ORIGINAL ARTICLE

# RADIOLOGICAL AND PHARMACOVIGILANCE COMPARISONS BETWEEN DRUG-RESISTANT TUBERCULOSIS AND DRUG SENSITIVE TUBERCULOSIS PATIENTS AT MARDAN MEDICAL COMPLEX

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**ABSTRACT**

**Objective:** To compare the radiological features and pharmacovigilance profile between drug-resistant TB (DR-TB) and drug-sensitive TB (DS-TB) patients.

**Study Design:** Retrospective, comparative cross-sectional study.

**Place and duration of Study:** Programmatic Management of Drug-Resistant Tuberculosis (PMDT) Center, Mardan Medical College, Mardan , 03 years(February 2022 to February 2025).

**Methodology:** Medical records of 200 tuberculosis patients (100 DR-TB and 100 DS-TB) were reviewed, using structured a proforma. Collected data consisted of demographic information, radiological features (extent of disease, infiltrates, consolidation, cavitary lesions, bronchiectasis, fibrosis, and non-parenchymal changes), and pharmacovigilance details like type, frequency, severity, causality, and outcomes of the adverse drug reactions (ADR). SPSS version 26 was used for data analysis. Chi-square and Fisher's exact tests were applied to assess significance, keeping a $p \leq 0.05$ , significant.

**Results:** DR-TB patients were found to have a significantly greater extent of pulmonary involvement, more cavitary lesions, consolidation, bronchiectasis, and destructive pulmonary changes than DS-TB patients ($p<0.05$). The proportion of DR-TB patients with ADRs was much higher when compared with DS-TB patients ($p<0.001$).

**Conclusions:** DR-TB patients have more a severe radiological disease and have a higher burden of adverse drug reactions, when compared to DS-TB patients. It is important that radiology is recognized early and pharmacovigilance is reinforced to achieve better treatment results.

**Keywords:** *Antitubercular agents; Drug resistance; Tuberculosis; Radiography; Pharmacovigilance*

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## INTRODUCTION

One of the most serious infectious illnesses in the world, tuberculosis (TB), is a public health concern, especially in low- and middle-income nations[1]. Mycobacterium tuberculosis is the cause, and although it can happen in extrapulmonary locations, it is typically linked to pulmonary illness [2]. Although the treatment is effective, TB is still a major cause of morbidity and mortality because of late diagnosis, non-adherence to treatment, socioeconomic inequities, and emergence of drug-resistant strains[3]. Year 2023 witnessed approximately 10.8 million individuals contracting TB globally, and around 1.25 million, dying of it. Globally ,TB is among the top 10 causes of death by an infectious disease [4].

Drug-resistant tuberculosis (DR-TB) and an even more problematic form, multidrug-resistant tuberculosis (MDR-TB), are becoming a serious problem for TB control programs worldwide[5]. MDR-TB is a type of tuberculosis that is resistant

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to isoniazid and rifampicin, the two most potent medications used in first-line anti-tuberculous therapy[6]. According to WHO, around 390,000 to 400,000 new cases of multidrug-resistant or rifampicin-resistant TB are reported annually across the globe [7]. Unfortunately, only a small number of these patients are diagnosed and treated on time, leading to continued transmission and sub-optimal treatment outcomes. DR-TB is especially prevalent in South Asian countries. Pakistan is one of the countries with highest TB burden in the world[8]. Drug resistance has become more common and has made disease management more difficult since patients with such resistance must be treated for longer periods with second-line drugs that are frequently accompanied by severe adverse drug reactions, higher healthcare costs, and reduced treatment success rates[9].

## CAPSULE SUMMARY

The radiological features and pharmacovigilance profile between drug-resistant TB (DR-TB) and drug-sensitive TB (DS-TB) patients was compared. DR-TB patients had more a severe radiological disease and a higher burden of adverse drug reactions(ADRs).Radiological features should be recognized early, and pharmacovigilance reinforced, to achieve better treatment results.

Radiological imaging is important in the diagnosis, assessment, and monitoring of TB[10]. The chest radiograph and computed tomography (CT) scan are useful in determining the severity and extent of pulmonary disease[11]. Patients with drug-sensitive tuberculosis (DS-TB) are more likely to have infiltrates, cavitary lesions, nodules, fibrosis, and pleural effusions in the upper lobes, whereas patients with DR-TB typically have more extensive lung disease with multiple thick-walled cavities, bronchiectasis, fibrosis, and destructive lung changes[12]. These differences in the radiology may be due to chronicity of the disease, delayed diagnosis, and inadequate response to therapy in resistant cases. A comparative evaluation of the radiological manifestations of DS-TB patients with DR-TB patients, therefore, can help the clinician in early detection of resistance patterns and prompt intervention[13].

Pharmacovigilance has also become an integral part of TB management as well as the radiological assessment[14]. Tuberculous drugs, particularly second-line drugs for DR-TB, have a broad range of adverse drug reactions that may involve hepatotoxicity, nephrotoxicity, ototoxicity, peripheral neuropathy, gastrointestinal disturbances, psychiatric manifestations, and dermatological complications[15]. These adverse events must be monitored, as they have a tremendous impact on adherence, patient quality of life, and therapeutic outcomes. The pharmacovigilance systems are designed to identify, document, and manage TB-related complications, thereby enhancing the safety and effectiveness of TB treatment programs[16]. However, there is limited data on comparing the pharmacovigilance profile of DR-TB patients with that of DS-TB patients in the local Pakistani healthcare facilities.

There is limited local data available, which compares the radiological manifestations and pharmacovigilance profile of DR-TB and DS-TB patients in Pakistan, particularly in Khyber Pakhtunkhwa. The burden of disease, access to health care, treatment adherence, and socioeconomic status may all play large roles in both imaging results and adverse drug reactions(ADRs) to treatment in the local population. Comparative comparison of these parameters may be helpful to recognize resistant cases early, to assess the severity of the disease, and to manage the disease on time, without complications due to the use of drugs. This study will contribute to the understanding of the situation and help clinicians, radiologists, pulmonologists, and public health officials in making better diagnoses, enhancing pharmacovigilance practices, optimizing patient management strategies, and ultimately improving the treatment outcomes of TB patients. The present study aimed to compare the radiological findings and pharmacovigilance profiles between DR-TB and DSTB.

## METHODOLOGY

The study was a retrospective comparative cross-sectional study that was done at the Programmatic Management of Drug-Resistant Tuberculosis (PMDT) Center, Mardan Medical College. Medical record of patients who had been treated for TB from 1st February 2022 until 1st February 2025 were reviewed. Ethical approval was obtained from the Association for Community Development, Khyber Pakhtunkhwa.

The sample size was not determined in advance, but for comparative analysis, a total of 200 patients were involved, consisting of 100 DR-TB and 100 DS-TB, selected consecutively. All eligible cases registered and managed at the PMDT Center, Mardan Medical Complex, were reviewed, patients who had complete medical records, and fulfilled the inclusion criteria were included. The final sample size was based on the availability of complete records over the time period of the study.

Patients with pulmonary tuberculosis who attended the PMDT Center, MMC, Mardan, from 1st February 2022 to 1st February 2025 were included, regardless of gender. This included both DR-TB and DS-TB cases, diagnosed using GeneXpert, culture, drug susceptibility testing, and/or medical records with radiological and clinical evaluation. All patients with complete clinical, radiological, and pharmacovigilance data available in their files were included in the final analysis. The cases were retrieved from hospital record archives for all eligible cases. Those who had incomplete or missing medical or ADR recording/reporting were excluded. Patients who were lost to follow-up before the baseline assessment and patients with co-existing major chronic diseases, including advanced malignancy or severe immunosuppressive conditions other than those related to TB, that could affect radiological and pharmacovigilance outcomes were also excluded.

A structured data collection proforma was employed to gather

information, including the demographic variables (like age and gender), radiological data including extent of disease, infiltrates, consolidation, cavitary disease, bronchiectasis, fibrosis, calcification, lymph node involvement, atelectasis, bullae formation, hyper-aeration, and non-parenchymal changes, and pharmacovigilance including type, frequency, severity, causality assessment, preventability, and outcomes of ADRs. Radiological findings were documented in chest X-ray and/or CT scan reports interpreted by radiologists, and adverse drug reactions were detected and classified from patient treatment records and pharmacovigilance reporting forms.

The data were analyzed through the use of the Statistical Package for Social Sciences (SPSS) Version 26. The quantitative variables, like age, were reported in mean ± SD, and the qualitative variables, like gender, radiological findings, and adverse ADRs were reported in frequencies and percentages. Categorical variables were compared between DR-TB and DS-TB groups by either the Chi-square test or the Fisher exact test, and continuous variables were compared by the independent sample t-test. A p-value of ≤0.05 was considered significant.

## RESULTS

The demographic characteristics of patients with DR-TB and DS-TB are summarized in Table 1. There were statistically significant differences in gender distribution between the two groups, but not in age distribution. Participants' mean ages were similar across both groups. There were significant differences between the two groups for lesions, infiltrative changes, consolidation, cavitary lesions, bronchiectasis, calcification pattern, selected nodular changes, and non-parenchymal abnormalities. Patients with DR-TB had more extensive pulmonary involvement, and they were more likely than DS-TB patients to have cavitary and destructive lung alterations. However, no significant differences were noted for most cases of ground glass opacity, atelectasis, bullae formation, hyper-aeration, and several nodal characteristics (Table 2).

**Table 1. Demographic Characteristics of DR-TB and DS-TB Patients (n =200)**

| Characteristic | DR-TB (n=100) | DS-TB (n=100) | p-value |
|---|---|---|---|
| Gender | | | 0.014 |
| Male | 52 (52.0) | 69 (69.0) | |
| Female | 48 (48.0) | 31 (31.0) | |
| Age Group (Years) | | | 0.063 |
| <30 | 19 (19.0) | 27 (27.0) | |
| 30–39 | 30 (30.0) | 21 (21.0) | |
| 40–49 | 31 (31.0) | 23 (23.0) | |
| 50–59 | 16 (16.0) | 16 (16.0) | |
| >59 | 4 (4.0) | 13 (13.0) | |
| Mean Age ± SD | 39.87 ± 11.59 | 41.03 ± 12.82 | — |

**Table 2. Comparison of Radiological Findings between DR-TB and DS-TB Patients (n=200)**

| Variable | DR-TB (n=100) | DS-TB (n=100) | p-value |
|---|---|---|---|
| Area of Lesion | | | <0.001 |
| Small | 0 (0.0) | 30 (30.0) | |
| Medium | 3 (3.0) | 43 (43.0) | |
| Large | 97 (97.0) | 27 (27.0) | |
| Infiltrates | | | |
| Lung Region | | | |
| Upper right lung | 37 (37.0) | 67 (67.0) | <0.001 |
| Upper left lung | 23 (23.0) | 55 (55.0) | <0.001 |
| Middle right lung | 27 (27.0) | 42 (42.0) | 0.026 |
| Middle left lung | 25 (25.0) | 38 (38.0) | 0.048 |
| Lower right lung | 12 (12.0) | 27 (27.0) | 0.007 |
| Lower left lung | 9 (9.0) | 28 (28.0) | <0.001 |
| Consolidation | | | |
| Lung Region | | | |
| Upper right lung | 57 (57.0) | 21 (21.0) | <0.001 |
| Upper left lung | 53 (53.0) | 17 (17.0) | <0.001 |
| Middle right lung | 48 (48.0) | 15 (15.0) | <0.001 |
| Middle left lung | 56 (56.0) | 15 (15.0) | <0.001 |
| Lower right lung | 21 (21.0) | 10 (10.0) | 0.032 |
| Lower left lung | 25 (25.0) | 7 (7.0) | <0.001 |
| Cavitary Lesions | | | |
| Location of Cavities | | | |
| Upper right lung | 58 (58.0) | 6 (6.0) | <0.001 |
| Upper left lung | 49 (49.0) | 7 (7.0) | <0.001 |
| Middle right lung | 39 (39.0) | 7 (7.0) | <0.001 |
| Middle left lung | 52 (52.0) | 5 (5.0) | <0.001 |
| Lower right lung | 7 (7.0) | 3 (3.0) | 0.194 |
| Lower left lung | 9 (9.0) | 3 (3.0) | 0.074 |
| Cavity Characteristics | | | |
| Cavity less than or equal to 4 cm | 66 (66.0) | 14 (14.0) | <0.001 |
| Cavity more than 4 cm | 14 (14.0) | 2 (2.0) | 0.002 |
| Solitary cavity | 5 (5.0) | 2 (2.0) | 0.248 |
| Multiple cavities | 68 (68.0) | 14 (14.0) | <0.001 |
| Ground Glass Opacity | | | |
| Lung Region | | | |
| ‘Upper right lung | 1 (1.0) | 3 (3.0) | 0.312 |
| ‘Upper left lung’ | 1 (1.0) | 1 (1.0) | 1.000 |

| | | | |
|---|---|---|---|
| 'Middle right lung' | 1 (1.0) | 2 (2.0) | 0.561 |
| 'Middle left lung' | 1 (1.0) | 1 (1.0) | 1.000 |
| 'Lower right lung' | 1 (1.0) | 1 (1.0) | 1.000 |
| 'Lower left lung' | 0 (0.0) | 1 (1.0) | 0.316 |
| Fibrosis | | | |
| Lung Region | | | |
| Upper right lung | 23 (23.0) | 15 (15.0) | 0.149 |
| Upper left lung | 11 (11.0) | 13 (13.0) | 0.663 |
| Middle right lung | 8 (8.0) | 7 (7.0) | 0.788 |
| 'Middle left lung' | 7 (7.0) | 8 (8.0) | 0.788 |
| 'Lower right lung' | 0 (0.0) | 4 (4.0) | 0.043 |
| Lower left lung | 1 (1.0) | 7 (7.0) | 0.030 |
| Bronchiectasis | | | |
| Lung Region | | | |
| Upper right lung | 4 (4.0) | 5 (5.0) | 0.733 |
| 'Upper left lung' | 3 (3.0) | 2 (2.0) | 0.651 |
| 'Middle right lung' | 14 (14.0) | 3 (3.0) | 0.005 |
| 'Middle left lung' | 9 (9.0) | 4 (4.0) | 0.152 |
| 'Lower right lung' | 9 (9.0) | 5 (5.0) | 0.268 |
| Lower left lung | 5 (5.0) | 2 (2.0) | 0.248 |
| Calcification | | | |
| Lung Region | | | |
| Upper right lung | 6 (6.0) | 3 (3.0) | 0.306 |
| 'Upper left lung' | 8 (8.0) | 0 (0.0) | 0.004 |
| 'Middle right lung' | 4 (4.0) | 1 (1.0) | 0.174 |
| 'Middle left lung' | 6 (6.0) | 0 (0.0) | 0.013 |
| 'Lower right lung' | 2 (2.0) | 0 (0.0) | 0.155 |
| 'Lower left lung' | 2 (2.0) | 0 (0.0) | 0.155 |
| Location of Nodes | | | |
| 'Upper right lung' | 5 (5.0) | 6 (6.0) | 0.756 |
| 'Upper left lung' | 4 (4.0) | 2 (2.0) | 0.407 |
| 'Middle right lung' | 5 (5.0) | 2 (2.0) | 0.248 |
| 'Middle left lung' | 6 (6.0) | 2 (2.0) | 0.149 |
| 'Lower right lung' | 2 (2.0) | 1 (1.0) | 0.561 |
| 'Lower left lung' | 4 (4.0) | 0 (0.0) | 0.043 |
| Lymph Nodes | | | |
| Node Characteristics | | | |
| '1–2 cm nodes' | 10 (10.0) | 7 (7.0) | 0.447 |
| '2–3 cm nodes' | 0 (0.0) | 0 (0.0) | — |
| 'Solitary node' | 5 (5.0) | 2 (2.0) | 0.248 |
| Multiple nodes | 5 (5.0) | 5 (5.0) | 1.000 |
| Atelectasis | | | |
| Lung Region | | | |
| Upper right lung | 2 (2.0) | 4 (4.0) | 0.407 |
| Upper left lung | 2 (2.0) | 0 (0.0) | 0.155 |
| 'Middle right lung' | 1 (1.0) | 1 (1.0) | 1.000 |
| 'Middle left lung' | 1 (1.0) | 3 (3.0) | 0.312 |
| 'Lower right lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| 'Lower left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| Bullae and Hyper-aeration | | | |
| Bullae | | | |
| 'Upper right lung' | 2 (2.0) | 1 (1.0) | 0.561 |
| 'Upper left lung' | 3 (3.0) | 0 (0.0) | 0.081 |
| 'Middle right lung' | 2 (2.0) | 1 (1.0) | 0.561 |
| 'Middle left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| 'Lower right lung' | 1 (1.0) | 1 (1.0) | 1.000 |
| 'Lower left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| Hyper-aeration | | | |
| 'Upper right lung' | 0 (0.0) | 0 (0.0) | — |
| 'Upper left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| 'Middle right lung' | 0 (0.0) | 0 (0.0) | — |
| 'Middle left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| 'Lower right lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| 'Lower left lung' | 1 (1.0) | 0 (0.0) | 0.316 |
| Non-Parenchymal Findings | | | |
| Right tracheal deviation | 13 (13.0) | 3 (3.0) | 0.009 |
| Left tracheal deviation | 17 (17.0) | 3 (3.0) | <0.001 |
| 'Right hilar elevation' | 19 (19.0) | 2 (2.0) | <0.001 |
| 'Left hilar elevation' | 16 (16.0) | 2 (2.0) | <0.001 |

A higher proportion of ADRs was seen in DR-TB than DS-TB patients. There were considerable variations in causality assessment, severity of ADRs, treatment interruption because of ADRs, preventable ADRs, and formal pharmacovigilance reporting. Gastrointestinal, hepatological, neurological, psychiatric, musculoskeletal, haematological, cardiac, auditory, skin-related, and/or general systemic adverse drug reactions were reported more frequently among DR-TB patients. Some adverse reactions, such as hyperuricaemia, hypothyroidism, myalgia, thrombocytopenia, renal impairment, skin hyperpigmentation, hair-related complaints, and drug fever, however, did not show statistically significant differences between the two groups (Table 3).

ADR reporting, causality assessment, severity of reaction, and pharmacovigilance-related outcomes were more prominent among DR-TB patients. The DR-TB group experienced greater gastrointestinal, hepatic, neurological, psychological, musculoskeletal, haematological, cardiac, renal, auditory, cutaneous, and general systemic adverse medication responses than the DS-TB group. Additionally, the picture shows that several ADR-related factors differed statistically substantially between the two groups, indicating that DR-TB patients

**Table 3. Comparison of Pharmacovigilance Profile and Reported ADRs Between DR-TB and DS-TB Patients (n=200)**

| Variable | DR-TB (n=100) | DS-TB (n=100) | p-value |
|---|---|---|---|
| Overall ADR Reporting | | | |
| At least one ADR reported | 52 (52.0) | 10 (10.0) | <0.001 |
| No ADR reported | 48 (48.0) | 90 (90.0) | <0.001 |
| Causality Assessment | | | |
| Possible ADR | 10 (10.0) | 2 (2.0) | 0.040 |
| Probable ADR | 30 (30.0) | 7 (7.0) | <0.001 |
| Definite ADR | 5 (5.0) | 1 (1.0) | 0.165 |
| Severity of ADRs | | | |
| Mild ADR | 25 (25.0) | 5 (5.0) | 0.003 |
| Moderate ADR | 15 (15.0) | 3 (3.0) | 0.004 |
| Severe ADR | 10 (10.0) | 1 (1.0) | 0.005 |
| Serious ADR | 7 (7.0) | 1 (1.0) | 0.015 |
| Pharmacovigilance Outcomes | | | |
| ADR requiring treatment interruption | 12 (12.0) | 1 (1.0) | 0.013 |
| ADR requiring hospitalization | 5 (5.0) | 1 (1.0) | 0.067 |
| Suspected drug withdrawn/changed | 3 (3.0) | 1 (1.0) | 0.315 |
| Preventable ADR | 20 (20.0) | 3 (3.0) | <0.001 |
| ADR was formally reported to the pharmacovigilance center | 50 (50.0) | 1 (1.0) | <0.001 |
| Gastrointestinal ADRs | | | |
| Gastrointestinal disturbance | 25 (25.0) | 7 (7.0) | <0.001 |
| Nausea and vomiting | 20 (20.0) | 5 (5.0) | <0.001 |
| Abdominal pain and anorexia | 14 (14.0) | 4 (4.0) | 0.014 |
| Diarrhea | 8 (8.0) | 2 (2.0) | 0.052 |
| Hepatic and Metabolic ADRs | | | |
| Hepatotoxicity / raised liver enzymes/jaundice | 10 (10.0) | 2 (2.0) | 0.022 |
| Hyperuricaemia | 5 (5.0) | 1 (1.0) | 0.089 |
| Hypothyroidism | 2 (2.0) | 0 (0.0) | 0.176 |
| Neurological and Psychiatric ADRs | | | |
| Peripheral neuropathy | 10 (10.0) | 1 (1.0) | 0.027 |
| Dizziness/vertigo | 5 (5.0) | 1 (1.0) | 0.058 |
| Psychiatric issues | 9 (9.0) | 0 (0.0) | 0.001 |
| Visual disturbance / optic neuritis | 4 (4.0) | 0 (0.0) | 0.059 |
| Musculoskeletal ADRs | | | |
| Arthralgia | 9 (9.0) | 1 (1.0) | 0.004 |
| Myalgia | 3 (3.0) | 1 (1.0) | 0.244 |
| Haematological ADRs | | | |
| Anemia/ myelosuppression | 8 (8.0) | 0 (0.0) | 0.003 |
| Thrombocytopenia/ leukopenia | 2 (2.0) | 0 (0.0) | 0.157 |
| Cardiac ADRs | | | |
| QT interval prolongation | 8 (8.0) | 0 (0.0) | 0.019 |
| Palpitation / ECG abnormality other than QT prolongation | 2 (2.0) | 0 (0.0) | 0.314 |
| Renal and Auditory ADRs | | | |
| Renal impairment | 3 (3.0) | 0 (0.0) | 0.085 |
| Ototoxicity | 4 (4.0) | 0 (0.0) | 0.028 |
| Skin ADRs | | | |
| Rash/itching/ hypersensitivity | 11 (11.0) | 4 (4.0) | 0.035 |
| Skin hyperpigmentation | 3 (3.0) | 0 (0.0) | 0.058 |
| Hair fall / hair-related complaints | 2 (2.0) | 1 (1.0) | 0.476 |
| General Symptoms | | | |
| Fatigue/weakness | 15 (15.0) | 6 (6.0) | 0.018 |
| Drug fever | 3 (3.0) | 0 (0.0) | 0.071 |

were more likely to experience treatment-related side effects (Figure 1).

## DISCUSSION

In terms of radiological severity and pharmacovigilance profile, the current investigation demonstrated clinically significant differences between DR-TB and DS-TB patients. Patients with DR-TB were more likely than DS-TB cases to have pulmonary involvement, cavitary lesions, bronchiectasis, consolidation, and destructive lung alterations. They also experienced more ADRs.

The majority of the DR-TB patients in our study had large areas of lung involvement and multiple cavitary lesions, especially in the upper lung zones. This is in line with the findings of Cheng

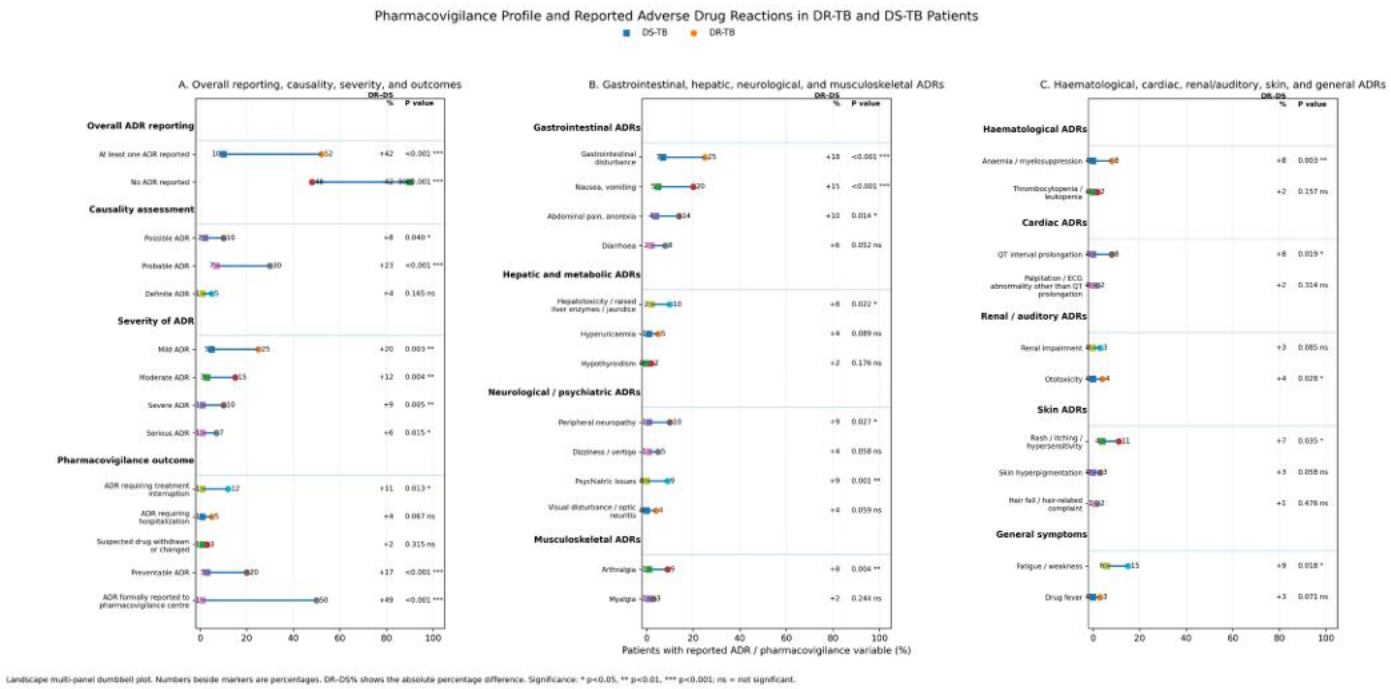


**Figure 1. Comparison of ADRs between DR-TB and DS-TB patients.**

et al. (2021) where DR-TB cases showed more bilateral, more extensive, and more cavitary disease patterns in their computed tomography (CT) scans, which may be attributed to delayed diagnosis and long disease course of DR-TB[17]. Similarly, comparative radiological studies from China and other high-burden countries have revealed that cavitary disease and upper lobe destruction occur much more frequently in DR-TB, as a result of higher bacillary load and treatment resistance[18].

Increased prevalence of bronchiectasis and fibrosis in DR-TB patients in our study is similar to the findings of imaging-based studies that consistently showed that drug resistance is linked with chronic structural lung damage and post-infective sequelae. The findings indicate that DR-TB is a more advanced and progressive form of pulmonary destruction than DS-TB.

Our results also showed significantly higher consolidation and infiltrative changes in DR-TB patients. The same was observed in the retrospective study in Pakistan by Atif et al. 2022, where radiological severity scores were found to be significantly higher in MDR-TB patients than in DS- TB patients, suggesting more aggressive disease behavior in the resistant strains[19]. The differences in these radiological parameters may be due to delayed diagnosis, inadequate initial treatment, and continued bacterial multiplication in the DR-TB patients.

Pharmacovigilance findings of our study showed that the burden of ADRs in DR-TB was much higher than in DS-TB, with 52% and 10% of the patients, respectively, having at least one ADR, respectively. This finding is robustly supported by Massud et al. (2022), who noted that a large proportion (over 50%) of DR-TB patients experienced multiple ADRs while receiving second-line treatment, including gastrointestinal and neurological ADRs[20]. Likewise, Khan et al. (2022) from Pakistan found that there was a strong association between second-line anti-TB drugs and frequency of adverse events necessitating clinical intervention[21].

Gastrointestinal, hepatic, neurological, psychiatric, and musculoskeletal ADRs were significantly more prevalent among DR-TB patients in our study. These results corroborate worldwide pharmacovigilance data, which have shown that linezolid, fluoroquinolones, and aminoglycosides can be associated with a broad range of toxicities, such as neuropathy, QT prolongation, and ototoxicity. A study from India, in 2024, also identified gastrointestinal and neurologic side effects as the commonest side effects among DR-TB patients, especially among those receiving the longer oral treatment regimens[22].

Moreover, treatment disruptions, preventable ADRs, and formal pharmacovigilance reporting were significantly higher in DR-TB patients. This is an indication of the complexity of DR-TB management and the need for better monitoring systems. Similar observations have been made in international pharmacovigilance databases, which show that DR-TB treatment is linked with increased treatment discontinuation and the need for well-designed supervision systems to enhance treatment adherence and safety[23]. In our study, the difference in causality and severity of DR-TB and DS-TB further corroborates the findings of earlier studies that second-line anti-TB drugs are more toxic and need to be adjusted on an individual basis and monitored closely.

Overall, the results of the present study are aligned with the

global and regional literature and confirm that DR-TB is accompanied by a significantly increased burden of radiological disease and a greater burden of complications related to pharmacovigilance as part of TB management programs.

**Limitations:** A retrospective study relying on medical records may not be accurate or complete, including reports on ADRs and radiologic interpretations. Second, the study was carried out in a single tertiary care PMDT centre, making it difficult to extrapolate the results to other areas or healthcare environments. Thirdly, radiological findings were not reassessed independently, which could have led to inter-observer variation in findings. Further, the study did not measure the long-term outcome of treatment, like cure rate, relapse, or mortality, which might have strengthened the clinical implications of differences between DR-TB and DS-TB patients in both radiological and pharmacovigilance parameters.

**Recommendations**: Routine radiological evaluation of all suspect cases of tuberculosis is suggested to facilitate early detection of drug-resistant tuberculosis, especially in cases with extensive and/or cavitary lungs. Enhancing pharmacovigilance systems, with active monitoring of ADRs in particular, for DR-TB patients on second-line anti-TB treatment is needed. Health care workers need to be trained regularly in recognizing, documenting, and reporting ADRs to enhance patient safety and adherence to treatment. Larger, multicenter prospective trials are also advised to confirm these outcomes and investigate the long-term effects of TB treatment based on the radiological severity and burden of adverse drug reactions.

## CONCLUSION

Drug resistant tuberculosis that is resistant to any drug has a significantly more extensive and destructive radiological involvement of the lung tissue when compared with drug-sensitive TB. Furthermore, ADR frequency, severity, and complexity are significantly higher in DR-TB patients, leading to an increased pharmacovigilance burden in this population. DR-TB is not just a microbiological problem but a more aggressive clinical form of TB and one with increased toxicity of the treatment. To achieve the best patient care, minimize complications, and maximize therapeutic success in TB treatment, it is critical to identify resistant patterns early in the course of disease and to have strong pharmacovigilance monitoring.

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***AUTHORS' CONTRIBUTION***

- ***Laila khan:*** *Conceptualization of study, supervision of research work, and final approval of manuscript.*
- ***Sajjad Ali:*** *Study design, radiological interpretation, and critical revision of the manuscript.*
- ***Rumman:*** *Data collection, literature review, and manuscript drafting.*
- ***Aleina Ali Shah:*** *Statistical analysis, interpretation of results, and preparation of tables.*
- ***Akmal Naveed:*** *Data acquisition, clinical evaluation of patients, and proofreading of the manuscript.*
- ***Nazar ul Islam:*** *Manuscript editing, review of references, and coordination of final submission.*

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