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Research Article

Acute Respiratory Deterioration in Post-Tuberculosis Lung Disease: Differential Diagnosis, Clinical Assessment, and Management in High-Burden Settings

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ABSTRACT

Background: Post-tuberculosis lung disease (PTLD) encompasses persistent respiratory symptoms, structural lung abnormalities, and functional impairment after TB treatment. Survivors may experience episodes of acute respiratory deterioration, but the cause cannot safely be inferred from a history of TB or from residual radiographic abnormalities alone. Recurrent TB, bacterial infection, bronchiectasis exacerbation, chronic pulmonary aspergillosis, airflow obstruction, pulmonary vascular disease, and non-respiratory conditions may present with overlapping symptoms. **Objective:** To outline a clinically oriented approach to recognising acute deterioration in people with prior pulmonary TB, prioritising urgent triage, differential diagnosis, targeted investigations, and follow-up after the acute episode. **Approach:** This narrative review synthesises selected PTLD standards, recent reviews, and clinical concepts relevant to post-TB respiratory care. The search for this working draft was not systematic and does not support claims of exhaustive evidence coverage. The proposed framework is intended to structure clinical reasoning, not replace local protocols or specialist assessment. **Clinical framework:** Initial assessment should identify physiological instability and red flags, establish the tempo and nature of symptoms, compare current status with baseline, and investigate active TB or other treatable conditions when indicated. Investigations should be guided by presentation and available resources, and may include oxygen saturation, chest imaging, sputum testing for TB and bacterial pathogens, blood tests, and targeted evaluation for fungal disease, pulmonary embolism, cardiac disease, or other diagnoses. Management should target the identified cause, with antimicrobial stewardship and appropriate escalation. A documented post-episode review can reassess lung function, inhaled treatment, airway clearance, rehabilitation needs, and recurrence risk. **Conclusion:** Acute deterioration in a TB survivor requires a structured, safety-focused assessment rather than automatic attribution to chronic sequelae. A practical pathway should protect against delayed recognition of recurrent TB and other serious conditions while supporting appropriate treatment and continuity of post-TB care.

KEYWORDS: Post-tuberculosis lung disease; acute respiratory deterioration; recurrent tuberculosis; bronchiectasis; chronic pulmonary aspergillosis; differential diagnosis; high-burden settings.

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1. INTRODUCTION

Successful TB treatment does not guarantee complete recovery of lung structure or function. Post-TB sequelae may include bronchiectasis, fibrosis, residual cavities, pleural thickening, airflow obstruction, reduced exercise tolerance, and chronic respiratory symptoms.[1,2] Some survivors remain clinically stable, while others experience episodic worsening that leads to emergency visits, hospitalisation, repeated antibiotic exposure, or renewed TB investigations.

An acute episode in a TB survivor is not itself a diagnosis. New or worsening cough, sputum, breathlessness, fever, chest pain, haemoptysis, hypoxaemia, or systemic symptoms can arise from several overlapping causes. Recurrent or persistent TB must remain in the differential when clinically appropriate, but other causes—including bacterial infection, bronchiectasis exacerbation, chronic pulmonary aspergillosis (CPA), COPD/asthma, pulmonary embolism, heart failure, and malignancy—may be missed if the history of TB dominates clinical reasoning.

Recent mapping of the PTLD literature and guidance has identified less consistent operational guidance for acute-on-chronic complications than for routine assessment and rehabilitation.[3] This creates a rationale for a focused clinical framework, while recognising that the current evidence base is heterogeneous and that the framework proposed here requires prospective validation.

2. Review approach and scope

This is a narrative clinical review intended to organise clinical reasoning for high-burden settings. The current draft draws on selected international PTLD standards and recent reviews identified during preliminary searching. It does not claim a systematic search, comprehensive study selection, or formal risk-of-bias assessment. Before submission, the authors should document database-specific search strings and dates, expand the primary-study evidence base, and verify all references and management recommendations against current guidelines.

The review focuses on acute or subacute respiratory deterioration in people with previously treated pulmonary TB. It does not define a single validated PTLD exacerbation syndrome, nor does it propose one universal diagnostic panel or treatment regimen.

3. Establishing severity before establishing cause

The first task is to determine whether the patient is physiologically unstable. Assessment should include respiratory rate, work of breathing, oxygen saturation where available, pulse, blood pressure, mental status, temperature, and ability to speak or mobilise. Compare findings with the person’s known baseline, especially when chronic hypoxaemia or severe functional limitation is present.

Urgent assessment or emergency referral is warranted for severe or rapidly worsening breathlessness, cyanosis or significant hypoxaemia, altered consciousness, haemodynamic instability, major haemoptysis, suspected pulmonary embolism, severe chest pain, or signs of sepsis. In settings with limited diagnostics, clinical instability should trigger escalation rather than delay while awaiting routine tests.

Haemoptysis deserves particular attention. Potential causes include active TB, bronchiectasis, CPA, malignancy, and vascular complications of chronic cavitary disease. The amount, rate, physiological effect, and recurrence of bleeding determine urgency; any substantial or ongoing bleeding requires urgent evaluation.[4]

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4. Differential diagnosis

Potential cause	Clues that may raise suspicion	Diagnostic considerations
Recurrent or persistent TB	New or progressive cough, fever, night sweats, weight loss, haemoptysis, new radiographic change, exposure risk	Follow current national algorithms; obtain sputum molecular testing and additional microbiology as indicated. Prior treatment or residual imaging does not exclude active disease.
Bacterial respiratory infection	Acute change in sputum volume or purulence, fever, focal chest findings, systemic illness	Sputum culture where feasible, chest imaging and severity assessment; interpret colonisation cautiously in bronchiectasis.
Bronchiectasis exacerbation	Increased cough, sputum volume/purulence, breathlessness, fatigue or haemoptysis relative to baseline	Compare with usual symptoms; sputum culture where feasible; assess severity and airway-clearance needs.
Chronic pulmonary aspergillosis	Chronic symptoms, weight loss, persistent or recurrent haemoptysis, cavities or progressive radiographic change	Consider chest CT and Aspergillus-specific IgG or other locally available tests in an appropriate clinical context; exclude active TB and alternative causes.
COPD or asthma exacerbation	Wheeze, chest tightness, increased dyspnoea, known obstructive disease or relevant exposure	Assess oxygenation and severity; review inhaler technique and prior diagnosis. Spirometry is generally performed when clinically stable if diagnosis is uncertain.
Pneumonia or other acute lung disease	Fever, hypoxaemia, focal findings, acute imaging changes	Chest radiography and investigations guided by severity; consider local epidemiology and immunocompromise.
Pulmonary embolism	Sudden dyspnoea, pleuritic pain, unexplained hypoxaemia, syncope or thromboembolic risk	Use validated clinical assessment and appropriate urgent imaging/testing where available.
Cardiac disease, anaemia, other causes	Orthopnoea, oedema, palpitations, pallor, fatigue out of proportion to respiratory findings	Investigate based on examination and history; avoid assuming all breathlessness is pulmonary.

5. Clinical history and examination

5.1 Define the change from baseline

Record onset, duration, progression, fever, sputum volume and character, haemoptysis, chest pain, breathlessness at rest or on exertion, exercise tolerance, sleep disturbance, and systemic symptoms. Ask what has changed compared with the person's usual state. Review prior TB episodes, treatment completion, drug-resistance history, previous microbiology, imaging, hospital admissions, and known residual lung disease.[5]

5.2 Identify risk modifiers

Relevant factors include smoking and second-hand smoke, biomass-fuel exposure, occupational dust or silica exposure, diabetes, HIV or other immunosuppression, undernutrition, chronic kidney disease, cardiovascular disease, and medication use. Clarify recent antibiotic exposure, allergies, prior sputum microbiology, inhaler use, and possible treatment adverse effects.

5.3 Examine for alternative explanations

Look for respiratory distress, focal crackles, wheeze, signs of consolidation, clubbing, cyanosis, oedema, raised jugular venous pressure, calf asymmetry, pallor, and signs of dehydration or malnutrition. Examination findings are not sufficiently specific to distinguish all causes, so the differential should guide targeted investigations.

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6. Investigations: targeted rather than indiscriminate

Testing should be proportionate to severity, clinical suspicion, local availability, and the consequences of missing a diagnosis. A chest radiograph can identify new consolidation, pneumothorax, or changes in chronic abnormalities, but comparison with prior images is often essential. CT is not required for every episode; it may be appropriate when complications, CPA, malignancy, pulmonary embolism, or unexplained deterioration are suspected.

When recurrent or persistent TB is possible, collect appropriate respiratory specimens and follow current national diagnostic algorithms. A negative result from a single test should be interpreted in context, particularly where clinical suspicion remains high. Sputum bacterial culture may inform treatment in bronchiectasis or severe infection where available. Blood tests, electrocardiography, blood gas analysis, echocardiography, fungal investigations, or vascular imaging should be selected according to the differential and severity.

Once the acute episode has stabilised, spirometry and other functional testing can help characterise persistent impairment. Performing spirometry during severe acute illness may be inappropriate or yield results that do not reflect baseline function. The timing should be guided by clinical recovery and local protocols.

7. Management principles

Treatment should target the most likely or confirmed cause, while avoiding diagnostic anchoring. Suspected active TB requires prompt investigation and management according to current national guidance; empiric treatment decisions must consider severity, test availability, resistance risk, and specialist advice. Antibiotics for bacterial infection should follow local guidance and be informed by microbiology when feasible. Bronchiectasis management may include airway-clearance techniques, hydration advice, treatment of identified infection, and review of underlying causes.

Bronchodilators and inhaled corticosteroids should be used for appropriate indications rather than prescribed solely because a patient has a history of TB. CPA requires specialist-informed diagnosis and management because radiographic and symptom overlap with TB is substantial and antifungal therapy has important monitoring and interaction considerations. Suspected pulmonary embolism, major haemoptysis, severe hypoxaemia, sepsis, or acute cardiac disease requires urgent condition-specific management.

Antimicrobial stewardship is important. Repeated empiric antibiotics or anti-TB treatment without adequate reassessment can delay the correct diagnosis and increase adverse effects. Where diagnostic capacity is limited, referral and a documented safety-net plan are essential when symptoms persist, worsen, or recur.

8. After the acute episode: prevent the next avoidable deterioration

Discharge or outpatient review should include a documented diagnosis or working differential, investigations pending, medication plan, warning signs, and a clear follow-up appointment. Recurrent episodes should trigger reassessment of the underlying phenotype rather than repeated treatment of symptoms alone. Review smoking and occupational exposures, inhaler technique where relevant, vaccination according to current national recommendations, nutrition, physical activity, and comorbidities.

Patients with persistent breathlessness or functional limitation may benefit from pulmonary rehabilitation after clinical stabilisation and appropriate assessment. People with chronic sputum production may need airway-clearance education

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and specialist review. Rehabilitation should complement, not substitute for, investigation of ongoing infection, CPA, or other treatable disease.[5]

9. Proposed practical pathway

Step	Action
1. Triage	Assess physiological stability and red flags; escalate immediately when indicated.
2. Compare with baseline	Define symptom onset and change in sputum, breathlessness, function, fever, haemoptysis, and oxygenation.
3. Build differential	Consider recurrent TB, bacterial infection, bronchiectasis, CPA, obstructive disease, and non-respiratory causes.
4. Investigate selectively	Use imaging, TB microbiology, bacterial cultures, blood tests, and specialist investigations according to clinical suspicion.
5. Treat the cause	Follow current condition-specific guidelines; avoid repeated empiric therapy without reassessment.
6. Close the loop	Arrange follow-up, review pending results, provide safety-net advice, and reassess chronic lung-health needs after recovery.

10. Implementation considerations in high-burden settings

Where CT, spirometry, microbiology, and respiratory specialists are not readily available, a tiered pathway can still improve safety if it prioritises triage, appropriate TB testing, access to chest radiography, reliable referral, and follow-up of pending results. A minimum documentation tool could record baseline symptoms, acute changes, red flags, investigations requested, working diagnosis, treatment, and the follow-up plan.

Implementation research should assess time to appropriate evaluation, the proportion of suspected recurrent TB cases investigated, referral completion, avoidable antibiotic or anti-TB treatment, emergency admissions, patient costs, and equity of access. These indicators should be piloted and refined with clinicians, TB programme teams, respiratory services, and TB survivors before routine adoption.

11. Evidence gaps and research priorities

Key gaps include the absence of a universally accepted definition of acute PTLD exacerbation; limited prospective data on causes and incidence of acute deterioration after TB; uncertain diagnostic performance of symptom-based pathways; and limited evidence on cost-effective test combinations in low-resource settings. Research should distinguish acute infection from chronic structural disease and should include patient-reported outcomes, recurrence, hospitalisation, antimicrobial exposure, and function after recovery.

Prospective multicentre cohorts could characterise episodes and diagnostic outcomes. Pragmatic implementation studies could compare usual care with a structured triage-and-follow-up pathway. Studies should prespecify definitions, include relevant comorbidities and exposure histories, and report missing data and loss to follow-up.

12. Limitations

This manuscript is a preliminary narrative review. The literature search is not systematic, no formal risk-of-bias appraisal has been conducted, and the proposed pathway has not been prospectively validated. It should not be used as a stand-alone clinical protocol. Before journal submission, the authors should update the search, add primary studies and current official guidance, verify all references, and ensure that recommendations are consistent with local emergency, TB, antimicrobial, and respiratory-care protocols.

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13. CONCLUSION

Acute respiratory deterioration in a person previously treated for TB is a clinical event requiring fresh assessment, not a diagnosis of PTLD exacerbation by default. Early severity assessment, a structured differential diagnosis, targeted investigation for recurrent TB and other treatable causes, appropriate treatment, and a documented follow-up plan can reduce diagnostic anchoring and fragmented care. A focused pathway should be validated in real-world high-burden settings before it is recommended for broad implementation.

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