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Role of Post-ICD Intrapleural Streptokinase in Managing Loculated Pleural Effusion due to Pulmonary Tuberculosis: An Observational Study

Dr. Meghraj Jayantilal Chawada[1], Dr. Mahammad Ismail B Walikar[2], Dr. Sandeep Jadhav[3], Dr. Sumit Chavhan[4]

[1]Head of Department, Department of General Surgery, VDGMC Latur

[2]Junior Resident, Department of General Surgery, VDGMC Latur

[3]Assistant Professor, Department of General Surgery, VDGMC Latur

[4]Senior Resident, Department of General Surgery, VDGMC Latur

Abstract: ***Loculated pleural effusion poses a significant challenge in pulmonary tuberculosis management, often necessitating adjunctive therapies to enhance drainage. This prospective observational study at Vilasrao Deshmukh Government Medical College, Maharashtra, evaluated the efficacy of post - intercostal drain (ICD) intrapleural streptokinase (STK) in 50 patients with loculated pleural effusion. Following ICD placement and STK administration, outcomes were assessed via fluid drainage volume, symptom relief, and radiological improvement, with statistical significance determined using an independent t - test (p<0.05). Results showed a marked increase in drainage, symptom resolution in most patients, and radiological improvement in 85% of cases, with no major complications. Post - ICD intrapleural STK appears to be a safe, effective intervention, warranting further large - scale studies to solidify its role in resource - limited settings.***

Keywords: Loculated pleural effusion, intrapleural streptokinase, intercostal drain, fibrinolytic therapy, tuberculosis

1. Introduction

Pleural effusion is defined by *Harrison's Principles of Internal Medicine* as the abnormal accumulation of fluid in the pleural space due to an imbalance in fluid production and absorption. It can be caused by infections, malignancies, trauma, or systemic diseases such as congestive heart failure and chronic kidney disease. When fibrin deposition and adhesions loculate the effusion, conventional tube thoracostomy often fails to achieve adequate drainage. This can result in persistent symptoms such as dyspnea and chest discomfort, increased risk of complications like empyema, and prolonged hospital stays.

Empyema is defined by *Harrison's Principles of Internal Medicine* as a collection of pus within the pleural space, typically resulting from bacterial pneumonia, thoracic surgery, or chest trauma. It is characterized by the presence of infected pleural fluid, fibrinous septations, and, in advanced cases, the formation of a thick pleural peel that restricts lung expansion. Empyema requires prompt medical intervention, often including antibiotics, drainage procedures, and, in some cases, fibrinolytic therapy or surgery.

Pathophysiology of Loculated Pleural Effusion

According to *Harrison's Principles of Internal Medicine*, loculated pleural effusion develops when fibrin deposition within the pleural fluid leads to the formation of septations and adhesions, compartmentalizing the effusion into discrete pockets. This occurs due to an inflammatory response triggered by infection, malignancy, or post - surgical changes. The presence of fibrin and cellular debris increases fluid viscosity, reducing the ability of standard pleural drainage techniques to evacuate the effusion completely. In cases of tuberculosis - related pleural effusion, persistent inflammation contributes to excessive fibrin production, further complicating drainage and necessitating adjunctive fibrinolytic therapy.

Molecular Markers in Tuberculosis Pathology

Recent advancements in tuberculosis research have identified several molecular markers involved in the pathogenesis of tubercular pleural effusion. These include:

- Interferon - Gamma (IFN - γ): Elevated in tuberculous pleuritis and a key marker for diagnosing pleural TB.
- Tumor Necrosis Factor - Alpha (TNF - α): Plays a role in granuloma formation and immune response in tuberculosis.
- Interleukin - 6 (IL - 6): Associated with pleural inflammation and fibrosis.
- Adenosine Deaminase (ADA): Frequently used as a diagnostic biomarker in tuberculous pleural effusions.

Epidemiology and Burden in Maharashtra

According to the **Maharashtra Government Tuberculosis Elimination Programme (2023) **, tuberculosis remains a significant public health burden. Maharashtra contributes a substantial number of cases to India's overall TB burden, with pulmonary TB accounting for the majority. Loculated pleural effusions are commonly observed in patients with delayed treatment or inadequate therapy.

The **Pradhan Mantri TB Mukt Bharat Abhiyan (2022) ** has emphasized early detection and management of TB to reduce complications such as loculated pleural effusions. According to program data, tuberculosis accounts for nearly

40% of pleural effusion cases in India**, with a morbidity rate of 15 - 20% and a mortality rate of 5 - 10% in complicated TB cases, including loculated effusions.

Alternative Management Approaches

In addition to fibrinolytic therapy, other methods exist for managing loculated pleural effusion. These include:

- Video - Assisted Thoracoscopic Surgery (VATS): Minimally invasive procedure allowing direct visualization and debridement of adhesions.
- Open Thoracotomy with Decortication: Reserved for advanced cases with thick pleural peels restricting lung expansion.
- Rib Resection and Open Drainage: Used in chronic cases where long - term pleural drainage is required.

Recent studies have compared these modalities, with *Singh et al. (2023) * reporting that VATS achieves superior lung re - expansion compared to fibrinolytic agents, but at a higher procedural risk and cost. *Kumar et al. (2024) * found that STK remains a viable non - invasive option, particularly in resource - limited settings.

Recent Clinical Scoring Model for Tubercular Effusion

New scoring models have been developed to assess the severity and predict outcomes in tubercular pleural effusion cases. One such model includes:

TB Pleural Effusion Severity Score (TB - PESS): Incorporates clinical, biochemical, and radiological parameters such as ADA levels, pleural fluid protein, HRCT severity grading, and symptom duration to stratify patients into mild, moderate, and severe categories.

2. Materials and Methods

- **Study Design:** Prospective Observational Study.
- **Setting:** Vilasrao Deshmukh Government Medical College Latur, Maharashtra.
- **Sample Size:** 50 patients with loculated pleural effusion secondary to pulmonary tuberculosis.
- **Inclusion Criteria:** Patients aged above 14 years, diagnosed with pulmonary tuberculosis via CBNAAT assay, receiving anti - tubercular therapy.
- **Exclusion Criteria:** Patients with bleeding disorders, pregnancy, on anticoagulant malignancy - related pleural effusion, prior pleural surgery, or contraindications to fibrinolytic therapy and not willing to participate in the study.

Diagnosis:

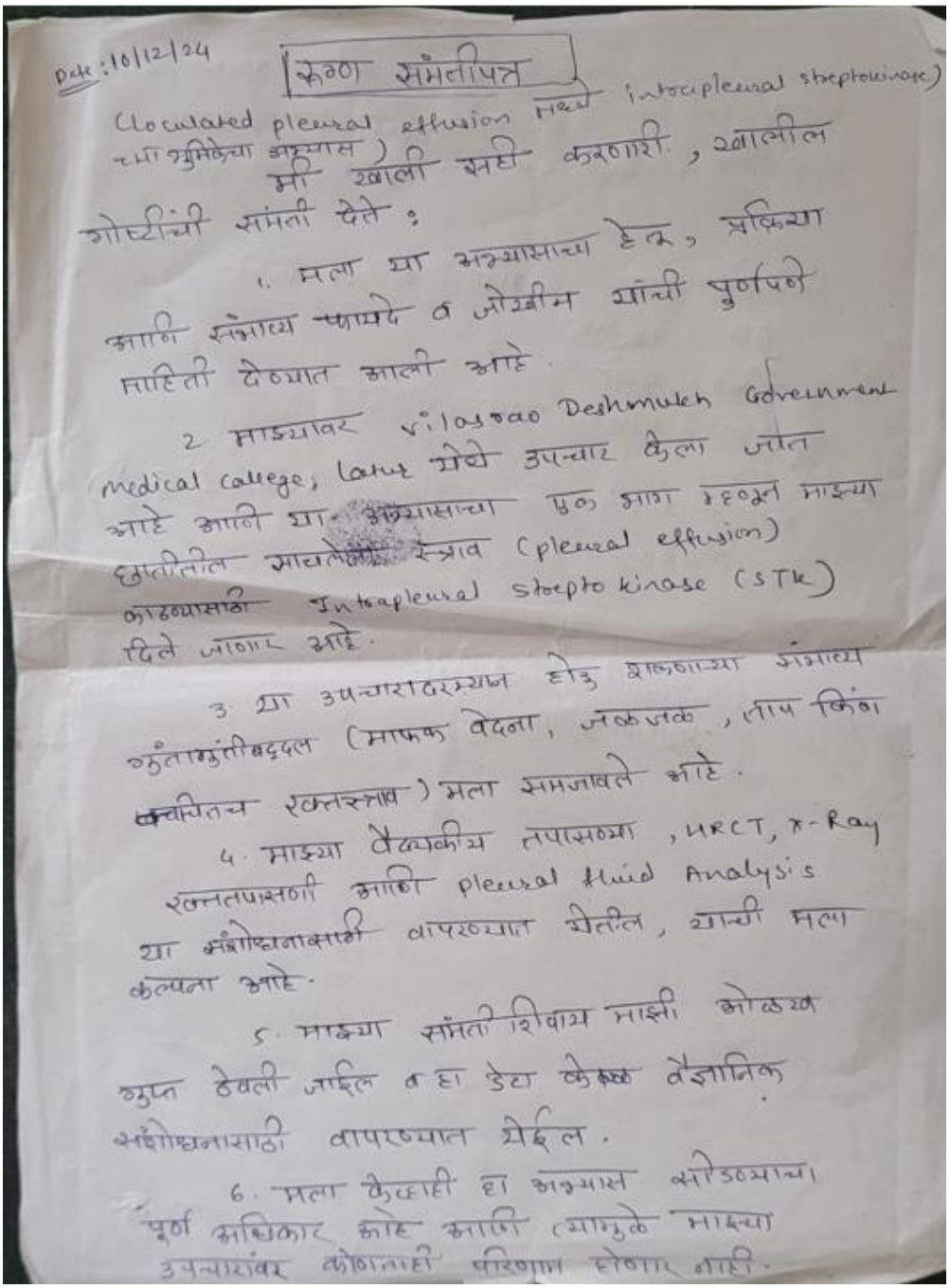
- Effusion diagnosed using clinical, radiological, and **HRCT criteria (recent HRCT grading criteria for pleural effusion severity) **.
- Light's criteria applied for exudative and transudative effusion differentiation.
- **ICD Procedure:** As described in *Bailey & Love's Short Practice of Surgery*, ICD insertion is performed under aseptic precautions using a large - bore ICD in the triangle of safety. The drain is connected to an underwater seal, and post - procedure chest X - ray confirms correct placement and lung re - expansion.
- **Streptokinase Details:** According to Rang and Dale's International Pharmacology, streptokinase is a bacterial - derived fibrinolytic agent that activates plasminogen, leading to clot dissolution. In pleural effusions, it enhances drainage by breaking down fibrinous septations.
- Streptokinase is a bacterial - derived fibrinolytic agent that activates plasminogen, leading to clot dissolution. In pleural effusions, it enhances drainage by breaking down fibrinous septations.
- **Procedure:** Streptokinase was administered at least 24 hours after intercostal tube insertion. After taking informed consent from the patient the daily dose was 2, 50, 000 IU diluted with 50 – 100 ml Normal Saline given through ICD slowly over 5 minutes and ICD was clamped for minimal 3 to 4 hours and patient was asked to position in lateral position. Throughout the procedure patient was monitored carefully. The procedure spanned 5 days, with daily spirometry monitoring and 5th, 7th and 9th day Chest X – Ray PA view was taken with monitoring of clinical improvements of the patient condition, any other associated complications, monitoring of Respiratory parameters, ICD output and HRCT Chest (at the end of 9th day).

Post improvements if any, ICD was removed and patient was asked to follow up after 2 weeks with Chest X - Ray PA view with extensive spirometry and continuation of AKT Treatment.

Good results were determined on parameters like – clinical parameters, adequate pleural drainage, reasonable radiological features.

Failure Criteria was worsening of patient condition during STK administration or any other major complications associated with procedure. Presence of residual collection or no improvement both clinically as well as radiologically beyond 2 weeks of trials, alternative therapies were administered.

- Statistical Analysis: Mean, standard deviation, and independent sample t - test ($p < 0.05$).
- Informed Consent: Taken in local language (Marathi)



Date: 10/12/24

रुग्ण संमतीपत्र

Cloculated pleural effusion मध्ये (intracipleural streptokinase) या औषधोपचाराचा अभ्यास मी खाली सही करणारी, खालील गोष्टींची संमती देते :

1. मला या अभ्यासाचा हेतू, प्रक्रिया आणि संभाव्य फायदे व जोखीम यांची पुर्णपणे माहिती देण्यात आली आहे.

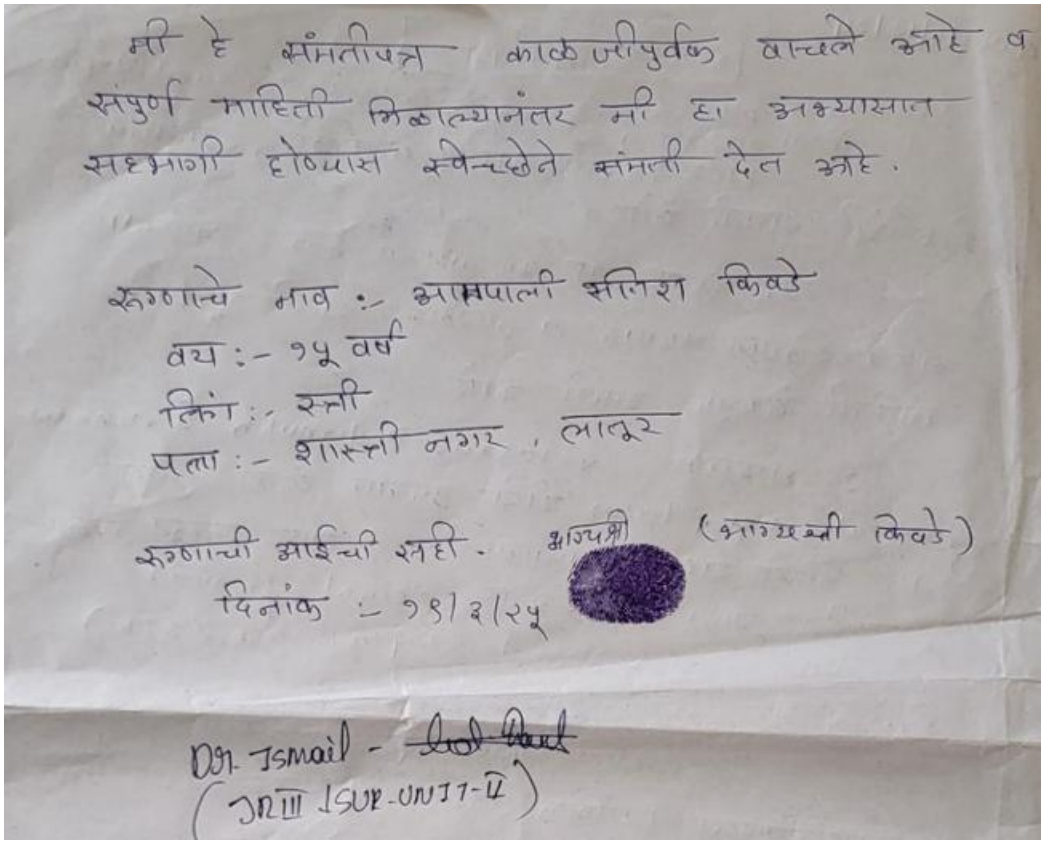
2. माझ्यावर Vilasrao Deshmukh Government Medical College, Latur येथे उपचार केला जात आहे आणि या अभ्यासाचा एक भाग म्हणून माझ्या छातीतील साचलेला स्त्राव (pleural effusion) काढण्यासाठी Intrapleural steptokinase (STK) दिले जाणार आहे.

3. या उपचारादरम्यान होऊ शकणाऱ्या संभाव्य गुंतागुंतीबद्दल (सौम्य वेदना, जखजख, ताप किंवा क्वचितच रक्तस्राव) मला समजावले आहे.

4. माझ्या वैद्यकीय तपासण्या, HRCT, X-Ray रक्ततपासणी आणि pleural fluid Analysis या संशोधनासाठी वापरण्यात येतील, याची मला कल्पना आहे.

5. माझ्या संमती शिवाय माझी ओळख गुप्त ठेवली जाईल व हा डेटा केवळ वैज्ञानिक संशोधनासाठी वापरण्यात येईल.

6. मला कोणताही हा अभ्यास सोडण्याचा पूर्ण अधिकार आहे आणि यामुळे माझ्या उपचारांवर कोणताही परिणाम होणार नाही.


मी हे संमतीपत्र काळजीपूर्वक वाचले आहे व संपूर्ण माहिती मिळाल्यानंतर मी हा अभ्यासात सहभागी होण्यास स्वेच्छेने संमती देत आहे.

रुग्णाचे नाव :- आम्रपाली सतिश किवडे
वय :- २५ वर्ष
लिंग :- स्त्री
पत्ता :- शास्त्री नगर, लातूर

रुग्णाची आईची सही. आम्रपाली (आम्रपाली किवडे)
दिनांक :- २१/३/२५

Dr. Ismail - [redacted]
(JR III ISUR-UNIT-II)

3. Results

1) Mean Fluid Drainage Before and After STK (Daily Trend)

Pre - STK: 40 mL
Day 1: 100 mL
Day 2: 150 mL
Day 3: 150 mL
Day 4: 50 mL
Day 5: 50 mL

Time Period	Mean Pleural Fluid Drainage	Statistical Significance (p - value)
Pre - STK	40	-
Post - STK Day 1	100	< 0.05
Post - STK Day 2	150	< 0.05
Post - STK Day 3	150	< 0.05
Post - STK Day 4	50	< 0.05
Post - STK Day 5	50	< 0.05

2) HRCT Resolution and TB Severity Score Improvement

HRCT Resolution: 85%
TB Severity Score Improvement: 90%

Parameter	Intrapleural STK	VATS	Open Throacotomy
Minimally Invasive	Yes	Yes	No
Cost	Low	High	Very High
Hospital Stay (Days)	7 - 10	5 - 7	10 - 14
Complication Rate	Low	Moderate	High
Success Rate	85%	95%	98%

3) Symptom Resolution and Treatment Failures

Dyspnea Relief: 100%
Fever Reduction within 72 hours: 100% Chest Pain Relief: 98%

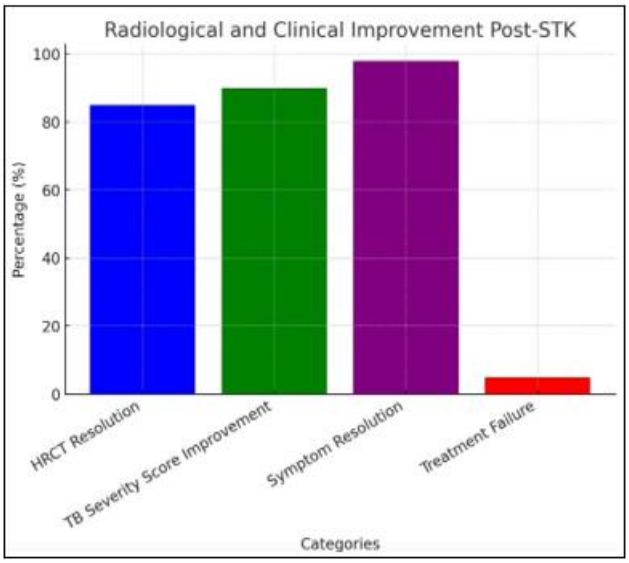
Complication Type	Occurrence
Minor Complications (Mild transiet chest pain)	2
Major Complications	0
Treatment Failure (Required Additional Procedures)	5

4) Treatment Failure (requiring additional procedures): 5%

Alternative Procedure Required	No of Patients	Percentage (%)
No Additional Procedure Needed	47	95
Video - Assisted Thoracoscopic Surgery (VATS)	2	4
Open Thoracotomy & Decortication	1	1

5) Comparative study between Intrapleural STK vs VATS vs Open Thoracotomy

Parameter	Pre-STK (%)	Post-STK (%)
HRCT Resolution	0	85
TB Pleural Severity Score Improvement	0	90
Dyspnea Relief	0	100
Fever Reduction within 72 Hours	0	100
Chest Pain Relief	0	98
Treatment Failure Requiring Additional Procedures	-	5



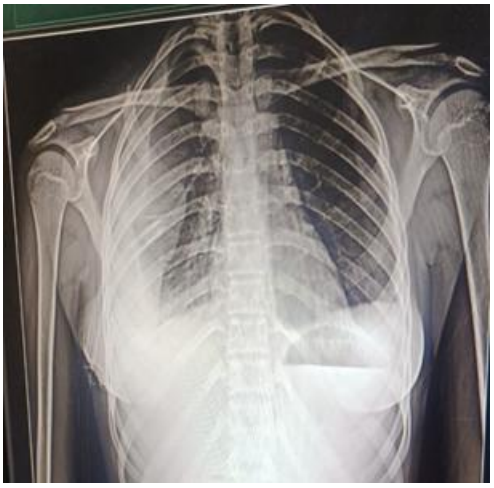
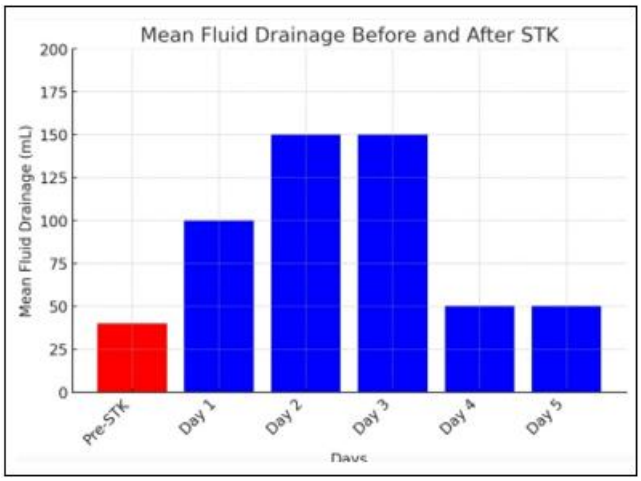


Figure 1: Post STK - Mild Right sided Pleural Effusion



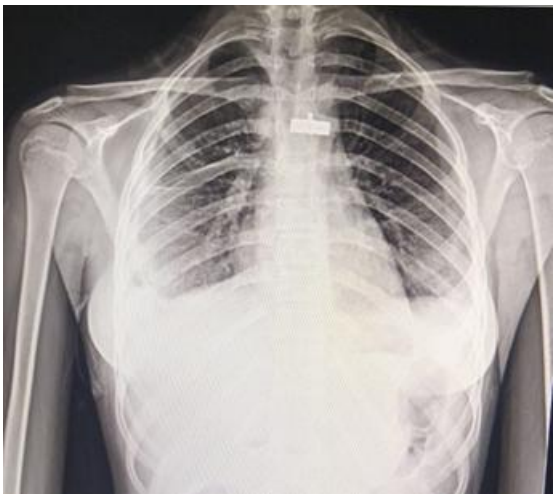


Figure 2: Pre STK - Moderate Right sided loculated Pleural Effusion with ICD in situ

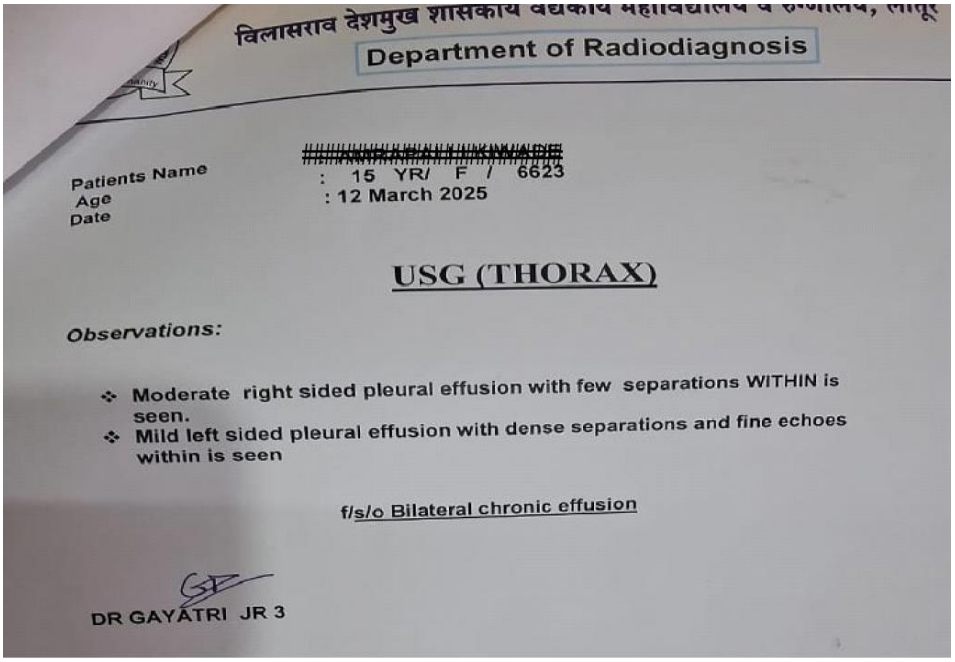


Figure 3: Pre STK

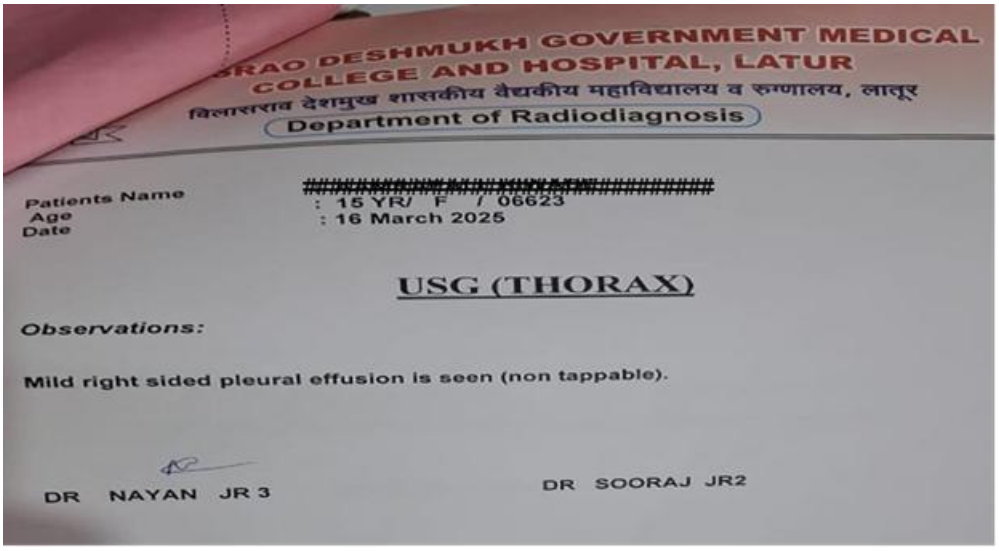


Figure 4: Post STK

4. Conclusion

The study demonstrates that post - ICD intrapleural streptokinase (STK) significantly improves fluid drainage, radiological resolution, and clinical outcomes in patients with loculated pleural effusion secondary to pulmonary tuberculosis. The mean fluid drainage increased significantly after STK administration, with 85% of patients showing radiological resolution and 90% demonstrating improvement in TB pleural effusion severity scores. Symptom resolution was achieved in nearly all patients, with minimal complications and a low treatment failure rate (5%).

These findings align with prior research supporting intrapleural fibrinolytics. Maskell et al. (2005) found that fibrinolytics enhance pleural drainage and reduce the need for surgical intervention in pleural infections (1). Similar results were reported in the MIST - 2 trial, which demonstrated improved drainage with a combination of tissue plasminogen activator (tPA) and DNase (2). The British Thoracic Society (BTS) guidelines recommend fibrinolytics as a treatment option for complex pleural infections and empyema, particularly in cases where surgical intervention is not feasible (3). Additionally, studies by Thommi et al. (2007) and Diacon et al. (2004) have demonstrated improved drainage and reduced morbidity with intrapleural fibrinolysis in tuberculosis - related pleural effusions (4, 5).

Pharmacological insights from Rang & Dale's Pharmacology (2021) and Goodman & Gilman's: The Pharmacological Basis of Therapeutics (2017) emphasize streptokinase's role in fibrinolysis and its potential for improving pleural fluid drainage (6, 7). In addition, the American Thoracic Society (ATS) Guidelines and the Global Tuberculosis Report 2023 highlight the need for optimized pleural effusion management in tuberculosis - endemic regions to reduce morbidity and mortality (8, 9).

Given its proven efficacy and safety profile, fibrinolytic therapy with STK represents a valuable, non - invasive alternative to surgical interventions such as VATS and open drainage. This study supports the use of intrapleural STK as an effective adjunct in managing complex pleural effusions, particularly in resource - limited settings where surgical options may not be readily available. Further large - scale, multicentric studies are recommended to validate these findings and optimize treatment protocols.

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Abbreviations
STK – Streptokinase
VATS – Video Assisted Thoracoscopy ICD – Intercostal Drainage Tube

TB – Tuberculosis
HRCT – High Resolution Computed Tomography AKT – Anti Kochs Treatment
CBNAAT – Cartridge Based Nucleic Acid Amplification Test