normal	15.4	2.1	17	0.26	N	N

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							Time since 1st	No of Times	Sensitive/ Resistant	Outcome		Zones	Side	Lesion	FVC (% Pred)	FEV1(% Pred)	FEV1/FVC (%)	Result	Size of mpa	TRV	Spap	Severity	End diastolic dimension	Tapse	Tasv	Rvmpi	Iv septum bulge	Rv dysfunction
23	Uchimahali	33	F	14	N	N	1	1	Sensitive	Default	Y	3	Unilateral	F Bu	58.9	56.7	72.1	Restriction	3.4	3.1	42	Mild	16.1	1.8	11	0.31	N	N
24	Kaviarasan	45	M	13	N	700	3	2	Sensitive	Default	Y	4	Bilateral	F Bu	36.6	23.1	50	Mixed	3.4	3.2	45	Mild	20.4	1.5	9	0.33	N	Y
25	Muniyammal	27	F	19	N	N	5	3	Resistant	Complete	Y	2	Unilateral	C P	46.9	37.5	68.9	Mixed	3.1	2.6	31	Normal	16.8	1.9	12	0.28	N	N
26	Ganesan	50	M	14.5	Y	849	2	1	Sensitive	Default	Y	3	Unilateral	F	52	64	72.2	Restriction	2.8	2.3	25	Normal	17.3	2.1	13	0.27	N	N
27	Nainar	65	M	14	N	560	5	1	Sensitive	Default	N	3	Unilateral	F C	49.2	33.9	51	Mixed	2.7	2.5	29	Normal	16.2	1.9	13	0.23	N	N
28	Nandhini	24	F	13	N	N	3	2	Sensitive	Default	Y	3	Bilateral	F Bu	47.7	32.3	60.1	Mixed	3.6	4.2	74	Moderate	24.7	1.4	9	0.42	Y	Y
29	Sivashankar	38	M	25	N	N	10	1	Sensitive	Default	Y	3	Unilateral	F C	58.4	29.3	40.8	Mixed	3.4	3.8	62	Moderate	17.8	1.7	11	0.24	N	N
30	Chinnadurai	63	M	20	N	462	10	1	Sensitive	Cured	N	3	Bilateral	F B	81.1	46.9	43.4	Obstruction	3.1	2.6	31	Normal	16.8	1.8	12	0.3	N	N
31	Lakshmanan	68	M	16.3	Y	N	10	2	Sensitive	Default	Y	3	Unilateral	F C Bu	81.7	84.5	76.1	Normal	2.5	1.9	19	Normal	15.4	1.9	16	0.3	N	N
32	Muppidathy	55	M	17.1	N	1155	3	1	Sensitive	Complete	Y	3	Bilateral	F C	49.1	43.9	68.7	Mixed	3.9	3.7	61	Moderate	23.2	1.4	9	0.4	Y	Y
33	Subbaiah	73	M	20	Y	N	4	1	Sensitive	Complete	N	1	Unilateral	F C	82.1	79.7	70.5	Normal	2.9	2.1	22	Normal	15.4	2.1	15	0.24	N	N
34	Muthulalshmi	38	F	19	N	N	10	1	Sensitive	Complete	Y	2	Bilateral	B	21	25	99	Restriction	2.8	1.9	18	Normal	13.4	2	16	0.27	N	N
35	Ganapathy	65	M	21	N	840	13	2	Resistant	Default	N	1	Unilateral	P	80.2	43.1	40.1	Obstruction	3.1	2.5	29	Normal	16.6	1.9	11	0.29	N	N
36	Neelavathy	53	F	22.4	Y	N	20	1	Sensitive	Complete	Y	3	Bilateral	B	46.8	39.3	66.2	Mixed	3.5	4.8	99	Severe	26.7	1.2	7	0.46	Y	Y
37	Subbaiah p	62	M	21	N	2240	3	1	Sensitive	Complete	N	2	Bilateral	F	85.2	69.3	61.2	Obstruction	2.7	2.3	26	Normal	16.7	1.8	12	0.26	N	N
38	Amalesh	40	M	18	N	560	10	1	Sensitive	Default	N	4	Bilateral	F Bu C	22.1	17.2	62.3	Mixed	3.9	4.7	93	Severe	26.8	1.2	8	0.49	Y	Y
39	Paramasivam	65	M	20	N	675	30	1	Sensitive	Complete	Y	2	Bilateral	F	42.2	25.2	44.5	Mixed	3.8	3.5	53	Mild	23.9	1.1	7	0.45	Y	Y
40	Malaiyandi	62	M	22	N	N	10	1	Sensitive	Complete	Y	1	Unilateral	F B	83.1	78.5	71	Normal	3.4	3.3	48	Mild	17.6	1.7	12	0.28	N	N
41	Gomathi	42	F	20	N	N	5	1	Sensitive	Complete	N	1	Unilateral	B	38	29	62.3	Mixed	2.5	1.5	14	Normal	14.4	1.9	16	0.25	N	N
42	Lakshmi	60	F	21	N	N	10	1	Sensitive	Complete	N	3	Unilateral	F C	65.1	71.7	85.1	Restriction	2.7	2.2	23	Normal	13.8	2.2	18	0.31	N	N
43	Ananthavalli	40	F	19	N	N	10	1	Sensitive	Default	N	3	Unilateral	F	81.5	83.9	84.4	Normal	2.6	1.7	16	Normal	16.7	1.8	13	0.22	N	N

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44	Gowrithangam	40	F	23	N	N	5	1	Sensitive	Complete	Y	3	Unilateral	F	83.6	75.3	73.9	Normal	2.9	2.5	28	Normal	14.3	1.8	19	0.26	N	N
45	Panchangam	68	M	20	N	1032	10	1	Sensitive	Complete	Y	2	Bilateral	F	68.1	78.2	74	Restriction	3.1	2.6	29	Normal	16.2	1.9	12	0.28	N	N
46	Petchiammal	35	F	20	N	N	3	1	Sensitive	Complete	N	3	Unilateral	F Bu	53.8	55.1	85.1	Restriction	3.5	3.5	52	Mild	23.4	1.6	9.8	0.32	Y	Y
47	Maduraiveeran	54	M	17.5	N	952	11	1	Sensitive	Default	Y	3	Unilateral	F C	33.3	24.8	57.4	Mixed	3.8	3.9	67	Moderate	28.6	1.4	8	0.41	Y	Y
48	Thangam	35	F	14	Y	N	24	2	Resistant	Default	N	2	Unilateral	F C	68.4	64.4	78.2	Restriction	2.8	2.6	32	Normal	16.7	1.8	12	0.31	N	N
49	Arunachalam	64	M	20	N	560	7	1	Sensitive	Complete	N	1	Unilateral	A	86.1	83.8	72.8	Normal	2.6	2.4	27	Normal	12.7	1.8	13	0.26	N	N
50	Sankarapandi	42	M	17	Y	560	2	1	Sensitive	Complete	Y	3	Bilateral	F C P	44.7	35.7	63.7	Mixed	3.4	3.2	44	Mild	22.6	1.5	9	0.32	Y	Y
51	Sudalaivadivu	35	F	17.3	N	N	2	1	Sensitive	Complete	Y	3	Bilateral	F C B	72	58.7	67.2	Mixed	3.4	3.1	42	Mild	16.2	1.8	11	0.29	N	N
52	Navnithakrishnan	65	M	22	N	400	5	2	Sensitive	Default	N	2	Bilateral	F	81.7	64.4	60.4	Obstruction	2.5	2.1	22	Normal	15.3	2.1	16	0.23	N	N
53	Alagurajan	23	M	11.4	N	N	4	2	Sensitive	Default	Y	5	Bilateral	Bu	50.5	39.9	66	Mixed	3.8	4.8	97	Severe	33.5	1.4	8	0.57	Y	Y
54	Namakani	63	F	19	N	N	30	1	Sensitive	Complete	Y	1	Unilateral	B	63	57	74.5	Restriction	1.9	1.7	15	Normal	16.5	1.7	13	0.26	N	N
55	Petchidurai	40	M	14	N	840	2	1	Sensitive	Default	Y	4	Bilateral	F C	58.7	50.4	68.7	Mixed	3.7	4.7	94	Severe	30.2	1.3	8	0.49	Y	Y
56	Shanmugaiah	61	M	15	N	1064	7	3	Resistant	Default	Y	4	Bilateral	F Bu C	32.1	22.9	53.7	Mixed	3.9	4.8	98	Severe	38	1.3	7	0.52	Y	Y
57	Amutha	33	F	27	N	N	13	1	Sensitive	Complete	N	1	Unilateral	B	83.7	75.4	75.8	Normal	2	1.8	17	Normal	17.3	1.7	12	0.25	N	N
58	Balakrishnan	33	M	23	Y	N	2	1	Sensitive	Default	N	3	Bilateral	C	64.2	52.1	66.1	Mixed	3.1	2.7	33	Normal	16.9	1.8	11	0.29	N	N
59	Thayammal	60	F	19	N	N	27	1	Sensitive	Complete	N	1	Unilateral	F	81.5	77.9	73.9	Normal	2.3	2.1	22	Normal	15.3	2.2	14	0.26	N	N
60	Kailasam	50	M	21	N	448	4	2	Sensitive	Cured	N	2	Bilateral	F	58.9	54.7	72.4	Restriction	2.6	2.3	25	Normal	17.4	2	14	0.29	N	N
61	Sudalai	80	M	15	N	N	10	1	Sensitive	Default	N	2	Bilateral	F	52	67	99.1	Restriction	3.5	3.5	52	Mild	17.2	1.8	12	0.26	N	N
62	Beer mohammed	44	M	16.9	Y	N	3	1	Sensitive	Complete	N	1	Unilateral	F	68	63	77.1	Restriction	2.2	2.1	22	Normal	15.4	2.2	15	0.27	N	N
63	Rajagopalan	47	M	15.1	N	430	5	1	Sensitive	Complete	N	2	Bilateral	F	48	50	86.1	Restriction	3.7	4.3	79	Moderate	17.9	1.7	11	0.31	N	N
64	Lakshmi	60	F	16	N	N	5	1	Sensitive	Default	N	3	Unilateral	F	35	37	88.6	Restriction	2.7	2.6	32	Normal	17.1	1.8	13	0.29	N	N
65	Sankaran	68	M	21	N	462	25	2	Sensitive	Complete	N	2	Unilateral	F	83.5	78.2	74	Normal	2.8	2.5	28	Normal	14.5	1.9	19	0.26	N	N
66	Paulraj	61	M	18.7	N	574	4	1	Sensitive	Default	N	1	Unilateral	A	35	31	72.3	Restriction	1.8	1.7	16	Normal	15.8	2	15	0.24	N	N

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67	Arumugam	50	M	16.2	N	N	35	1	Sensitive	Complete	N	4	Bilateral	B P	93	83	72.8	Normal	2.8	2.5	30	Normal	16.7	1.8	11	0.29	N	N
68	Subbulakshmi	45	F	18.8	N	N	12	1	Sensitive	Complete	N	2	Unilateral	F	48	40	70.2	Restriction	2.7	2.2	24	Normal	13.9	2.1	18	0.3	N	N
69	Subramanian	40	M	17.5	N	300	7	1	Sensitive	Default	Y	3	Unilateral	F C	72	59.2	66.4	Mixed	3.9	4.4	82	Moderate	31.3	1.3	7	0.45	Y	Y
70	Karuppusamy	75	M	22	N	N	10	1	Sensitive	Complete	N	1	Unilateral	F A	55	61.9	81	Restriction	2.1	1.8	17	Normal	17.4	1.9	13	0.29	N	N
71	Samuel	58	M	17.9	N	1350	5	1	Sensitive	Default	N	4	Bilateral	F C	37	35	77.3	Restriction	3.6	3.6	49	Mild	23.3	1.5	9.8	0.33	Y	Y
72	Pushpam	50	F	20	N	N	2	1	Sensitive	Default	N	2	Unilateral	F	85.4	80.6	75	Normal	2.5	2.1	22	Normal	15.5	2.1	15	0.21	N	N
73	Subbaiah	46	M	18	N	1092	1	1	Sensitive	Default	N	3	Bilateral	F C	64.4	69.9	86.5	Restriction	3.8	3.5	52	Mild	17.8	1.8	11	0.31	N	N
74	Arumugam	43	M	13.3	N	400	3	3	Sensitive	Default	Y	3	Unilateral	F	31	20	52.6	Mixed	2.6	2.7	34	Normal	16.6	1.8	12	0.26	N	N
75	Ganesan	46	M	24.8	N	600	23	1	Sensitive	Complete	Y	3	Unilateral	F	70.2	69.9	79.4	Restriction	2.8	2.5	30	Normal	16.7	1.8	12	0.31	N	N
76	Mayandi	47	M	22	N	378	20	2	Sensitive	Complete	N	4	Bilateral	F B	82.3	59.6	57.6	Obstructio n	3.8	3.6	56	Mild	23.8	1.1	8	0.46	Y	Y
77	Kannan	57	M	16.5	Y	420	5	2	Sensitive	Default	N	1	Unilateral	F	81	79	74.6	Normal	1.7	2	16	Normal	17.5	1.8	19	0.23	N	N
78	Ananthakumar	60	M	20.7	N	280	10	1	Sensitive	Complete	Y	3	Bilateral	F C	69.3	56.5	61.7	Mixed	3.5	4.2	75	Moderate	25.2	1.3	9	0.33	Y	Y
79	Sankaran	69	M	21	N	980	25	1	Sensitive	Complete	N	3	Bilateral	F	65	41	50.4	Mixed	2.7	2.7	34	Normal	15.7	2	15	0.24	N	N
80	Ramalakshmi	45	F	19	N	N	15	1	Sensitive	Default	N	1	Unilateral	F B	83.1	78.3	76.3	Normal	2.1	1.9	20	Normal	16.4	1.9	18	0.23	N	N
81	Thangavel	58	M	16.5	N	N	5	1	Sensitive	Default	N	1	Unilateral	F	26	22	66.2	Mixed	2.7	2.5	28	Normal	14.7	1.9	18	0.27	N	N
82	Ganapathy	66	M	14.3	N	868	20	1	Sensitive	Default	N	2	Unilateral	F	48	35	56.9	Mixed	3.5	3.8	62	Moderate	23.4	1.4	9.8	0.39	Y	Y
83	Arulmani	55	M	18.7	N	N	15	2	Sensitive	Default	N	1	Unilateral	F	85	80.7	73.1	Normal	2	1.8	17	Normal	16.4	1.8	13	0.25	N	N
84	Muthu	55	M	17.5	N	140	20	1	Sensitive	Default	N	2	Unilateral	F	54	56	83.9	Restriction	3.4	3.1	42	Mild	16.4	1.8	12	0.28	N	N
85	Karuppusamy	65	M	18.7	Y	N	15	1	Sensitive	Complete	N	1	Unilateral	F	62	53	72.7	Restriction	1.9	1.9	20	Normal	16.9	1.8	19	0.24	N	N
86	Kanammal	40	F	16.5	N	N	1	1	Sensitive	Complete	N	1	Unilateral	F	81.2	71.3	72.3	Normal	1.8	1.7	16	Normal	15.6	2	15	0.23	N	N
87	Pandarathi	35	F	20.1	N	N	1	1	Sensitive	Complete	N	2	Bilateral	F	70.5	72.7	86.5	Restriction	2.8	2.5	28	Normal	14.9	1.8	16	0.29	N	N
88	Sankarammal	47	F	18.5	N	N	3	1	Sensitive	Complete	N	3	Unilateral	F	64.1	67.7	85	Restriction	3.4	3.3	48	Mild	17.4	1.7	11	0.27	N	N
89	Thiraviyam	40	M	18.1	N	N	8	1	Sensitive	Complete	Y	2	Bilateral	B	21	16	62.7	Mixed	3.4	3.7	65	Moderate	29.1	1.3	8	0.42	Y	Y

Sl no	Name	Age	Sex	Bmi	Diabetes	Smoking index	PULMONARY TUBERCULOSIS HISTORY				Respiratory distress	RADIOLOGICAL FINDING			PFT				ECHOCARDIOGRAPHY								
							Time since 1st	No of Times	Sensitive/ Resistant	Outcome		Zones	Side	Lesion	FVC (% Pred)	FEV1(% Pred)	FEV1/FVC (%)	Result	Size of mpa	TRV	Spap	Severity	End diastolic dimension	Tapse	Tasv	Rvmpi	Iv septum bulge	Rv dysfunction
90	Murugan	66	M	15.4	N	1288	2	1	Sensitive	Default	Y	3	Unilateral	F	70.4	57.2	60.1	Mixed	3.5	4.5	84	Moderate	27.1	1.4	9	0.43	Y	Y
91	Chelladurai	40	M	16.9	N	840	10	1	Sensitive	Complete	N	3	Bilateral	F B	58.2	43.4	60.1	Mixed	3.4	3.1	41	Mild	22.4	1.6	9	0.33	Y	Y
92	Petchimuthu	42	M	14.9	N	N	17	1	Sensitive	Complete	N	4	Bilateral	B	58.8	50.1	68.3	Mixed	3.5	4.4	82	Moderate	28.3	1.3	8	0.44	Y	Y
93	Mariammal	52	F	17.8	N	N	4	2	Sensitive	Complete	N	3	Unilateral	F C	66.2	62.4	74.6	Restriction	3.4	3.4	50	Mild	17.2	1.9	13	0.24	N	N
94	Ramasubbu	56	M	21	N	300	15	1	Sensitive	Complete	Y	1	Unilateral	F	83	85	78.6	Normal	2.1	1.9	18	Normal	16.6	1.8	18	0.26	N	N
95	Murugan	47	M	18.3	N	N	2	1	Sensitive	Default	N	1	Unilateral	F	82.9	77.6	73.9	Normal	1.7	1.5	14	Normal	12.1	1.8	13	0.27	N	N
96	Arputhamani	64	F	17	N	N	2	1	Sensitive	Complete	N	1	Unilateral	B	89.3	63.2	54.1	Obstructio n	1.7	1.6	15	Normal	16.7	1.7	13	0.25	N	N
97	Sudalai	45	M	17.9	Y	1050	3	1	Resistant	Default	Y	2	Bilateral	F C	64	62	77.6	Restriction	3.4	3.4	49	Mild	17.6	1.8	11	0.29	N	N
98	Manikandan	47	M	19	N	200	3	1	Resistant	Complete	Y	2	Unilateral	F C	64.9	59.6	73.1	Restriction	2.2	2.1	21	Normal	16.2	2	18	0.26	N	N
99	Kumar	35	M	15.2	N	840	5	2	Sensitive	Default	Y	5	Bilateral	F C Bu	47.4	35.9	62.8	Mixed	3.5	4.9	101	Severe	34.5	1.1	7	0.54	Y	Y
100	Bhagavathi	65	F	23	N	N	10	1	Sensitive	Complete	N	1	Unilateral	A	82.6	83.9	77.5	Normal	2.2	1.5	13	Normal	13.9	2	15	0.26	N	N