

Frequency of Deranged Liver Enzymes in Patients Receiving Anti-Tuberculous Therapy

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ABSTRACT

Objective: To determine the frequency of deranged liver enzymes in patients receiving ATT.

Background: Drug-induced liver injury is a common complication of anti-tuberculous therapy (ATT) and may lead to treatment interruption and poor outcomes. It ranges from mild liver enzyme elevation to severe hepatic dysfunction. Early detection is essential to ensure patient safety.

Methodology: This prospective Observational study conducted after approval of study during 15 december 2025 to 15 march 2026 at Prince Fahad Hospital Dalbandin. All patients fulfilling inclusion criteria at Outpatient department. A total of 126 patients receiving ATT were included using non-probability consecutive sampling. Liver function tests were performed at baseline and after 8 weeks. Data were analyzed using SPSS version 22, and $p \leq 0.05$ was considered significant.

Results: The mean age was 38.23 ± 12.56 years, with 57.1% aged 14–40 years. Males were 57.9% of the sample. Overall, 24.6% of patients developed deranged liver enzymes. Elevated ALT was seen in 19.0%, AST in 9.5%, and ALP in 10.3% of patients.

Conclusion: Nearly one-quarter of patients receiving ATT developed liver enzyme derangement. Regular monitoring of liver function is recommended for early detection and prevention of hepatotoxicity.

Keywords: Anti-tuberculous therapy, liver enzymes, hepatotoxicity, tuberculosis

How to Cite: Ghayas A, Inam U, Aman M. Frequency of Deranged Liver Enzymes in Patients Receiving Anti-Tuberculous Therapy. Bolan Journal of Medical and Allied Health Sciences. 2026 Apr;2(1):28-33.

INTRODUCTION

When treating tuberculosis (TB), drug-induced liver damage (DILI) is a significant clinical issue. Hepatotoxicity was the most frequent severe side effect of anti-tubercular treatment (ATT), requiring medication cessation in 11% of patients, followed by exanthem (6%) and arthralgia (2%), according to a retrospective examination of 519 TB patients.¹

DILI may cause severe morbidity and mortality, poor treatment adherence, and acute liver failure (ALF) or acute-chronic liver failure (ACLF). Since there are no reliable diagnostic tests, DILI is difficult to detect; instead, it is a diagnosis of exclusion made by definitively ruling out infectious and other possible noninfectious causes.

DILI is often categorised as idiosyncratic and intrinsic (or direct). Drugs that are intrinsically harmful to the liver are the cause of intrinsic DILI. This kind of DILI has a brief onset period of hours to days, is often dose-related and is predictable. Hazardous free radicals cause hepatocyte necrosis in areas that are furthest from the hepatic arterioles, where metabolism is quickest and antioxidant detoxifying ability is lowest.²

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Manuscript Received: 1 March 2026, Revised: 15 March 2026, Accepted: 1 April 2026

However, medications that are not intrinsically harmful to the liver may elicit idiosyncratic DILI. It might take days, weeks, or months for this kind of DILI to appear, and it is unexpected and dose-independent. Instead of being zonal, as is often seen with predicted DILI, hepatocyte necrosis is extensively spread across hepatic lobules.³

The most frequent cause of idiosyncratic DILI globally is ATT-related DILI (ATT-DILI).⁴ Given the prevalence of TB in many Asian nations, ATT is the most frequent cause of drug-induced ALF and DILI.^{5,6} The second most frequent medication that causes ACLF is ATT.⁷

Because DILI is defined differently over time, the incidence of ATT-DILI varies. Hepatitis affected 2.3% to 28% of patients with ATT-DILI,⁸⁻¹⁰ and acute liver failure (ALF) affected 25% of patients, with overall and ALF death rates of 22.7% and 69.6%, respectively.⁶ ATT-related ALF, which has a more aggressive course, accounts for 5.7% of all ALF at a tertiary facility with a death rate more than 60%.¹¹⁻¹⁵

Given the high burden of tuberculosis and widespread use of ATT, drug-induced liver injury remains a significant yet under-recognized cause of treatment interruption and adverse outcomes. This study aims to determine the frequency of ATT-related DILI to support early detection and improve patient management.

METHODOLOGY

This Prospective Observational study was conducted at the Outpatient Department of Prince Fahad Bin Sultan Hospital Dalbandin from 15 December 2025 to 15 March 2026. Prior ethical approval was obtained from the institutional review board.

A sample size of 126 patients was calculated using the WHO sample size calculation formula, considering the prevalence of deranged liver enzymes as 20%, a margin of error of 7%, and a confidence level of 95%. Non-probability consecutive sampling techniques were employed.

INCLUSION CRITERIA

Patients aged 14 to 65 years of either gender who had been receiving anti-tuberculous therapy (ATT) for a minimum duration of 8 weeks, were included. The ATT regimen consisted of first-line drugs namely

isoniazid, rifampicin, ethambutol, and pyrazinamide.

EXCLUSION CRITERIA

Patients with pre-existing liver enzyme derangement prior to initiation of ATT (ALT >40 IU/L, AST >50 IU/L) were excluded. Additionally, patients with known liver diseases—including acute viral hepatitis (ALT >10 times normal), chronic viral hepatitis (confirmed by liver biopsy), alcoholic liver disease (AST:ALT ratio of 2:1 with biopsy confirmation), and autoimmune hepatitis (positive ANA, ASMA, and biopsy findings)—were excluded. Patients with suspected malignancies such as hepatocellular carcinoma or metastatic liver disease (diagnosed via alpha-fetoprotein levels and liver biopsy) were also excluded to minimize confounding and bias.

Written informed consent was obtained from all participants prior to enrollment. Patients meeting the inclusion criteria were recruited from the outpatient department based on documented history of tuberculosis and ongoing ATT, verified through medical records. All participants were interviewed and examined in a confidential setting to ensure privacy and minimize social stigma. Baseline liver function tests (LFTs) were recorded at initiation (week 0) and repeated at 8 weeks. Blood samples were processed at the institutional laboratory of Prince Fahad Bin Sultan Hospital Dalbandin.

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26. Quantitative variables such as age were presented as mean $\pm$ standard deviation or median (interquartile range), depending on normality assessed using the Shapiro–Wilk test. Qualitative variables including gender, residence, family history of liver disease, diabetes, hypertension, obesity, employment status, education level, and liver enzyme status (ALT, AST, ALP, and overall derangement) were presented as frequencies and percentages.

Stratification was performed with respect to age, gender, residence, family history of liver disease, diabetes, hypertension, employment status, and education level to assess their effect on the outcome variable (deranged liver enzymes). Post-stratification analysis was conducted using chi-square test or Fisher's exact test, as appropriate. A p-value of ≤ 0.05 was considered statistically significant.

RESULTS

A total of 126 patients fulfilling the inclusion criteria were enrolled in this study. The mean age of the participants was 38.23 ± 12.56 years. Most patients, 72 (57.1%), were aged between 14 and 40 years, while 54 (42.9%) were between 41 and 65 years.

Of the total participants, 73 (57.9%) were male and 53 (42.1%) were female, showing a male predominance.

Regarding residence, 44 (34.9%) patients belonged to urban areas, whereas 82 (65.1%) were from rural areas. A family history of liver disease was present in 24 (19.0%) patients, while 102 (81.0%) had no such history. Diabetes mellitus was observed in 34 (27.0%) patients, whereas 92 (73.0%) were non-diabetic. Hypertension was present in 26 (20.6%) patients and absent in 100 (79.4%). Obesity was reported in 45 (35.7%) patients, while 81 (64.3%) were non-obese. Regarding socioeconomic characteristics, 67 (53.2%) patients were employed, whereas 59 (46.8%) were unemployed. Educational status showed that 57 (45.2%) patients had education up to matric level, while 69 (54.8%) had graduation or higher levels of education (Table I).

With respect to liver enzyme levels, elevated alanine aminotransferase (ALT >40 IU/L) was observed in 24 (19.0%) patients, while 102 (81.0%) had normal ALT levels. Elevated aspartate aminotransferase (AST >40 IU/L) was noted in 12 (9.5%) patients, whereas 114 (90.5%) had normal AST levels. Similarly, elevated alkaline phosphatase (ALP >180 IU/L) was found in 13 (10.3%) patients, while 113 (89.7%) had normal ALP levels (Table II).

Overall, 31 (24.6%) patients had deranged liver enzymes, whereas 95 (75.4%) maintained normal liver enzyme levels while receiving anti-tuberculous therapy (ATT) (Figure 1).

Stratification analysis showed that age ($p = 0.591$), residence ($p = 0.340$), employment status ($p = 0.063$), and education level ($p = 0.670$) were not significantly associated with deranged liver enzymes.

However, a significant association was observed with gender ($p = 0.038$), with females showing a higher frequency of liver enzyme derangement. Similarly, diabetes ($p = 0.031$), hypertension ($p = 0.001$), and obesity ($p = 0.001$) were significantly associated with

an increased risk of hepatotoxicity. Family history of liver disease also showed statistical significance ($p = 0.001$); however, this finding should be interpreted cautiously, as no cases of deranged liver enzymes were observed in that group (Table III).

Table I: distribution of Residence, family history of liver disease, diabetes, hypertension, obesity, employment status & education. (n=126)

Variables		Frequency (%)
Residence	Urban	44 (34.9%)
	Rural	82 (65.1%)
Family history of liver disease	Yes	24 (19.0%)
	No	102 (81.0%)
Diabetes	Yes	34 (27.0%)
	No	92 (73.0%)
Hypertension	Yes	26 (20.6%)
	No	100 (79.4%)
Obesity	Yes	45 (35.7%)
	No	81 (64.3%)
Employment status	Employed	67 (53.2%)
	Unemployed	59 (46.8%)
Education	Upto matric	57 (45.2%)
	Graduation and above	69 (54.8%)
	Total	126 (100.0%)

Table II: distribution of ALT, AST & ALP. (n=126)

Variables		Frequency (%)
ALT	> 40 IU/L	24 (19.0%)
	≤ 40 IU/L	102 (81.0%)
AST	> 40 IU/L	12 (9.5%)
	≤ 40 IU/L	114 (90.5%)
ALP	> 180 IU/L	13 (10.3%)
	≤ 180 IU/L	113 (89.7%)
	Total	126 (100.0%)

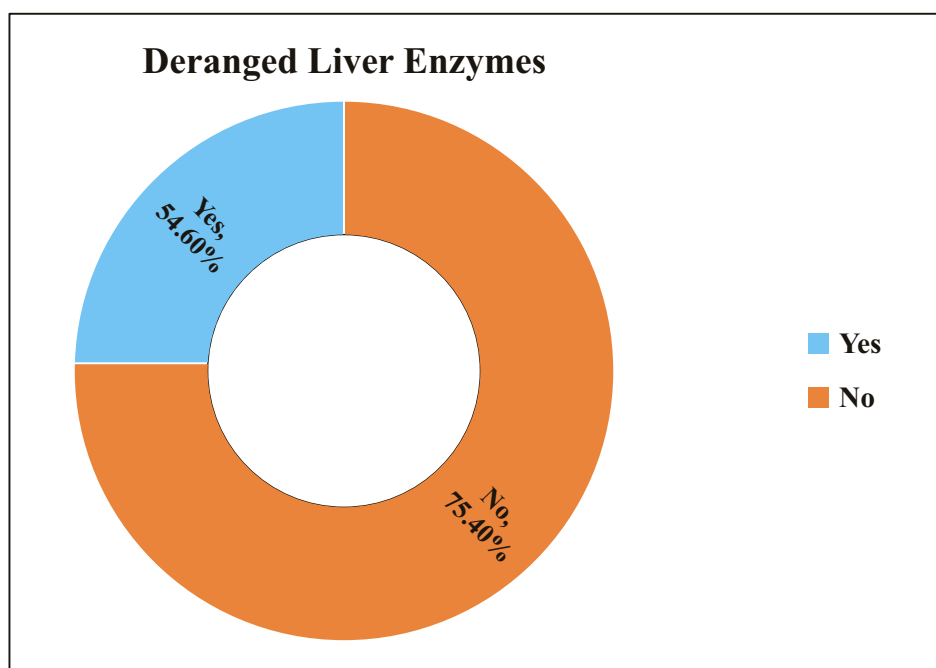


Figure 1: Frequency of Deranged Liver Enzymes in patients taking ATT. (n=126)

Table III: Stratification of DLE with different variables.

Variables		Deranged Liver Enzymes		Total	P - Value
		Yes	No		
Age	14 - 40 Years	19	53	72	0.591
	41 - 65 Years	12	42	54	
Gender	Male	13	60	73	0.038
	Female	18	35	53	
Residence	Urban	13	31	44	0.34
	Rural	18	64	82	
Family history of liver disease	Yes	0	24	24	0.001
	No	31	71	102	
Diabetes	Yes	13	21	34	0.031
	No	18	74	92	
Hypertension	Yes	19	7	26	0.001
	No	12	88	100	
Obesity	Yes	19	26	45	0.001
	No	12	69	81	
Employment Status	Employed	12	55	67	0.063
	Unemployed	19	40	59	
Education	Upto matric	13	44	57	0.670
	Graduation and above	18	51	69	
Total		31	95	126	

DISCUSSION

This Prospective observational study assessed the frequency of deranged liver enzymes in patients receiving anti-tuberculous therapy (ATT) at a tertiary care hospital. Out of 126 patients, 31 (24.6%) developed deranged liver enzymes, indicating that approximately one-quarter of patients on ATT experienced hepatotoxicity. This finding is consistent with previous literature, where the prevalence of ATT-induced hepatotoxicity ranges between 10% and 30%.^{11,12}

The demographic profile of this study showed a predominance of males (57.9%), younger age group (57.1% aged 14–40 years), and rural population (65.1%), which aligns with regional patterns of tuberculosis distribution. However, no significant association was observed between liver enzyme derangement and age or residence, suggesting that hepatotoxicity may occur irrespective of these demographic factors.

A significantly higher frequency of deranged liver enzymes was observed among females ($p = 0.038$), indicating a possible increased susceptibility to ATT-induced hepatotoxicity. Similarly, metabolic comorbidities including diabetes ($p = 0.031$), hypertension ($p = 0.001$), and obesity ($p = 0.001$) were significantly associated with liver enzyme abnormalities. These findings are supported by existing evidence suggesting that metabolic disorders increase vulnerability to drug-induced liver injury due to altered hepatic metabolism and underlying inflammatory states.

No significant association was found with employment status or educational level, indicating that socioeconomic factors had limited influence on hepatotoxicity in this cohort. Although family history of liver disease showed statistical significance ($p = 0.001$), this finding should be interpreted cautiously, as no cases of deranged liver enzymes were observed in that group, suggesting possible sample distribution bias.

The hepatotoxic effects observed in this study are likely attributable to commonly used ATT drugs such as Isoniazid, Rifampicin, and Pyrazinamide, which are known to cause liver injury through various mechanisms including oxidative stress and enzyme induction.

These findings highlight the importance of routine liver function monitoring, particularly in patients with metabolic risk factors, to ensure early detection and prevention of severe hepatotoxicity.

STUDY LIMITATIONS

This study has several limitations. Being a single-center cross-sectional study, the findings may not be generalizable to wider populations. The cross-sectional design limits assessment of temporal changes in liver enzyme levels while ATT. Additionally, important confounding factors such as alcohol consumption, drug interactions, and viral hepatitis status were not fully explored. The absence of longitudinal follow-up may have underestimated the true burden of hepatotoxicity.

The study had a small sample size and was conducted at a single center, so the results may not represent the general population. Also, because this was an observational study, it can show association only and cannot prove cause and effect.

CONCLUSION

Liver enzyme derangement was common in patients receiving ATT. Female gender and metabolic diseases were important risk factors. Regular monitoring is necessary to prevent complications.

ETHICAL APPROVAL

Ethical approval was obtained from the IRB of Prince Fahad Hospital (Approval No. ERC-2025/A-601). All study procedures were carried out according to ethical research standards.

ACKNOWLEDGMENT

The authors would like to acknowledge the support and cooperation of the administration and staff of Prince Fahad Hospital for facilitating this research. We also thank all study participants for their valuable contribution and participation in the study.

CONFLICT OF INTEREST

The authors declare no conflicts of interest. The research was conducted independently without any personal, financial, or professional influence on study design, analysis, or reporting.

FUNDING DISCLOSURE

No external funding was received. All research-related

expenses were borne by the authors without financial support from any institution or organization.

AUTHORS' CONTRIBUTIONS

AG: Conceptualization, supervision, resources, writing.

UI: Investigation, writing – original draft.

MA: Investigation, writing and editing.

TK: statistical analysis, interpretation of results, and preparation of tables and figures.

KJ: patient recruitment, data entry, and proofreading of the final manuscript.

LS: Literature review, data collection, manuscript review, and proofreading.

All authors have read and agreed to the published version of the manuscript.

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