



BALANCING TUBERCULOSIS TREATMENT EFFICACY AND HEPATOTOXICITY IN LIVER DYSFUNCTION

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ABSTRACT

Tuberculosis (TB) remains a major global health burden. Despite the high efficacy of first-line anti-tuberculosis therapy, treatment is frequently complicated by drug-induced liver injury (DILI), particularly in patients with pre-existing liver dysfunction. This review aimed to evaluate the balance between treatment efficacy and hepatotoxicity during TB therapy in patients with liver dysfunction and to summarise current management strategies. A literature review was conducted using studies retrieved from Scopus, PubMed, and Google Scholar. Articles published between 2015 and 2025 were identified using predefined search terms. After applying inclusion and exclusion criteria, ten eligible studies were qualitatively synthesised. The findings identified baseline liver dysfunction, hepatitis C co-infection, metabolic-associated steatotic liver disease, alcohol consumption, and poor nutritional status as major risk factors for hepatotoxicity. DILI was consistently associated with treatment interruption, regimen modification, delayed recovery, and reduced therapeutic success. Regular liver function monitoring, risk stratification, individualised treatment adjustments, and selective use of hepatoprotective agents were reported to minimise hepatotoxicity while preserving treatment effectiveness. Patient-centred, risk-based management and early identification of high-risk individuals are essential to optimise clinical outcomes and safely maintain effective anti-tuberculosis therapy.

Keywords: drug-induced liver injury; hepatotoxicity; liver dysfunction; pharmacotherapy; tuberculosis

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INTRODUCTION

Tuberculosis (TB) remains one of the leading infectious diseases worldwide and continues to impose a substantial public health burden despite considerable advances in prevention, diagnosis, and treatment. According to the latest global estimates, approximately 10.7 million people developed TB in 2024, while more than one million deaths were attributed to the disease, highlighting that TB remains a major cause of morbidity and mortality globally. Although global TB control programmes have improved case detection and treatment coverage, progress towards the targets of the End TB Strategy remains insufficient, particularly in low- and middle-income countries where healthcare resources, socioeconomic disparities, and delayed diagnosis continue to hinder disease control. These challenges are especially pronounced in countries with a high TB burden, where ongoing transmission and treatment-related complications remain major obstacles to successful disease management (World Health Organization, 2025).

The standard treatment for drug-susceptible TB relies on a multidrug regimen consisting of first-line anti-tuberculosis drugs, including isoniazid, rifampicin, pyrazinamide, and ethambutol. This regimen has achieved high cure rates when administered appropriately and remains the cornerstone of global TB management. Nevertheless, treatment success depends not only on the bactericidal efficacy of these agents but also on their safety profile. Among the various adverse drug reactions associated with anti-tuberculosis therapy, drug-induced liver injury (DILI) represents the most clinically significant complication because it frequently necessitates treatment interruption, regimen modification, or permanent drug discontinuation. Consequently, hepatotoxicity has become one of

the principal barriers to maintaining uninterrupted TB therapy and achieving favourable clinical outcomes (Lewis et al., 2024; Prasad et al., 2026).

Anti-tuberculosis drug-induced liver injury exhibits a broad clinical spectrum, ranging from asymptomatic elevations in liver enzymes to acute hepatitis, acute liver failure, and, in severe cases, death. Recent evidence indicates that hepatotoxicity remains one of the most common serious adverse events associated with first-line anti-TB therapy, particularly because isoniazid, rifampicin, and pyrazinamide are all intrinsically hepatotoxic. The pathogenesis of DILI is complex and multifactorial, involving oxidative stress, mitochondrial dysfunction, immune-mediated responses, and the formation of reactive metabolites during hepatic drug metabolism. These mechanisms contribute to hepatocellular injury and may be exacerbated by genetic susceptibility and underlying liver disease. Because the severity of hepatotoxicity is highly variable among individuals, predicting which patients will develop clinically significant liver injury remains a considerable challenge in routine clinical practice (Kumar, Kumar, & Kumar, 2025; Prasad et al., 2026).

Patients with pre-existing liver dysfunction constitute one of the most vulnerable populations during anti-tuberculosis treatment. Chronic viral hepatitis, metabolic dysfunction-associated steatotic liver disease (MASLD), alcohol-related liver disease, malnutrition, and other chronic hepatic disorders may substantially reduce hepatic reserve, thereby increasing susceptibility to drug-induced toxicity. Furthermore, impaired liver function may alter drug metabolism and clearance, resulting in higher exposure to hepatotoxic metabolites and an increased likelihood of liver injury. Recent systematic reviews and meta-analyses consistently demonstrate that liver-related comorbidities, hepatitis C virus infection, alcohol consumption, hypoalbuminaemia, and poor nutritional status significantly increase the risk of anti-tuberculosis drug-induced liver injury. These findings emphasise that hepatotoxicity is not solely determined by drug characteristics but also by patient-specific clinical factors that require careful evaluation before initiating treatment (Kumar, Kumar, & Kumar, 2025; Prasad et al., 2026). Beyond its direct hepatic consequences, hepatotoxicity has substantial implications for TB treatment effectiveness. The occurrence of liver injury frequently results in temporary discontinuation of therapy, delayed treatment completion, sequential drug reintroduction, or substitution with less effective regimens. These modifications may prolong the infectious period, reduce treatment adherence, increase healthcare costs, and potentially contribute to treatment failure or the emergence of drug resistance. Consequently, clinicians are often confronted with a therapeutic dilemma in which maintaining effective antimicrobial therapy must be balanced against preventing progressive liver injury. This challenge is particularly relevant in patients with underlying liver disease, where both inadequate TB treatment and excessive hepatotoxicity may lead to serious clinical consequences (Kumar, Kumar, & Kumar, 2025; Prasad et al., 2026).

Several studies have investigated the mechanisms and risk factors of anti-tuberculosis drug-induced liver injury; however, the available evidence remains fragmented. Most published studies have focused on individual aspects of hepatotoxicity, including molecular mechanisms, genetic susceptibility, or isolated clinical risk factors, while relatively few have comprehensively examined how hepatotoxicity influences the overall effectiveness of tuberculosis treatment in patients with pre-existing liver dysfunction. Recent systematic reviews have confirmed that baseline liver disease, hepatitis C virus infection, malnutrition, alcohol consumption, and hypoalbuminaemia substantially increase the risk of drug-induced liver injury, yet the translation of these findings into practical treatment strategies remains limited. Consequently, clinicians continue to face uncertainty regarding how best to preserve treatment efficacy while minimising liver-related adverse events in high-risk patients (Kumar, Kumar, & Kumar, 2025; Liu et al., 2026).

Growing evidence also supports a shift towards personalised management of tuberculosis patients at risk of hepatotoxicity. Rather than applying a uniform treatment approach, recent studies recommend risk stratification based on baseline liver function, comorbidities, nutritional status, and other patient-specific characteristics. Advances in predictive models have demonstrated that pre-treatment risk assessment can identify patients with a higher likelihood of developing drug-induced liver injury before anti-tuberculosis therapy is initiated. Such approaches may facilitate closer

biochemical monitoring, timely therapeutic modification, and improved patient safety without unnecessarily compromising the bactericidal effectiveness of first-line anti-tuberculosis drugs. These developments highlight the increasing importance of precision medicine in tuberculosis management, particularly among patients with underlying liver disease (Liu et al., 2026; Prakongsup & Udomsinprasert, 2026).

Despite these advances, significant knowledge gaps remain regarding the optimal balance between therapeutic efficacy and hepatotoxicity. Current clinical recommendations largely emphasise the early detection and management of liver injury after its occurrence, whereas evidence integrating preventive strategies with sustained treatment effectiveness remains limited. Furthermore, considerable heterogeneity among previous studies in terms of patient populations, definitions of hepatotoxicity, study designs, and clinical outcomes has resulted in inconsistent recommendations for managing tuberculosis patients with impaired liver function. Recent reviews have therefore highlighted the need for comprehensive evidence synthesis to support evidence-based clinical decision-making and to guide individualised treatment strategies that reduce hepatotoxicity without compromising microbiological cure or treatment completion (Mustika & Susanti, 2025; Yang et al., 2026). Accordingly, this literature review aims to synthesise recent evidence regarding the relationship between treatment efficacy and hepatotoxicity during anti-tuberculosis therapy in patients with liver dysfunction. Specifically, this review examines the mechanisms underlying anti-tuberculosis drug-induced liver injury, identifies the major clinical risk factors associated with hepatotoxicity, evaluates its impact on treatment outcomes, and summarises current management strategies that may optimise both therapeutic effectiveness and patient safety. By integrating contemporary evidence from recent studies, this review seeks to provide a comprehensive scientific foundation for clinicians in selecting safer and more individualised therapeutic approaches for tuberculosis patients with impaired liver function.

METHOD

This study employed a literature review design to comprehensively synthesise current evidence regarding the balance between treatment efficacy and hepatotoxicity during anti-tuberculosis therapy in patients with liver dysfunction. The review was conducted following a structured and transparent approach to ensure the identification, selection, and synthesis of relevant scientific evidence. A systematic literature search was performed using three electronic databases: PubMed, Scopus, and Google Scholar. Publications published between January 2021 and June 2026 were considered eligible to ensure that the review reflected the most recent evidence. The search strategy combined Medical Subject Headings (MeSH) terms and free-text keywords using Boolean operators. The primary search string included: ("tuberculosis" OR "TB") AND ("drug-induced liver injury" OR hepatotoxicity OR DILI) AND ("liver dysfunction" OR "liver disease") AND ("anti-tuberculosis therapy" OR pharmacotherapy). Additional manual searches of the reference lists of eligible articles were conducted to identify potentially relevant studies that were not retrieved through the initial database search.

Studies were included if they: (1) investigated hepatotoxicity associated with first-line or second-line anti-tuberculosis treatment; (2) involved patients with liver dysfunction or evaluated risk factors related to drug-induced liver injury; (3) were original research articles, systematic reviews, or meta-analyses; (4) were published in peer-reviewed journals between 2021 and 2026; and (5) were available in full text and written in English. Studies were excluded if they were conference abstracts, editorials, letters, case reports, animal or in vitro studies, duplicate publications, or did not specifically address the relationship between tuberculosis treatment and hepatotoxicity. The study selection process consisted of four stages: identification, screening, eligibility assessment, and inclusion. All records retrieved from the electronic databases were exported to a reference management program, where duplicate records were removed. Titles and abstracts were independently screened to determine their relevance to the research question. Full-text articles that met the preliminary screening criteria were subsequently assessed against the predefined inclusion

and exclusion criteria. Disagreements during the selection process were resolved through discussion until consensus was reached. The final set of eligible studies was included for qualitative synthesis.

Relevant information was extracted from each included study using a standardised data extraction form. The extracted variables included author, publication year, country, study design, study population, sample size, treatment regimen, identified risk factors for hepatotoxicity, clinical outcomes, and recommended management strategies. The findings were synthesised using a qualitative descriptive approach by grouping the evidence into four principal themes: (1) mechanisms of anti-tuberculosis drug-induced liver injury, (2) risk factors associated with hepatotoxicity, (3) the impact of hepatotoxicity on tuberculosis treatment effectiveness, and (4) strategies to optimise treatment efficacy while minimising hepatotoxicity. Similarities and differences among studies were critically analysed to identify consistent evidence and remaining knowledge gaps.

RESULT

A comprehensive literature search was conducted using three electronic databases, namely PubMed, Scopus, and Google Scholar, to identify studies investigating the relationship between anti-tuberculosis therapy and hepatotoxicity. After removing duplicate records and applying predefined inclusion and exclusion criteria, 10 studies published between 2015 and 2025 were included in the qualitative synthesis. The study selection process is illustrated in Figure 1.

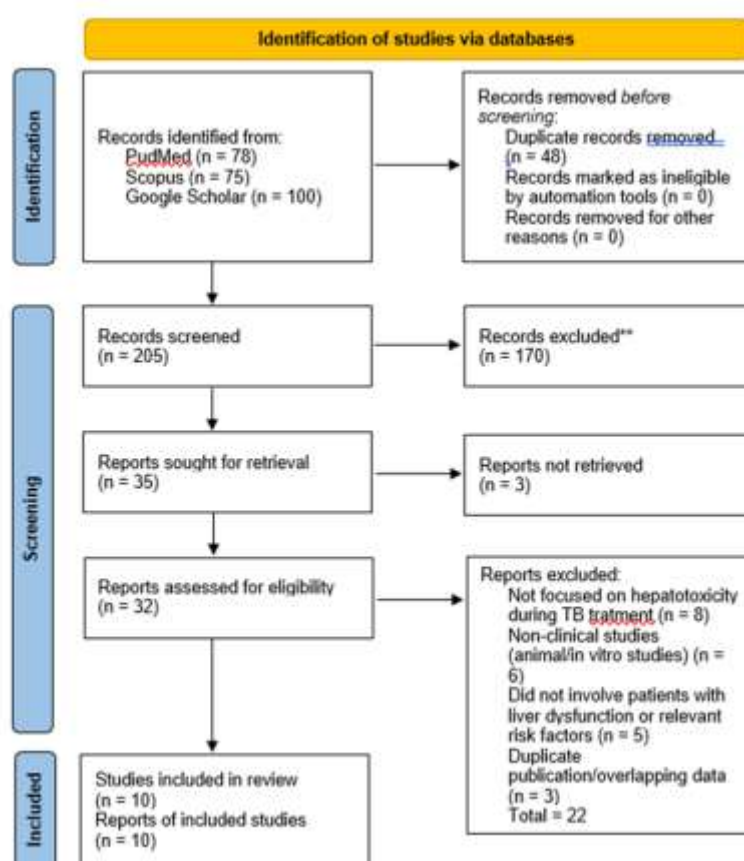


Figure 1. PRISMA 2020 Flow Diagram of Study Selection
Table 1.

Characteristics of Studies Included in the Literature Review

No	Author (Year)	Research Objectives	Metode	Temuan Utama	Implikasi
1	Chu et al., (2015)	Evaluating the role of bicyclol in preventing hepatotoxicity in TB patients with liver	Comparative clinical trials in TB patients with liver	Studies show that administration of bicyclol significantly reduced the incidence of elevated liver enzymes compared to the control group. The drug works by stabilizing the	The use of hepatoprotective agents such as bicyclol can be an additional strategy in reducing hepatotoxicity without compromising the

No	Author (Year)	Research Objectives	Metode	Temuan Utama	Implikasi
		liver disease	disorders	hepatocyte membrane and reducing the oxidative stress caused by anti-TB drugs. However, the effect does not completely eliminate the risk of hepatotoxicity, especially in patients with severe liver damage.	effectiveness of TB therapy. However, its use must be selective and still accompanied by strict monitoring of liver function.
2	Gray & Goldberg, (2016)	Assess the effect of early liver function on the risk of hepatotoxicity due to isoniazid	Retrospective cohort study in patients with latent TB therapy	The results showed that abnormalities of liver function before therapy were a stronger predictor of hepatotoxicity compared to age. Patients with elevated initial liver enzyme values have a higher risk of liver damage during therapy.	Screening of liver function before TB therapy is very important. Regimen adjustment and intensive monitoring are necessary in patients with abnormal baseline to prevent serious complications.
3	Kim et al., (2016)	Determining the role of hepatitis B and C infection against DILI in TB patients	Studi kohort observasional	It was found that Hepatitis C infection significantly increased the risk of hepatotoxicity, whereas hepatitis B did not show a significant association. This shows the difference in pathophysiological mechanisms between the two infections.	Hepatitis C screening needs to be part of the initial evaluation of TB patients. Management of TB patients with HCV requires a more careful approach to prevent DILI.
4	Kumar, Kumar, Patel, et al., (2025)	Identify the incidence and risk factors of DILI due to anti-TB drugs	Systematic review dan meta-analysis	The study shows that the incidence of hepatotoxicity is quite high, with the main risk factors including age, alcohol consumption, liver comorbidities, and malnutrition. Variation in incidence between studies showed a heterogeneity of populations and therapy regimens.	Early identification of risk factors allows for personalization of TB therapy. A risk stratification approach can help balance the effectiveness and safety of therapy.
5	Lee et al., (2016)	Determining the frequency and risk factors of DILI in MDR-TB patients	Cohort study in MDR-TB patients	DILI occurs with a fairly high frequency in MDR-TB patients. Risk factors include multiple drug use and long duration of therapy. Hepatotoxicity often leads to interruption of therapy.	In MDR-TB, monitoring must be more stringent due to the complexity of the regimen. Balancing strategies are more important to prevent therapy failure due to drug discontinuation.
6	Prasad et al., (2026)	Synthesizing the current understanding of DILI as a result of anti-TB drugs	Narrative review	This article describes the main mechanisms of hepatotoxicity, including the role of toxic metabolites, oxidative stress, and genetic factors. In addition, the management approaches such as phasing out the drug and phasing reintroduction were discussed.	Understanding the mechanism allows for the development of safer therapies. The individualized approach of therapy is key in balancing the effectiveness and risk of hepatotoxicity.
7	Shen & Liu, (2025)	Assessing the effect of fatty liver on DILI in TB patients	Observational studies	It was found that patients with metabolic-associated fatty liver disease had a higher risk of developing hepatotoxicity. This condition worsens the liver's response to anti-TB drugs.	Metabolic comorbidities should be considered in TB therapy. A comprehensive evaluation of the condition of the liver is necessary before starting therapy.
8	Song et al., (2019)	Assessing the clinical impact of hepatotoxicity on the success of TB therapy	Studi case-control	Hepatotoxicity leads to delayed therapy, discontinuation of medication, and decreased treatment success. Patients with DILI had worse outcomes than those who did not experience hepatotoxicity.	Hepatotoxicity is not only a side effect, but a determining factor for the success of therapy. Prompt and proper management is essential to maintain the effectiveness of TB treatment.
9	Wei et al., (2025)	Assessing the risk of DILI in TB patients with hepatitis C	Systematic review dan meta-analysis	Coinfection with Hepatitis C significantly increases the risk of DILI compared to patients without coinfection. The analysis showed a	TB patients with HCV are a high-risk group that requires specific therapeutic strategies, including intensive monitoring

No	Author (Year)	Research Objectives	Metode	Temuan Utama	Implikasi
		coinfection		consistent increase in risk across a variety of studies.	possible regimen modifications.
10	Yew et al., (2018)	Explaining the mechanism of oxidative stress in the hepatotoxicity of anti-TB drugs	Experimental and clinical reviews	First-line TB drugs such as isoniazid and rifampicin cause oxidative stress through the formation of reactive metabolites that damage hepatocytes. This mechanism is the main basis for the occurrence of DILI.	Therapeutic approaches that target oxidative stress may be a potential strategy to reduce hepatotoxicity without reducing the effectiveness of TB therapy.

Table 1 summarises the characteristics of the ten studies included in this literature review. The selected studies comprised a range of research designs, including observational cohort studies, case-control studies, clinical trials, systematic reviews, meta-analyses, and narrative reviews. These studies collectively investigated the occurrence, risk factors, mechanisms, clinical consequences, and management of anti-tuberculosis drug-induced liver injury (AT-DILI) in patients receiving anti-tuberculosis therapy. The included studies consistently demonstrated that hepatotoxicity remains one of the most frequently reported adverse effects associated with first-line anti-tuberculosis treatment. Several studies identified pre-existing liver dysfunction, hepatitis C co-infection, metabolic-associated fatty liver disease, alcohol consumption, advanced age, and poor nutritional status as important determinants of drug-induced liver injury. In addition, the reviewed evidence indicated that the incidence and severity of hepatotoxicity varied according to patient characteristics, underlying comorbidities, and treatment regimens.

The reviewed literature also showed that hepatotoxicity substantially affected tuberculosis treatment outcomes. Drug-induced liver injury frequently resulted in temporary treatment interruption, modification of anti-tuberculosis regimens, prolonged treatment duration, and reduced treatment success. Patients with multidrug-resistant tuberculosis or chronic liver disease were reported to be particularly vulnerable because they often required prolonged therapy with multiple potentially hepatotoxic medications. Furthermore, several studies highlighted strategies to minimise hepatotoxicity while maintaining treatment efficacy. These approaches included baseline liver function assessment, regular biochemical monitoring, identification of individual risk factors, temporary discontinuation of hepatotoxic drugs when clinically indicated, gradual drug reintroduction, and the selective use of hepatoprotective agents in high-risk patients. Collectively, these findings indicate that balancing therapeutic efficacy and hepatotoxicity requires careful patient evaluation and individualised clinical management.

Table 2.

Major Risk Factors for Anti-Tuberculosis Drug-Induced Liver Injury

Risk Factor	Evidence from Included Studies	Clinical Significance
Baseline liver dysfunction	Abnormal liver function before treatment was consistently associated with an increased risk of hepatotoxicity.	Requires pre-treatment liver function assessment and close monitoring.
Hepatitis C co-infection	Patients with hepatitis C showed a substantially higher incidence of drug-induced liver injury than those without co-infection.	Consider intensive liver function monitoring throughout treatment.
Metabolic-associated fatty liver disease (MAFLD/MASLD)	Fatty liver disease increased susceptibility to hepatotoxic effects of anti-tuberculosis drugs.	Baseline metabolic evaluation is recommended before therapy.
Alcohol consumption	Chronic alcohol intake was associated with greater liver injury due to impaired hepatic metabolism.	Alcohol cessation should be encouraged before and during treatment.
Advanced age	Older patients demonstrated a higher incidence of hepatotoxicity because of reduced hepatic metabolic capacity.	Elderly patients require closer clinical surveillance.
Malnutrition	Poor nutritional status was associated with increased susceptibility to liver injury during treatment.	Nutritional assessment and support should accompany anti-tuberculosis therapy.
Multidrug-resistant tuberculosis (MDR-TB)	Prolonged treatment and exposure to multiple drugs increased hepatotoxicity risk.	Regular biochemical monitoring is essential during extended treatment.

Table 2 summarises the principal risk factors associated with anti-tuberculosis drug-induced liver injury identified across the included studies. Baseline liver dysfunction emerged as the most consistently reported predictor of hepatotoxicity, indicating that patients with impaired hepatic function before treatment initiation are more likely to develop liver injury during anti-tuberculosis therapy. This finding highlights the importance of comprehensive pre-treatment clinical assessment to identify individuals at increased risk. Several patient-related comorbidities were also frequently associated with hepatotoxicity. Chronic hepatitis C infection and metabolic-associated fatty liver disease were repeatedly identified as conditions that increase hepatic susceptibility to anti-tuberculosis drugs. In addition, lifestyle-related factors, particularly chronic alcohol consumption and poor nutritional status, were reported to further increase the likelihood of liver injury by reducing hepatic metabolic capacity and impairing liver regeneration. Treatment-related characteristics also contributed to hepatotoxicity risk. Patients receiving prolonged multidrug regimens, especially those undergoing treatment for multidrug-resistant tuberculosis, experienced a higher frequency of liver injury because of cumulative drug exposure and the complexity of treatment. Collectively, these findings indicate that anti-tuberculosis drug-induced liver injury is a multifactorial complication resulting from the interaction between patient characteristics, underlying liver conditions, and treatment-related factors. Early identification of these risk factors may facilitate risk stratification and support safer clinical management during anti-tuberculosis therapy.

Table 3.

Clinical Impact of Anti-Tuberculosis Drug-Induced Liver Injury on Treatment Outcomes

Clinical Impact	Evidence from Included Studies	Clinical Implications
Treatment interruption	Hepatotoxicity frequently resulted in temporary discontinuation of anti-tuberculosis drugs until liver function improved.	Delayed treatment may compromise disease control and prolong recovery.
Regimen modification	Patients with significant liver injury often required dose adjustment or substitution of hepatotoxic drugs.	Alternative regimens should maintain therapeutic efficacy while reducing hepatotoxic risk.
Delayed treatment completion	Liver injury prolonged treatment duration because of drug withdrawal and gradual reintroduction.	Extended treatment may reduce patient adherence and increase healthcare utilisation.
Reduced treatment success	Patients experiencing hepatotoxicity showed lower treatment success rates than those without liver injury.	Effective hepatotoxicity management is essential to optimise treatment outcomes.
Increased risk in MDR-TB	Hepatotoxicity occurred more frequently among patients receiving prolonged multidrug-resistant tuberculosis regimens.	Intensive monitoring is required because treatment interruption may increase the risk of therapeutic failure.

Table 3 summarises the clinical consequences of anti-tuberculosis drug-induced liver injury reported across the included studies. Hepatotoxicity consistently disrupted tuberculosis treatment by necessitating temporary discontinuation of anti-tuberculosis drugs, followed by gradual drug reintroduction after recovery of liver function. Such interruptions frequently prolonged the overall duration of therapy and complicated clinical management. Several studies also reported that hepatotoxicity required modification of standard treatment regimens, particularly among patients who developed severe liver injury. These modifications included dose adjustment, replacement of hepatotoxic agents, or the use of alternative therapeutic regimens. Although these approaches aimed to reduce further liver damage, they occasionally compromised treatment continuity and increased the complexity of patient management. Furthermore, the reviewed studies demonstrated that hepatotoxicity adversely affected treatment outcomes by delaying treatment completion and reducing therapeutic success. These consequences were particularly evident among patients with multidrug-resistant tuberculosis, who required prolonged multidrug therapy and therefore experienced greater cumulative exposure to potentially hepatotoxic medications. Overall, the findings indicate that anti-tuberculosis drug-induced liver injury represents an important determinant of treatment effectiveness and should be recognised as a major clinical challenge during tuberculosis management.

Table 4.
Strategies for Balancing Treatment Efficacy and Hepatotoxicity

Management Strategy	Evidence from Included Studies	Expected Clinical Benefit
Baseline liver function assessment	Liver function evaluation before treatment identified patients at high risk of hepatotoxicity.	Facilitates early risk stratification and treatment planning.
Regular liver function monitoring	Periodic monitoring enabled early detection of liver injury during treatment.	Prevents severe hepatotoxicity through timely intervention.
Individualised treatment adjustment	Drug interruption, dose modification, and gradual reintroduction were recommended for patients developing hepatotoxicity.	Preserves treatment efficacy while reducing liver damage.
Identification of patient-specific risk factors	Assessment of viral hepatitis, alcohol consumption, nutritional status, and metabolic disorders improved clinical decision-making.	Supports personalised anti-tuberculosis therapy.
Selective use of hepatoprotective agents	Hepatoprotective therapy was beneficial in selected high-risk patients.	May reduce hepatotoxicity without compromising anti-tuberculosis efficacy.

Table 4 presents the principal management strategies identified across the included studies for balancing treatment efficacy with hepatotoxicity. Most studies emphasised that baseline liver function assessment before initiating anti-tuberculosis therapy is fundamental for identifying patients at increased risk of drug-induced liver injury. Early risk stratification enables clinicians to implement appropriate monitoring and therapeutic planning before clinically significant hepatotoxicity develops. Routine biochemical monitoring during treatment was consistently recommended as an effective strategy for detecting liver injury at an early stage. Early recognition of abnormal liver function allows timely clinical interventions, including temporary drug discontinuation, dose adjustment, or gradual reintroduction of anti-tuberculosis drugs after hepatic recovery. These approaches minimise liver damage while maintaining treatment continuity whenever possible. The reviewed evidence also highlighted the importance of individualised clinical management based on patient-specific risk factors, including underlying liver disease, viral hepatitis, alcohol consumption, nutritional status, and metabolic disorders. In selected high-risk patients, hepatoprotective agents were reported as supportive therapy to reduce hepatotoxicity, although their use should complement rather than replace careful clinical monitoring. Overall, the included studies indicate that successful tuberculosis treatment requires a patient-centred approach that balances therapeutic effectiveness with the prevention and management of hepatotoxicity.

DISCUSSION

The findings of this literature review indicate that anti-tuberculosis drug-induced liver injury (AT-DILI) is a multifactorial adverse event influenced by the interaction between patient-related characteristics, underlying liver conditions, and treatment-related factors. Across the included studies, baseline liver dysfunction consistently emerged as the strongest predictor of hepatotoxicity. Patients with pre-existing hepatic impairment possess reduced hepatic reserve and altered drug metabolism, making them more susceptible to toxic metabolites generated during first-line anti-tuberculosis therapy. Consequently, liver injury may develop even when standard treatment regimens are administered appropriately. These findings are supported by recent clinical guidelines, which recommend comprehensive baseline liver function assessment before initiating anti-tuberculosis therapy, particularly in patients with chronic liver disease or previous hepatic disorders (Yew et al., 2018).

This review also identified chronic viral hepatitis, particularly hepatitis C virus (HCV) infection, as an important determinant of hepatotoxicity. Chronic viral hepatitis promotes persistent hepatic inflammation and fibrosis, thereby reducing the liver's capacity to tolerate potentially hepatotoxic medications. A recent systematic review and meta-analysis involving more than 34,000 tuberculosis patients demonstrated that HCV infection significantly increased the risk of AT-DILI compared with patients without viral hepatitis. Similarly, hepatitis B virus infection, HIV co-infection, and disseminated tuberculosis were recognised as additional clinical conditions associated with increased susceptibility to liver injury during treatment (Liu et al., 2026). Lifestyle and nutritional factors also play a critical role in the development of hepatotoxicity. Alcohol consumption enhances

oxidative stress and interferes with hepatic detoxification pathways, whereas malnutrition and hypoalbuminaemia impair hepatic regeneration and reduce the body's capacity to metabolise anti-tuberculosis drugs safely. The recent meta-analysis by Kumar, Kumar, Patel, et al., (2025) reported that malnutrition, alcohol intake, and reduced serum albumin levels were among the strongest non-genetic predictors of AT-DILI. These findings reinforce the importance of nutritional assessment and counselling before treatment initiation, particularly in resource-limited settings where malnutrition remains highly prevalent among tuberculosis patients (Liu et al., 2026).

In addition to clinical risk factors, treatment-related characteristics contribute substantially to hepatotoxicity. First-line anti-tuberculosis drugs, particularly isoniazid, rifampicin, and pyrazinamide, undergo extensive hepatic metabolism and may generate reactive metabolites capable of inducing mitochondrial dysfunction, oxidative stress, cholestasis, and immune-mediated hepatocellular injury. Recent reviews have highlighted that these mechanisms often occur simultaneously rather than independently, explaining the considerable variability in clinical presentation among patients. Furthermore, prolonged multidrug therapy, especially in patients with multidrug-resistant tuberculosis, increases cumulative exposure to hepatotoxic agents and consequently elevates the risk of liver injury (Kumar, Kumar, & Kumar, 2025; Mustika & Susanti, 2025). Collectively, these findings demonstrate that hepatotoxicity during anti-tuberculosis therapy cannot be attributed to a single factor. Instead, it results from the complex interaction of host characteristics, underlying liver disease, nutritional status, and pharmacological exposure. Therefore, effective prevention requires comprehensive risk stratification before treatment initiation, allowing clinicians to identify high-risk patients who may benefit from closer biochemical monitoring and individualised therapeutic strategies. Such a patient-centred approach is increasingly recommended in recent evidence and may improve treatment safety without compromising the efficacy of anti-tuberculosis therapy (Liu et al., 2026; Yew et al., 2018).

CONCLUSION

This literature review demonstrates that balancing treatment efficacy and hepatotoxicity remains a critical challenge in the management of tuberculosis patients with liver dysfunction. The findings indicate that anti-tuberculosis drug-induced liver injury is influenced by multiple factors, including pre-existing liver disease, viral hepatitis co-infection, metabolic disorders, alcohol consumption, and poor nutritional status, all of which may compromise treatment continuity and therapeutic success. Effective management therefore requires early risk stratification, comprehensive baseline liver function assessment, regular biochemical monitoring, and individualised treatment adjustments to minimise hepatotoxicity while maintaining the effectiveness of anti-tuberculosis therapy. By integrating recent evidence, this review provides a comprehensive synthesis of current knowledge regarding the clinical relationship between hepatotoxicity and treatment outcomes, highlighting the importance of patient-centred management in improving treatment safety and effectiveness. The findings also contribute to the growing evidence supporting personalised therapeutic strategies for high-risk tuberculosis patients.

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