**Case Report**

# Management of Pulmonary Tuberculosis in Patient with Schizophrenia

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***Abstract***

*Schizophrenia affects human cognition, emotion, perception, and other psychosocial skills which is prone to medical noncompliance. Medication adherence or compliance of people with schizophrenia will not be achieved without a shared understanding between professionals, carers and patients regarding medication efficacy, insight, side effects, medication attitudes, and external factors. Recent study found that 32.8% of tuberculosis patients in Indonesia were also managed for psychotic disorders. Furthermore, the treatment coverage of tuberculosis in Aceh Province in 2022 was far below the national average (74,7%), which only reached 52,6%. Rifampicin, a potent anti-tubercular agent, is known to significantly induce several CYP enzymes. As a result, rifampicin may accelerate metabolism of other drugs, in this case antipsychotics, leading to reduced plasma concentrations and potentially diminishing their therapeutic effects. This article reported a case of newly diagnosed pulmonary tuberculosis of a 41-year-old male with schizophrenia in primary healthcare.*
***Keywords:*** *pulmonary tuberculosis, schizophrenia, drug interactions, medications adherence, case report.*

# Penatalaksanaan Tuberkulosis Paru pada Pasien Skizofrenia

***Abstrak***

*Skizofrenia mempengaruhi tingkat kognitif, emosi, persepsi, serta keterampilan psikososial lainnya, yang membuat penderita rentan terhadap ketidakpatuhan pengobatan. Kepatuhan pengobatan pada pasien skizofrenia tidak dapat tercapai tanpa adanya kerjasama antara tenaga medis, pengasuh, dan pasien terkait pemahaman berbagai macam aspek seperti efektivitas pengobatan, wawasan tentang kondisi klinis, efek samping, sikap terhadap pengobatan, dan faktor eksternal. Sebuah penelitian menemukan bahwa 32,8% pasien tuberkulosis di Indonesia juga mendapatkan pengobatan antipsikotik. Selain itu, cakupan pengobatan tuberkulosis di Provinsi Aceh pada tahun 2022 masih jauh di bawah rata-rata nasional (74,7%), hanya mencapai 52,6%. Rifampisin, agen anti-tuberkulosis yang kuat, diketahui dapat menginduksi beberapa enzim CYP secara signifikan. Akibatnya, rifampisin dapat mempercepat metabolisme obat lain, termasuk antipsikotik, sehingga dapat mengurangi konsentrasi plasma dan berpotensi menurunkan efektivitas terapeutiknya. Artikel ini melaporkan kasus seorang pria berusia 41 tahun dengan skizofrenia yang baru didiagnosis dengan tuberkulosis paru di fasilitas kesehatan primer.*
***Kata kunci:*** *tuberculosis paru, skizofrenia, interaksi obat, kepatuhan berobat, laporan kasus.*

## Introduction

Schizophrenia affects human cognition, emotion, perception, and other psychosocial skills which is prone to medical noncompliance.[1,2] Drug factors, patient's insight, marital status, education level, life satisfaction, and comorbidities have been known to associate with medication adherence of people with schizophrenia.[3–5] Medication adherence or compliance of people with schizophrenia will not be achieved without a shared understanding between professionals, carers and patients: medication efficacy, insight, side effects, medication attitudes, and external factors.[6] Recent study showed that medication compliance in schizophrenic patients commonly worsened in a year, urging routine follow up.[7] Comorbidity and multitherapy is likely to cause further medication noncompliance.

Tuberculosis infection remains an unfinished agenda in Indonesia.[8] Despite tuberculosis challenging therapeutic regimen, the risk of transmission is increased in schizophrenic patients due to multiple factors.[9] Recent study found that 32.8% of tuberculosis patients in Indonesia were also managed for psychotic disorders.[10] Furthermore, the treatment coverage of tuberculosis in Aceh Province in 2022 only reached 52,6%, which was far below the national average (74,7%).[11]

Pharmacokinetic interactions between atypical antipsychotics and anti-infective agents predominantly arise through the modulation of drug-metabolizing enzymes, most notably the hepatic cytochrome P450 (CYP) system, uridine diphosphate glucuronosyltransferase (UGT) system, and drug transporters such as P-glycoprotein (P-gp).[12] Rifampicin, a potent anti-tubercular agent, is known to significantly induce several CYP enzymes. As a result, rifampicin may accelerate metabolism of other drugs, in this case antipsychotics, leading to reduced plasma concentrations and potentially diminishing their therapeutic effects, which might cause an acute episode of psychosis.[13,14] Therefore, tuberculosis detection and medication supervision in patients with psychotic disorders is highly crucial to be implemented, especially in Aceh. This article reported a case of newly diagnosed pulmonary tuberculosis infection in a patient with chronic schizophrenia in limited clinical settings.

## Case Description

A 41-year-old male with schizophrenia in primary healthcare was referred to a pulmonologist after his family complained that the patient almost always refused to eat for a month straight. Family also stated that he appeared less enthusiastic than usual, occasional cough and noticeable weight loss were seen. Symptoms of fever, difficulty of breathing, chest pain, palpitations, vomiting, nausea, and diarrhea were denied. There was no record of prior interactions with tuberculosis and HIV patients. History of similar complaints and previous TB medications were also denied. There was no familial history of tuberculosis, HIV, and malignancy. The patient works as a farmer, with a smoking habit of 12 cigarettes per day for more than 20 years. Exposure to other kinds of fumes was unclear. The patient was diagnosed with paranoid schizophrenia in 2009 with current medications of risperidone 2 mg /12 hours and THP 1 mg daily. The last acute episode was in 2023.

The patient was stable, with blood pressure of 90/60 mmHg, heart rate of 95 bpm, respiratory rate of 20 times per minute, body temperature of 37.3$^{o}$C, and body mass index (BMI) of 14.4 kg/m2 (underweight). On physical examination, there was bronchovesicular breathing sound accompanied by high-pitched rhonchi predominantly on the apex of both lungs, regular heart sounds were distinctly heard on the patient's right chest. Patient was referred to a referral hospital for pulmonologist consultation and diagnostic tests. Patient's chest x-ray was suggestive of active pulmonary tuberculosis (Figure 1). Patient's chest x-ray shows atelectasis and multicavity of the right lung, indicating destroyed lung. Calcification, pleural thickening and infiltrates were also found on both lungs, suggestive of re-activation of pulmonary tuberculosis (Figure 1).

Patient's collapsed right lung causes tracheal and heart shift toward the ipsilateral side, resulting in right-sided heart sounds. Patient was not cooperative thus sputum GeneXpert examination could not be performed.

Fixed-dose combination (FDC) therapy for rifampicin sensitive pulmonary tuberculosis consisting of 150 mg rifampicin, 75 mg isoniazid, 400 mg pyrazinamide, and 275 mg of ethambutol were initiated and maintained until 2 months of therapy. Patient was given mucolytic, proton-pump inhibitor, and supplementary vitamins to reduce symptoms and improve his appetite. Patient's schizophrenia medications were maintained, there were no signs of side effects observed after two weeks of anti tuberculosis medications. The patient was advised to undergo a routine follow up to respective pulmonologist and psychiatrist in charge for any effect of drug interactions.

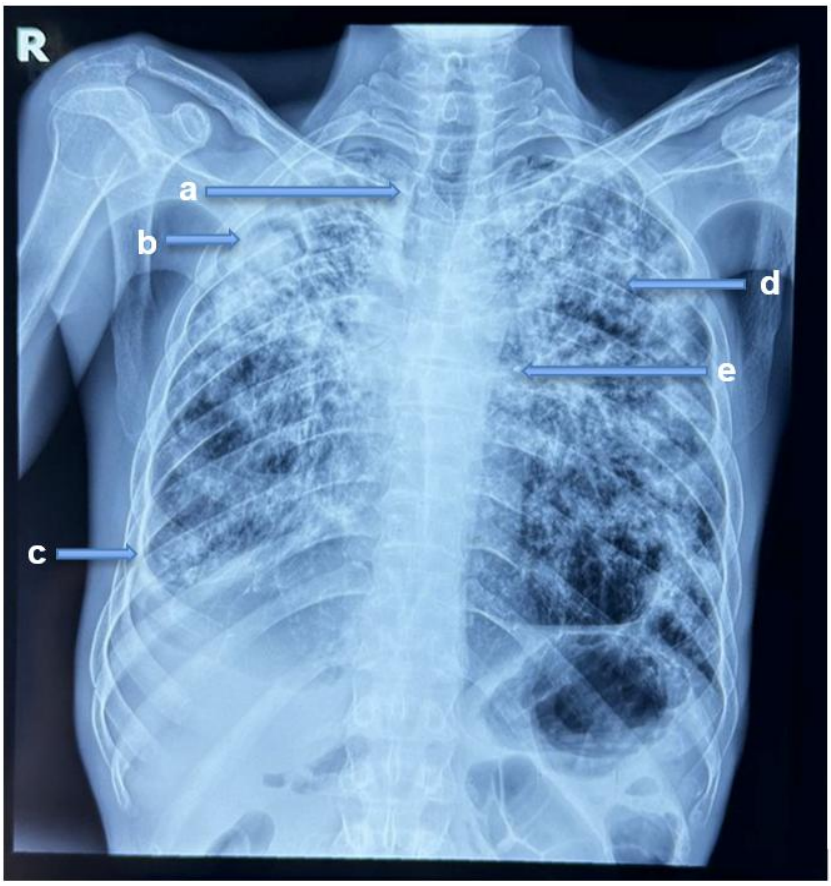


**Figure 1. Patient's chest x-ray result: a) Shifting of trachea into ipsilateral side, b) Multicavity, c) Pleuralthickening, d) Fibrosis, e) Calcification**

## Discussion

Pulmonary tuberculosis (TB) is still prevalent especially in developing countries, and individuals with schizophrenia are at a higher risk of this infection compared to the general population.[15] Schizophrenic patients with tuberculosis should be managed comprehensively as it requires complex management strategy. Recovery of pulmonary

tuberculosis depends on completing 6-months anti tuberculosis regimen treatment and requires internal motivation and cognitive function from the patients and surrounding family. However, individuals with schizophrenia often face cognitive and behavioral challenges that hinder medication adherence, increasing the risk of treatment failure.[4,16,17] Destroyed lung syndrome (DLS) is a condition of extensive lung damage, commonly consists of atelectasis, multiple cavities, and parenchymal lung fibrosis in radiological examination.[18,19] This often happened as a result of chronic or recurrent lung infections, particularly TB. This syndrome typically manifests after inadequate or irregular treatment of TB. Individuals with destroyed lung can be asymptomatic initially. However, they may gradually experience various issues such as breathing difficulty and frequent lung infections.[18] In patients with psychotic disorders, impaired cognition and poor self-care might cause them to be unaware of past or ongoing TB infection.[20] In these cases, antipsychotics offer protective factors for medication adherence to patients in completing their anti tuberculosis regimen, along with full support from caregivers.[21]

Atypical antipsychotics, such as clozapine and olanzapine, are primarily metabolized via CYP1A2, while aripiprazole, brexpiprazole, iloperidone, and risperidone are predominantly processed by CYP2D6, with secondary contributions from CYP3A4.[12] Rifampicin, a potent anti-tubercular agent, is known to greatly increase the activity of several CYP enzymes, including CYP1A2, CYP3A4, CYP2B, CYP2C, and CYP2D6, along with P-glycoprotein (P-gp).[13,14,22] A previous randomized study showed that the area under the concentration-time curve (AUC) for risperidone reduces by 43-51% in patients co-treated with rifampicin compared to those receiving risperidone alone, which may lead to antipsychotic treatment failure.[14,22,23] Generally, enzyme induction by rifampicin often takes 2-3 weeks to fully develop after initiation, and may persist up to 2 weeks after discontinuation.[24,25] However, despite these interactions, clinically significant effects of rifampicin on clozapine (antipsychotic) are generally observed in only a small number of patients. These effects depend on various individual factors such as genetics, overall health, age, nutrition, and the use of other medications.[15,26]

Attending physician must closely monitor patients who are on both antipsychotic and anti-infective regiments. Treatment strategy can be optimised by: 1. routine follow-up, and 2. establishing committed treatment goals with the patient, family, and care providers. Regular assessment of patient's condition is essential to maintain continuity of care. In a more advanced settings, therapeutic drug monitoring (TDM) can be used as a tool to assess drug interactions and treatment efficacy by measuring blood drug concentration at given time. The result can be used as a guide for dose adjustments to prevent psychotic relapse and other adverse outcomes. To achieve treatment success, medication compliance should be encouraged by requiring support from caregiver and family, as family knowledge has been found to increase schizophrenia patients' adherence to medication on top of another risk factors (problem behavior, low income, low education level, low life satisfaction, female, and old age (>50 years)).[3,27] Adequate information regarding treatment and follow-up guidelines of schizophrenia and national TB program from health care providers is also critical for successful outcome.

Up to two weeks after the administration of anti tuberculosis medications, there have been no complaints regarding patient's current psychological conditions yet. However, this case report was made to emphasize the importance of integrated TB-Schizophrenia management in limited settings as anti tuberculosis can impact the efficacy of psychiatric medications. It also highlights the recommendation for stakeholders to provide routine screening and tracing to control tuberculosis transmission in patients with mental illness such as schizophrenia, given the non-negligible prevalence

of tuberculosis among schizophrenia patients and the current poor TB treatment coverage especially in Aceh.[9,23] To ensure successful treatment outcomes, a comprehensive strategy focusing on regular follow-ups, family involvement, and medication adherence should be employed. Patient compliance is critical, and educating caregivers and family members can greatly improve adherence rates. Furthermore, clinicians must be aware of other risk factors for non-adherence, such as age, socioeconomic status, and disease-related factors, and work to address these challenges.

## Conclusion

In conclusion, this case report highlights the need for comprehensive TB-Schizophrenia management in resource-limited settings as it requires a multidisciplinary approach due to the complex interplay between antipsychotic medications and anti-tuberculosis drugs, and other factors that can complicate treatments such as cognitive impairments and medication adherence issues. This also calls for stakeholders to provide routine screening and tracking to prevent tuberculosis transmission among individuals with mental health conditions like schizophrenia.

## Consent Form

Patient and the family had given verbal permission regarding publication of medical data with confidentiality of patient personal information.

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