International Journal of Basic & Clinical Pharmacology
Kumari N et al. Int J Basic Clin Pharmacol. 2025 Sep;14(5):803-806
http://www.ijbcp.com
pISSN 2319-2003 | eISSN 2279-0780

DOI: https://dx.doi.org/10.18203/2319-2003.ijbcp20252580

Original Research Article

Adverse drug reactions to antitubercular therapy in osteoarticular tuberculosis: a retrospective observational study from a tertiary care center

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Received: 19 June 2025
Revised: 20 July 2025
Accepted: 21 July 2025

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ABSTRACT

Background: Osteoarticular tuberculosis (OATB) is a challenging form of extrapulmonary tuberculosis (TB) that often requires long-term multidrug regimens. Antitubercular therapy (ATT) can lead to significant adverse drug reactions (ADRs), potentially affecting patient adherence and outcomes. Objectives were to assess the types and frequencies of ATT-induced ADRs in patients treated for osteoarticular TB.
Methods: This retrospective observational study included 27 patients diagnosed with OATB, who were treated at Dr. RPGMC Tanda. Patient records and telephone interviews were used to collect data on ADRs. Descriptive statistics were used for analyses.
Results: Of 27 patients, 13 (48.1 %) experienced ADRs. GI symptoms were the most common (18.5%), followed by dermatological (11.1%) and neurological (11.1%) side effects. One case each of hepatotoxicity with liver failure and epistaxis, and two cases of ocular symptoms were recorded.
Conclusions: Nearly half of the patients developed ADRs to ATT. Regular monitoring and early intervention are essential to improve treatment compliance and patient safety.

Keywords: Osteoarticular tuberculosis, Antitubercular therapy, Adverse drug reactions, Retrospective study, Extrapulmonary tuberculosis, Treatment adherence, Tertiary care center

INTRODUCTION

Tuberculosis (TB) remains one of the top ten causes of death worldwide and is the leading cause of death from a single infectious agent, ranking above HIV/AIDS.[1] In 2018 alone, approximately 10 million new TB cases were reported globally, with a disproportionate burden in developing nations, such as India.[2] While pulmonary TB accounts for the majority of cases, extrapulmonary TB accounts for up to 20% of all TB infections in immunocompetent individuals, and this figure rises to 50% in immunocompromised patients.[3] Among the extrapulmonary forms, osteoarticular TB accounts for nearly 10% of cases and often involves the spine, large weight-bearing joints, or long bones.[4]

Osteoarticular TB typically results from hematogenous dissemination from a latent or active primary focus such as the lungs or lymph nodes.[5] Skeletal involvement can present subtly with chronic pain and swelling, leading to a delayed diagnosis. The management of OATB hinges on a prolonged course of multidrug ATT, typically involving isoniazid, rifampicin, pyrazinamide, and ethambutol for an

initial 2-month intensive phase, followed by a continuation phase extending up to 10-16 months.[6]

Although ATT is highly effective, it is frequently associated with ADRs, including hepatotoxicity, peripheral neuropathy, ocular toxicity, hypersensitivity reactions, and gastrointestinal side effects. These ADRs not only impact the patient's quality of life, but also threaten treatment adherence and success.[7,8] In resource-limited settings, where diagnostic and monitoring facilities may be scarce, unrecognized ADRs can lead to severe morbidity or treatment default.

Despite the burden of OATB and the known side effects of ATT, there is limited literature from India focusing specifically on the safety profile of ATT in patients with osteoarticular TB. This study aimed to fill this gap by identifying and quantifying ADRs in this subgroup to guide better monitoring and management strategies.

METHODS

Study design and setting

This retrospective observational study was conducted jointly by the Department of pharmacology and orthopaedics at Dr. R. P. government medical college, Kangra at Tanda, a tertiary care referral center in Himachal Pradesh, India. The study was conducted after receiving approval from the institutional ethics committee. (HFW-H-DRPGMC/Ethics/2024/014).

Study population

The study population included all patients diagnosed with OATB who were initiated on ATT between January 2022 and January 2024 in the department of orthopaedics.

Inclusion criteria

Patients eligible for inclusion in the study were adults aged 18 years or older who had been clinically and/or radiologically diagnosed with OATB. Only those patients who had completed ATT or were currently receiving it within the past two years were considered. Additionally, inclusion required that patients had provided verbal consent for participation in telephonic interviews and for the collection of relevant data.

Exclusion criteria

Exclusion criteria included patients with incomplete treatment records or insufficient follow-up data, as well as those who were lost to follow-up before completing at least two months of ATT. Patients diagnosed with drug-resistant TB, including multidrug-resistant (MDR) or extensively drug-resistant (XDR) forms, were also excluded. Additionally, individuals who were concurrently receiving hepatotoxic medications for other medical conditions were not considered for inclusion in the study.

Data collection

Patient details were obtained from hospital records and confirmed via telephone interviews using a structured case record form. The form documented demographic details, ATT regimen, treatment duration, and any adverse symptoms. Baseline and follow-up laboratory investigations, such as liver function tests (LFTs), renal function tests (RFTs), and hematological parameters, were also noted where available.

Assessment of ADRs

ADRs were classified as follows:

Gastrointestinal: Nausea, vomiting and gastritis

Cutaneous: Rash, pruritus and drug-induced dermatitis

Neurological: Peripheral neuropathy

Ocular: Blurred vision and color vision disturbance

Hepatobiliary: Jaundice and elevated liver enzymes

Others: Bleeding manifestations such as epistaxis

Statistical analysis

Descriptive statistics were used to summarize frequencies and percentages of ADRs. No inferential statistical tests were performed owing to the small sample size.

RESULTS

Out of the 27 patients enrolled in the study, fourteen patients (51.9%) did not experience any adverse events during the course of treatment. In contrast, thirteen patients (48.1%) reported experiencing one or more adverse effects associated with ATT.

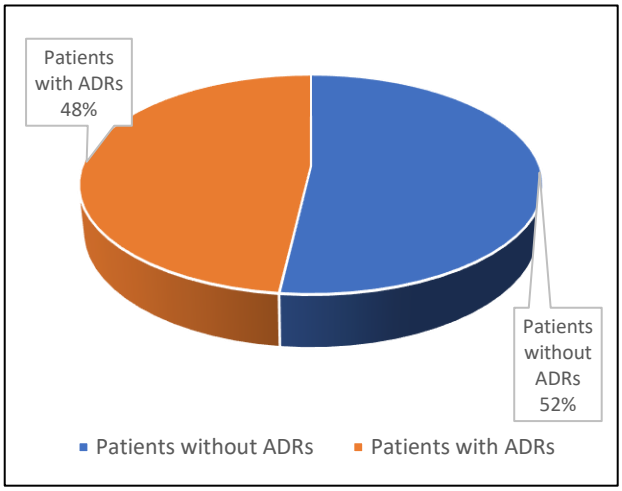

Figure 1: Proportion of patients with versus without ADRs.

This figure illustrates that nearly half of the study participants experienced at least one ADR during ATT. This emphasizes that ADRs are a common concern in osteoarticular TB treatment and merit close clinical attention.

Distribution of adverse events

Table 1: Distribution of adverse events by type.

Type of ADR	N	Percentage (%)
Gastrointestinal symptoms	5	18.5
Cutaneous dermatitis	3	11.1
Peripheral neuropathy	3	11.1
Ocular symptoms	2	7.4
Hepatotoxicity with liver failure	1	3.7
Epistaxis	1	3.7

Gastrointestinal symptoms were the most frequently reported ADR (18.5%), followed by cutaneous and neurological symptoms (11.1% each). Less commonly, ocular toxicity, hepatotoxicity, and epistaxis were noted. These findings underscore the broad spectrum of ADRs and highlight gastrointestinal and neurocutaneous reactions as key areas for proactive monitoring.

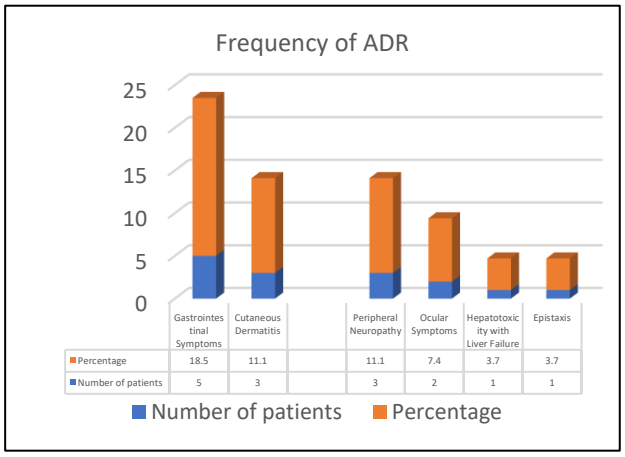

Figure 2: Frequency of ADRs.

The bar chart visually reinforces the numerical data in the table, showing that gastrointestinal symptoms were the predominant ADR, followed by cutaneous and neurological reactions. It helps identify the most prevalent ADRs that require early identification and patient education.

Although illustrative, this simulated line chart suggests a gradual accumulation of ADRs over time, emphasizing the importance of sustained pharmacovigilance and continuous follow-up throughout the treatment course to capture delayed-onset reactions.

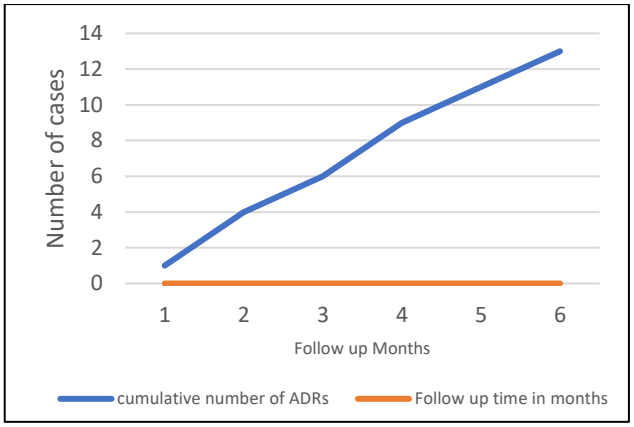

Figure 3: Line chart depicting a simulated cumulative trend of ADR reporting over a 6-month follow-up period for illustrative purposes.

DISCUSSION

Our study revealed that nearly half (48.1%) of the patients with osteoarticular TB experienced at least one adverse reaction to ATT. This is consistent with Koju et al who reported ADRs in 80% of patients with TB, with 34.3% experiencing major side effects.[9] Gastrointestinal symptoms were the most common, consistent with the findings of Forget and Menzies, who noted GI intolerance in 3-5% of patients.[7]

Cutaneous reactions such as drug-induced dermatitis were reported in 3 patients (11.1%), reflecting increased recognition of ATD-induced severe cutaneous adverse reactions (SCARs). Kim SH documented 56 SCAR cases associated with ATT, particularly DRESS syndrome, with isoniazid and rifampin as the most frequent offenders.[8]

Peripheral neuropathy, a known side effect of isoniazid, occurred in 11.1% of our patients, which is slightly higher than the 2-5% reported in Western cohort.[10] This discrepancy may be due to nutritional deficiencies or a lack of prophylactic pyridoxine supplementation.

Ocular toxicity, typically linked to ethambutol, was reported in two cases. While uncommon, ethambutol-induced optic neuropathy can lead to irreversible vision loss if not detected early.[11] The single case of hepatotoxicity leading to liver failure underscores the need for routine LFT monitoring, especially in elderly or alcoholic patients.

One patient developed epistaxis, a less commonly reported ADR, which may be related to thrombocytopenia or vascular fragility induced by drugs. Given the frequency and variety of ADRs, a multidisciplinary approach involving pharmacologists, orthopaedicians, and general physicians is crucial. Periodic monitoring, patient education, and early detection mechanisms should be institutionalized to ensure better adherence and safety.

Limitations

This study has several limitations. First, the retrospective design may have led to incomplete or inaccurate documentation of ADRs, particularly in cases where patients did not report mild or transient symptoms. Second, the small sample size (n=27) limits the generalizability of the findings and precludes the use of inferential statistics. Third, the reliance on patient self-reporting during telephonic interviews introduces recall bias. Additionally, not all patients had complete baseline and follow-up laboratory data, which may have resulted in underreporting of subclinical ADRs. Finally, drug causality assessment and severity grading of ADRs were not systematically applied due to data limitations.

CONCLUSION

ATT in osteoarticular TB, although effective, is associated with a significant burden of ADRs. This study highlights the need for active surveillance, early diagnosis, and management of ADRs to improve patient outcome and compliance.

Recommendations

To improve the safety of ATT in OATB, it is recommended to conduct routine baseline and follow-up investigations, including LFTs, RFTs, CBC, and vision checks. Pyridoxine should be supplemented with isoniazid to prevent neurotoxicity. Patients must be counselled to recognize and report early signs of ADRs. Additionally, establishing institutional pharmacovigilance systems is essential for effective monitoring and management of treatment-related complications.

ACKNOWLEDGEMENTS

Authors would like to thank to department of pharmacology and orthopaedics at Dr. R. P. G. M. C. Kangra at Tanda for support.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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Cite this article as: Kumari N, Sharma I, Kumar D, Goel K, Singh V, Katoch S. Adverse drug reactions to antitubercular therapy in osteoarticular tuberculosis: a retrospective observational study from a tertiary care center. Int J Basic Clin Pharmacol 2025;14:803-6.