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Original Research Article

Profile of Liver Function Tests in Patients Initiated on Anti-Tuberculous Therapy and Incidence of Anti-Tuberculous Drug-Induced Liver Injury

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Name of Author:
Dr Kiran Vadapalli*[1], Dr Revathi Boddepall[2]

Affiliation: *[1]MD, DM,DNB,MRCPUK,MRCPI,EDIC, IFCCM Assistant Professor of Medicine Govt General Hospital and Medical College Rajamahedravaram, Andhra Pradesh, India*
[2] MD General Medicine Senior Resident Dept of Medicine Great Eastern Medical School (GEMS) Srikakulam

Corresponding Author:
Dr Kiran Vadapalli

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Abstract: ***Background***: Anti-tuberculous therapy (ATT) is essential for tuberculosis management but is frequently complicated by drug-induced liver injury (DILI), which may lead to treatment interruption, liver failure, and death. The risk of ATT-induced DILI varies with baseline hepatic status and host factors, yet universal liver function monitoring is often impractical in resource-limited settings. This study evaluated liver function profiles, determined the incidence of ATT-induced DILI, and assessed associated risk factors and clinical outcomes. ***Methods:*** This prospective observational cohort study was conducted over 12 months at a tertiary care hospital in South India. One hundred adult patients initiated on ATT for pulmonary or extrapulmonary tuberculosis were enrolled and stratified based on baseline liver function tests into Group I (normal LFTs, n=75) and Group II (deranged LFTs, n=25). Serial clinical and biochemical monitoring was performed to identify DILI, assess severity, hepatic adaptation, treatment modification, and outcomes. ***Results:*** The overall incidence of ATT-induced DILI was 9%. DILI occurred in 6.67% of patients with normal baseline LFTs and 16% of those with deranged baseline LFTs (p=0.157). Alcohol use and diabetes mellitus were significantly associated with DILI. Among patients who developed DILI, 77.8% recovered following treatment modification, while DILI-related mortality was 22.2%. Hepatic adaptation was more frequent in patients with deranged baseline LFTs but did not independently predict prognosis. Clinical features such as jaundice, ascites, and hepatic encephalopathy were strongly associated with adverse outcomes. ***Conclusion:*** ATT-induced DILI remains a significant clinical challenge, particularly in patients with baseline liver dysfunction, alcohol use, and metabolic comorbidities. Risk-based monitoring, early recognition, and timely regimen modification are essential to minimize severe hepatotoxicity and improve outcomes while maintaining effective tuberculosis treatment.

Keywords: Anti-tuberculous therapy; Drug-induced liver injury; Liver function tests; Hepatotoxicity; Tuberculosis; Hepatic adaptation; Mortality

INTRODUCTION

Tuberculosis (TB) remains a leading cause of infectious morbidity and mortality, with a continuing global burden despite decades of programmatic control efforts. Contemporary burden analyses from the Global Burden of Disease collaboration show that TB continues to contribute substantially to deaths and disability worldwide, and that progress is uneven across regions and risk strata [1]. In parallel, the Asia–Pacific region carries a disproportionate share of chronic liver disease and metabolic risk factors that can modify drug handling and clinical vulnerability, creating a setting where TB treatment safety becomes inseparable from liver health [2]. For clinicians working in high-burden settings, the success of TB therapy therefore depends not only on microbiologic cure, but also on early recognition and mitigation of treatment-limiting toxicities most importantly anti-tuberculosis drug–induced liver injury (ATDILI) [3].

Drug-induced liver injury (DILI) is a syndromic

diagnosis defined by liver test abnormalities and/or liver dysfunction temporally related to an exposure, after alternative etiologies have been reasonably excluded. While many DILI episodes are mild and self-limited, a clinically meaningful minority progress to jaundice, coagulopathy, acute liver failure, or death. Modern guidance emphasizes structured causality assessment, careful phenotype characterization (hepatocellular, cholestatic, or mixed patterns), and risk-based monitoring rather than indiscriminate testing for all patients [3]. In TB care, the problem is amplified because first-line regimens rely on multiple drugs with overlapping hepatotoxic potential. Isoniazid, rifampicin, and pyrazinamide remain the core sterilizing agents for drug-susceptible TB, yet they are also the principal contributors to hepatotoxicity and treatment interruption, especially during the intensive phase when drug exposure is maximal [4].

The epidemiology of ATDILI varies widely across cohorts because of differences in diagnostic thresholds, monitoring intensity, background liver disease, nutrition, alcohol exposure, and genetic susceptibility. Large clinical datasets from hospital-based TB populations continue to demonstrate that a substantial fraction of ATDILI cases are clinically silent and detected only through biochemical surveillance, underscoring the limitation of symptom-triggered monitoring alone [5]. When hepatotoxicity is not recognized early, patients may present late with jaundice, encephalopathy, and decompensation, forcing regimen discontinuation and increasing the risk of poor TB outcomes through treatment interruption, regimen weakening, or delayed re-challenge [5]. In addition, the need to substitute less hepatotoxic regimens can compromise efficacy, prolong therapy, and contribute to programmatic costs.

Multiple interacting risk domains shape ATDILI susceptibility. Alcohol exposure is one of the most consistently reported clinical risks, and recent systematic review evidence supports an increased odds of ATDILI among patients who consume alcohol during therapy [6]. Nutritional compromise and anemia common in TB also appear to be relevant. Prospective cohort data have identified malnutrition and low hemoglobin as independent predictors of clinically important ATDILI, including moderate to severe events that drive hospitalization, interruption, and intensive follow-up [7]. Beyond clinical factors, host pharmacogenetic variability is increasingly recognized. For example, NAT2 polymorphisms influence isoniazid acetylation status; recent work links slow-acetylator genotypes with higher rates of liver injury and liver failure during anti-TB therapy, supporting a biologically plausible pathway from altered metabolism to reactive intermediates and hepatocellular stress [8]. These findings matter most in real-world settings where baseline liver reserve is heterogeneous particularly among patients with alcohol-associated liver disease, metabolic dysfunction–associated steatotic liver disease, or prior hepatic insults.

Risk prediction and targeted monitoring are therefore emerging as practical strategies. Contemporary modeling studies have proposed bedside nomograms that integrate age, bilirubin, inflammatory indices, uric acid, and alcohol exposure to estimate individual ATDILI risk before or early in treatment [9]. At the population level, interventional evidence remains limited; however, recent network meta-analytic syntheses of preventive approaches highlight the continued uncertainty about effective, universally recommended hepatoprotective prophylaxis, reinforcing that prevention currently relies more on risk stratification, patient education, and surveillance than on a single proven protective agent [4]. In high-burden, resource-constrained systems, this direction aligns with modern DILI guidance: intensify monitoring where risk is highest, and avoid unnecessary testing where pre-test probability is low without losing sensitivity for early detection in vulnerable groups [3].

Within this context, evaluating baseline liver function tests (LFTs), tracking dynamic changes after anti-tuberculous therapy initiation, and quantifying the incidence of clinically relevant ATDILI are directly actionable clinical goals. Identifying how frequently ATDILI arises in patients with normal versus deranged baseline LFTs can clarify who benefits most from intensified follow-up. Similarly, describing outcomes including recovery, mortality, and the need for regimen modification helps translate biochemical signals into patient-centered risk. As newer cohort evidence continues to refine the roles of alcohol, nutrition, anemia, and host genetics in ATDILI [6–9], locally generated data remain essential to adapt global guidance to regional realities. In TB-endemic settings with substantial background liver disease burden, an approach that integrates baseline LFT profiling, early surveillance, and risk-factor–anchored monitoring may reduce severe hepatotoxicity while preserving regimen effectiveness and completion rates [3,5,10].

Objectives

To evaluate liver function profiles and determine the incidence of anti-tuberculous drug–induced liver injury in patients starting anti-tuberculous therapy, comparing those with normal and abnormal baseline liver function tests.

To identify risk factors, assess hepatic adaptation, analyze clinical outcomes and mortality, and develop a practical monitoring strategy for early detection and prevention of severe hepatotoxicity.

MATERIAL AND METHODS

Study Design

This study was designed as a prospective observational cohort study conducted to evaluate the profile of liver function tests and the incidence of anti-tuberculous drug-induced liver injury in patients initiated on anti-tuberculous therapy. The study followed patients longitudinally from the initiation of therapy to assess biochemical changes, clinical outcomes, and mortality related to DILI.

Study Setting and Duration

The study was carried out in the Department of General Medicine at Government General Hospital, Kakinada, a tertiary care teaching hospital. The study duration was twelve months, from June 2023 to May 2024, which allowed adequate follow-up for detection of early and delayed hepatotoxicity associated with anti-tuberculous therapy.

Study Population

The study population comprised adult patients diagnosed with pulmonary or extra-pulmonary tuberculosis who initiated on anti-tuberculous therapy during the study period. Both outpatient and inpatient cases were included to reflect real-world clinical practice. Patients were enrolled consecutively to minimize selection bias.

Eligibility Criteria

Patients aged 18 years and above with microbiologically or clinically confirmed tuberculosis who were started on anti-tuberculous therapy were considered eligible for inclusion. Patients with HIV infection on hepatotoxic antiretroviral therapy, pregnant or postpartum women, patients receiving chemotherapy, individuals with known chronic liver disease, viral hepatitis, or those in a moribund state were excluded to avoid confounding liver injury unrelated to anti-tuberculous drugs.

Group Classification

Based on baseline liver function test values prior to initiation of anti-tuberculous therapy, patients were categorized into two groups. Group I included patients with normal baseline liver function tests, while Group II included patients with deranged baseline liver function tests. This stratification enabled comparison of incidence, severity, and outcomes of DILI between patients with and without pre-existing liver dysfunction.

Data Collection

After obtaining informed written consent, detailed demographic, clinical, and treatment-related data were collected using a structured case proforma. A thorough clinical examination was performed at baseline and during follow-up visits. Relevant history including alcohol consumption, diabetes mellitus, and other comorbidities was documented. Patients were monitored regularly for symptoms suggestive of hepatotoxicity such as jaundice, abdominal distension, altered sensorium, and constitutional symptoms.

Laboratory Evaluation

Baseline investigations included complete blood count, renal function tests, coagulation profile, viral markers, and comprehensive liver function tests comprising serum bilirubin, transaminases, alkaline phosphatase, gamma-glutamyl transferase, albumin, and globulin levels. Liver function tests were repeated periodically during follow-up or earlier if patients developed symptoms suggestive of liver injury. Imaging studies and microbiological investigations were performed as clinically indicated.

Definition and Assessment of DILI

Drug-induced liver injury was identified based on elevations in liver enzymes following initiation of anti-tuberculous therapy, after exclusion of alternative causes. The severity of DILI was graded using standardized criteria based on the degree of transaminase elevation. Hepatic adaptation was defined as transient elevation of liver enzymes with subsequent normalization despite continuation of therapy.

Outcome Measures

The primary outcome measure was the incidence of anti-tuberculous drug-induced liver injury. Secondary outcomes included severity grading of DILI, need for regimen modification, development of acute liver failure or acute-on-chronic liver failure, recovery, and mortality. Clinical predictors of adverse outcomes were also assessed.

Follow-up and Management

Patients diagnosed with DILI were managed according to standard clinical protocols, including withdrawal of offending drugs, modification of anti-tuberculous regimens, and supportive care. Sequential reintroduction of drugs was performed where appropriate under close biochemical monitoring. Patients were followed until recovery, death, or completion of the study period.

Statistical Analysis

All collected data were entered into a structured database and analyzed using appropriate statistical methods. Descriptive statistics were used to summarize demographic and clinical variables. Categorical variables were analyzed using the Chi-square test, while continuous variables were analyzed using the student's t-test. Statistical significance was considered at a p-value less than 0.05.

Ethical Considerations

The study was conducted after obtaining approval from the Institutional Ethics Committee. Written informed consent was obtained from all participants or their legally authorized representatives. Confidentiality of patient information was maintained throughout the study. Participants were informed of their right to withdraw from the study at any time without affecting their standard of care.

RESULTS

Baseline Characteristics of the Study Population

A total of 100 adult patients initiated on anti-tuberculous therapy were included in the study. Based on baseline liver function tests, 75 patients (75%) were categorized into Group I (normal baseline LFTs) and 25 patients (25%) into Group II (deranged baseline LFTs). Many patients in both groups were younger than 50 years, accounting for 70.7% in Group I and 64% in Group II. Patients aged 50 years or older constituted 29.3% of Group I and 36% of Group II.

Male predominance was observed overall, with a markedly higher male representation in Group II. The male-to-female ratio was 1.27:1 in Group I and 24:1 in Group II. Diabetes mellitus was present in 8 patients (10.7%) in Group I and 4 patients (16%) in Group II. Baseline demographic and clinical characteristics are summarized in Table 1.

Table 1. Baseline Characteristics of the Study Population

Variable	Group I (Normal LFTs) n=75	Group II (Deranged LFTs) n=25
Age ≥50 years	22 (29.3%)	9 (36.0%)
Age <50 years	53 (70.7%)	16 (64.0%)
Male sex	42 (56.0%)	24 (96.0%)
Female sex	33 (44.0%)	1 (4.0%)
Diabetes mellitus	8 (10.7%)	4 (16.0%)

Etiology and Baseline Biochemical Profile in Patients with Deranged LFTs

Among patients in Group II, alcohol-related liver disease was the predominant etiology for deranged baseline liver function tests, identified in 24 patients (96%). Non-alcoholic steatohepatitis accounted for one case (4%). Baseline hypoalbuminemia (serum albumin ≤2.5 g/dL) was observed in 4 patients (16%), while the remaining 21 patients (84%) had albumin levels above 2.5 g/dL. These findings are detailed in Table 2.

Table 2. Etiology and Baseline Biochemical Profile in Patients with Deranged LFTs (Group II)

Parameter	Number (n=25)	Percentage
Alcohol-related liver disease	24	96.0%
Non-alcoholic steatohepatitis	1	4.0%
Serum albumin ≤2.5 g/dL	4	16.0%
Serum albumin >2.5 g/dL	21	84.0%

Incidence and Severity of ATT-Induced Drug-Induced Liver Injury

Overall, 9 patients (9%) developed anti-tuberculous therapy–induced drug-induced liver injury during the study period. The incidence of DILI was 6.67% (5/75) in Group I and 16% (4/25) in Group II. Although the incidence was numerically higher in patients with deranged baseline LFTs, the difference did not reach statistical significance ($p = 0.157$).

Among DILI cases in Group I, WHO grade 2 and grade 3 liver injury were each observed in 40% of patients, while 20% had grade 1 injury. No grade 4 DILI was recorded. The distribution of incidence and severity of DILI across both groups is shown in Table 3.

Table 3. Incidence and Severity of ATT-Induced Drug-Induced Liver Injury

A. Incidence of DILI

Group	DILI cases / Total	Incidence (%)
Group I	5 / 75	6.67%
Group II	4 / 25	16.0%
p-value		0.157

B. Severity of DILI (WHO Grading)

WHO Grade	Number (n=5)	Percentage
Grade 1	1	20.0%
Grade 2	2	40.0%
Grade 3	2	40.0%
Grade 4	0	0%

Risk Factors Associated With DILI

Diabetes mellitus was significantly associated with the development of DILI. Among patients with diabetes, 33.3% developed DILI compared to a significantly lower proportion among non-diabetics (p = 0.0016). Alcohol use was strongly associated with DILI, particularly in Group II, where all but one patient had alcohol-related liver disease at baseline. Older age (≥50 years) and deranged baseline liver function tests were also associated with higher rates of DILI and adverse outcomes. Risk factor associations are summarized in Table 4.

Table 4. Risk Factors Associated with Development of DILI

Risk factor	DILI Present	DILI Absent	p-value
Diabetes mellitus	4	5	0.0016
No diabetes	5	86	
Alcohol use	4	20	—
No alcohol use	1	70	
Age ≥50 years (DILI cases)	1	—	—
Age <50 years (DILI cases)	3	—	—
Deranged baseline LFTs	4	21	

Note: Odds ratios calculated where applicable; alcohol and age trends interpreted descriptively due to small numbers.

Clinical Outcomes and Mortality

Of the 9 patients who developed DILI, 7 patients (77.8%) recovered following withdrawal or modification of anti-tuberculous therapy, while 2 patients (22.2%) died. The overall mortality rate in the entire cohort was 2%. DILI-related mortality was 20% (1/5) in Group I and 25% (1/4) in Group II. These outcomes are presented in Table 5.

Table 5. Clinical Outcomes and Mortality Among Patients With DILI

Group	DILI cases (n)	Recovered n (%)	Deaths n (%)
Group I	5	4 (80.0%)	1 (20.0%)
Group II	4	3 (75.0%)	1 (25.0%)
Total	9	7 (77.8%)	2 (22.2%)

Gender- and Diabetes-Specific Outcomes in DILI

In Group I, the single DILI-related death occurred in a female patient, while all male patients with DILI recovered; however, this association was not statistically significant (p > 0.05). In Group II, the DILI-related death occurred exclusively among male patients, with a statistically significant association between male sex and mortality (p < 0.001). No DILI-related deaths were observed among diabetic patients in either group. Gender- and diabetes-specific outcomes are summarized in Table 6.

Table 6. Gender- and Diabetes-Specific Outcomes in DILI

Subgroup	Recovered	Death	p-value
Group I – Male	2	0	>0.05
Group I – Female	2	1	
Group II – Male	3	1	<0.001
Group II – Female	0	0	
Diabetics (all DILI cases)	4	0	—
Non-diabetics (all DILI cases)	3	2	

Hepatic Adaptation, Treatment Modification, and Clinical Presentation

Hepatic adaptation, defined as transient elevation of liver enzymes with subsequent normalization despite continuation of therapy, was observed more frequently in Group II than in Group I. The odds of hepatic adaptation were significantly higher in Group II (odds ratio 0.1102; 95% CI 0.0377–0.3226; p = 0.0001).

Among DILI patients in Group II, alcohol-related cases accounted for all deaths, with a DILI-related mortality of 25% among alcohol users. Patients who required modification of the anti-tuberculous regimen recovered in all cases.

Clinically, jaundice and ascites were the most frequent presenting features of DILI in both groups, observed in 60% of Group I and 100% of Group II cases. Hepatic encephalopathy was present in 40% of Group I and all Group II patients with DILI. In Group II, mortality was highest among patients presenting with hepatic encephalopathy and ascites. Patients aged 50 years or older with DILI had a higher mortality compared to younger patients. These findings are detailed in Table 7.

Table 7. Hepatic Adaptation, Treatment Modification, and Clinical Presentation of DILI

A. Hepatic Adaptation

Group	Adaptation Present	Adaptation Absent	Odds Ratio (95% CI)	p-value
Group I	8	67	0.1102 (0.0377–0.3226)	0.0001
Group II	13	12		

B. Treatment Modification and Outcome (Group II DILI)

Parameter	Recovered	Death
Alcohol-related DILI	3	1
Regimen modified	2	0

C. Clinical Presentation and Outcome (Group II DILI)

Clinical feature	Recovered	Death	Total
Jaundice	1	3	4
Ascites	1	3	4
Pedal edema	1	1	2
Hepatic encephalopathy	1	3	4

DISCUSSION

In this prospective cohort of 100 adults initiated on anti-tuberculous therapy (ATT), the overall incidence of anti-tuberculosis drug–induced liver injury (ATDILI) was 9%, with a clear gradient according to baseline hepatic status. Patients with normal baseline liver function tests (Group I) experienced an incidence of 6.67%, whereas those with deranged baseline LFTs (Group II) demonstrated a higher incidence of 16%. This pattern reinforces the concept that ATDILI is not a uniform adverse effect but a risk-stratified phenomenon, in which pre-treatment hepatic reserve and host vulnerability shape both the likelihood and clinical course of hepatotoxicity. Contemporary DILI guidance emphasizes that baseline biochemical abnormalities represent clinically meaningful susceptibility markers rather than incidental findings, influencing both the threshold for injury and the margin of safety during exposure to hepatotoxic drugs. [11]

The higher ATDILI incidence observed in Group II is biologically plausible given the etiological composition of this cohort, in which alcohol-related liver disease accounted for 96% of baseline LFT derangements. Chronic alcohol exposure is known to induce oxidative stress, impair mitochondrial function, and disrupt hepatic adaptive pathways, all of which lower tolerance to toxic drug intermediates. Epidemiological syntheses consistently identify alcohol use and underlying liver disease as major determinants of DILI risk across drug classes, including first-line anti-tuberculous agents such as isoniazid and pyrazinamide. [21] Importantly, although ATT regimens in Group II were individualized according to baseline AST, ALT, and bilirubin levels, hepatotoxicity was not eliminated, suggesting that regimen tailoring may mitigate but cannot fully offset intrinsic host susceptibility once hepatic reserve is compromised. This observation supports the view that host factors often dominate risk once vulnerability is established. [12]

Despite the numerically higher ATDILI incidence in Group II, the between-group difference did not reach statistical significance ($p = 0.157$). This likely reflects limited statistical power, as only nine ATDILI events occurred overall. In such contexts, reliance solely on hypothesis testing may obscure clinically meaningful trends. Contemporary DILI methodology increasingly recommends interpretation based on effect direction, biological plausibility, and external consistency, alongside confidence intervals and absolute risk differences, particularly when event rates are low. [14] Within this framework, the observed incidence gradient remains clinically relevant and concordant with existing evidence.

Mortality patterns in this cohort provide important clinical insights. While overall mortality in the entire study population was low (2%), the case-fatality rate among patients who developed ATDILI was substantial (22.2%). Group-specific DILI-related mortality was comparable between patients with normal and deranged baseline LFTs (20% and 25%, respectively), indicating that once ATDILI occurs, outcomes can be poor regardless of baseline hepatic status. This aligns with broader DILI literature demonstrating that progression from biochemical injury to jaundice, encephalopathy, or liver failure is associated with sharply increased short-term mortality, emphasizing the critical importance of early detection and prompt withdrawal of offending agents. [11]

Clinical presentation strongly influenced outcomes. In Group II, jaundice, ascites, and hepatic encephalopathy clustered in not-recovered patients, suggesting progression to decompensated liver injury. Within chronic liver disease paradigms, these features reflect systemic inflammation and impaired hepatic reserve, conditions that predispose to acute-on-chronic liver failure (ACLF). Contemporary ACLF frameworks recognize drug toxicity as a potent precipitating factor capable of converting limited hepatic injury into multisystem dysfunction.

[19] From an ATT safety perspective, these findings underscore that baseline stratification alone is insufficient; dynamic monitoring and rapid response to early signs of clinical decompensation are decisive determinants of survival. [20]

Diabetes mellitus emerged as a strong risk factor for ATDILI in this cohort ($p = 0.0016$), with one-third of diabetic patients developing liver injury. Although no diabetes-associated ATDILI deaths occurred, the markedly increased incidence highlights metabolic vulnerability as a key modifier of hepatotoxic risk. Growing epidemiological and mechanistic evidence links metabolic dysfunction and steatotic liver changes to impaired hepatic resilience, altered drug metabolism, and heightened inflammatory signaling, thereby reducing tolerance to hepatotoxic exposures. [22] While formal metabolic phenotyping was beyond the scope of this study, the observed association supports routine metabolic risk assessment at baseline and closer early LFT surveillance in diabetic patients receiving ATT.

Sex-related findings should be interpreted cautiously. In Group I, a higher proportion of ATDILI cases occurred in females, and the only fatality in this group was female, whereas in Group II all patients were male and the single fatality occurred in a male patient. However, the extreme sex imbalance in Group II limits inference regarding sex-specific susceptibility. Although sex differences in adverse drug reactions and DILI have been reported in the literature, influenced by pharmacokinetic, hormonal, and immunological factors, the present data do not support definitive conclusions. [24] Rather, these findings highlight the need for balanced enrollment and adjusted analyses in future studies.

An important conceptual contribution of this study is the evaluation of hepatic adaptation. Hepatic adaptation was significantly more frequent in Group II than in Group I, despite higher ATDILI incidence and worse outcomes in the former. This apparent paradox is consistent with current DILI paradigms, which recognize that transient enzyme elevations may reflect adaptive responses rather than progressive injury. Adaptation may coexist with heightened susceptibility, particularly in chronically stressed livers where biochemical fluctuations occur against a backdrop of limited functional reserve. [15] In this context, the higher adaptation rate in Group II likely reflects ongoing hepatic stress rather than protective resilience, consistent with the finding that adaptation did not independently predict prognosis.

Regimen modification emerged as a clinically actionable intervention. All patients in Group II who underwent ATT regimen modification recovered, whereas mortality occurred exclusively among alcohol-associated DILI cases without successful mitigation. This reinforces a central principle of TB management: hepatotoxicity necessitates structured interruption and reassessment rather than abandonment of therapy. With evolving TB regimens emphasizing shorter courses and alternative drug combinations, hepatic safety remains a critical determinant of tolerability and completion. [16–18] These findings support the implementation of locally adapted monitoring algorithms grounded in baseline risk factors such as alcohol use, diabetes, hypoalbuminemia, and older age, with early biochemical follow-up to enable timely intervention. [13]

Age-related trends further support this approach. Although most participants were younger than 50 years, mortality among ATDILI cases in Group II aged 50 years or older was disproportionately high. While based on small numbers, this observation aligns with broader evidence identifying older age as a vulnerability factor for severe DILI outcomes across multiple drug classes. [21] Intensified early monitoring in older patients with baseline hepatic derangement appears justified.

Limitations

This study was conducted at a single center with a modest sample size and limited outcome events, restricting statistical power for subgroup analyses. The marked sex imbalance in Group II constrained interpretation of sex-specific effects. Baseline liver disease characterization relied on routine clinical and laboratory assessment rather than standardized fibrosis staging, potentially introducing heterogeneity within the deranged LFT group. Structured causality assessment tools and detailed drug exposure metrics were not applied, limiting phenotypic resolution. Additionally, the follow-up schedule for serial LFT monitoring was not standardized, constraining precise latency analysis.

Future Implementation

Future research should adopt multicentre designs with larger cohorts to enhance event capture and representativeness, ensure balanced sex distribution, and systematically quantify alcohol exposure, metabolic risk, nutritional status, and fibrosis burden. A pragmatic monitoring pathway can be operationalized, incorporating baseline risk stratification at ATT initiation, scheduled early LFT assessments in high-risk patients, defined clinical triggers for urgent evaluation, and standardized protocols for regimen modification and re-challenge. Integration of structured causality assessment and detailed drug exposure data would enable development of locally validated risk-prediction models and further refine ATT safety strategies.

CONCLUSION

Anti-tuberculous therapy–induced liver injury remains a clinically significant complication, particularly among patients with pre-existing hepatic dysfunction, alcohol use, and metabolic comorbidities. Although baseline liver function abnormalities increase susceptibility to hepatotoxicity, severe outcomes can occur regardless of initial hepatic status once liver injury develops. Early identification of high-risk patients, close biochemical and clinical monitoring, and prompt modification of anti-tuberculous regimens are critical to preventing progression to severe liver injury and reducing mortality. A risk-based, targeted monitoring approach offers a practical strategy to enhance treatment safety while maintaining effective tuberculosis control.

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