Evaluation of Drug-Induced Liver Injury in Patients Receiving Anti-tuberculosis Medications and Subsequent Management

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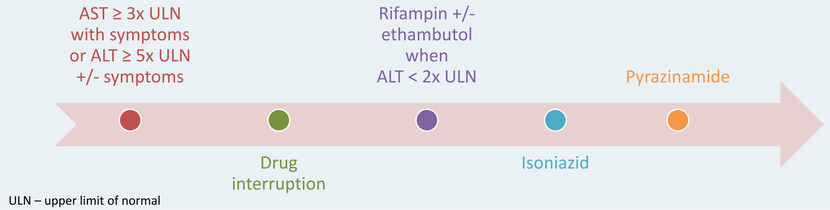
INTRODUCTION

- The risk of drug-induced liver injury (DILI) with anti-tubercular medications ranges from 5 – 33%.
- Risk factors associated with DILI include older age, advanced tuberculosis, heavy alcohol intake, and prior hepatic impairment.
- Patients with DILI may be asymptomatic or may present with fever, nausea, vomiting, anorexia, and lethargy.
- The Infectious Diseases Society of America and American Thoracic Society tuberculosis treatment guidelines provide recommendations regarding regimen interruptions and re-initiation of therapy for patients who develop DILI.



ULN – upper limit of normal

OBJECTIVES

Primary Objective: To describe the incidence of hepatoxicity associated with anti-tuberculous therapy, the management of DILI, and the re-initiation of therapy in patients with DILI.

METHODS

Study design: single center retrospective observational chart review that was deemed to be a quality improvement project by the Northwell IRB

Study period: July 1, 2017 – February 17, 2022

Population:

Inclusion Criteria	• Prescribed pyrazinamide during their hospitalization since isoniazid can be used as monotherapy and ethambutol/rifampin may be used for other indications • Intensive phase of therapy for drug-susceptible TB
Exclusion Criteria	• Age < 18 years

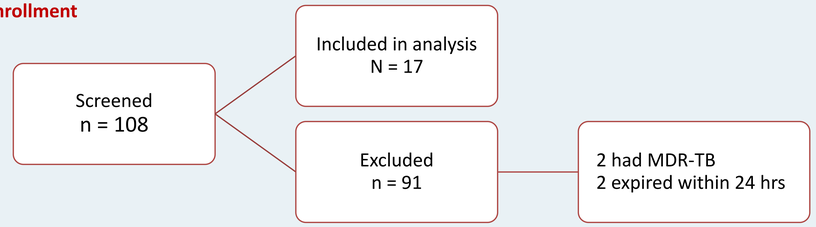
Data collection: Utilized the electronic medical record to screen subjects, collect demographics, concomitant hepatotoxic medications, laboratory values (e.g., alanine aminotransferase [ALT], aspartate aminotransferase [AST]), timing of drug interruption and sequence/timing of re-initiation.

Statistical analysis:

- Descriptive statistics were utilized to analyze the data.

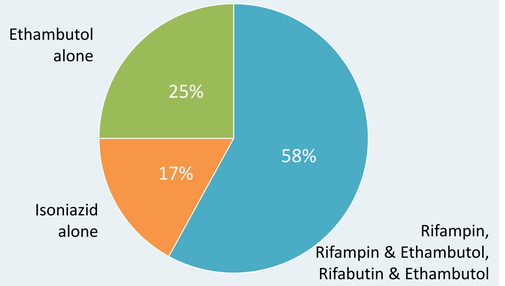
RESULTS

Enrollment



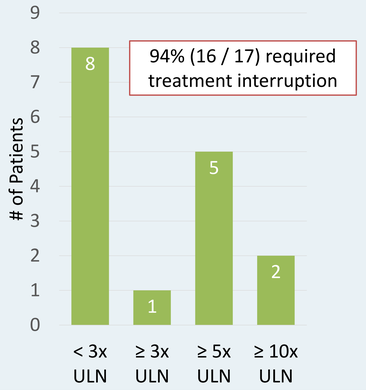
Baseline Characteristics	N = 17
Mean age (years)	57 ± 20
Sex, Female – n (%)	9 (53%)
Weight in kilograms (mean ± SD)	63 ± 15
Comorbidities – n (%)	
HIV	1 (6%)
Hepatitis, liver disease, or prior TB-DILI	0 (0%)
Alcohol consumption	0 (0%)
Length of hospital day, days (mean ± SD)	41 ± 31
Alanine Aminotransferase (U/L)	41 ± 43
Aspartate Aminotransferase (U/L)	55 ± 63
Alkaline Phosphatase (U/L)	116 ± 62
Total Bilirubin (mg/dL)	0.5 ± 0.3
Albumin (g/dL)	3.5 ± 0.7
Platelets (K/µL)	323 ± 138
Creatinine (mg/dL)	1.4 ± 1.6
	n = 11
Prothrombin Time (sec)	13.8 ± 1.3
INR	1.2 ± 0.1

Sequence of Re-initiation

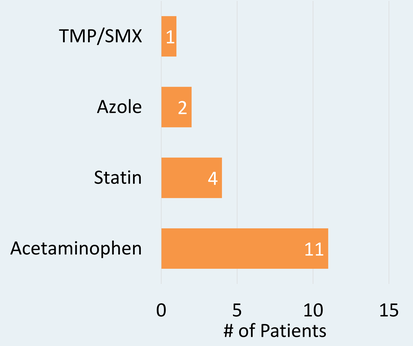


Timeframe to restart first drug (mean ± SD): 8 ± 4 days

Timing of Regimen Interruption



Concomitant Hepatotoxic Drugs



STUDY LIMITATIONS

- Small sample size
- Retrospective design
- Guidelines define DILI and base their recommendations for discontinuation and re-initiation on ALT values only
  - Does not factor in other lab values such as bilirubin, AST, alkaline phosphatase
- Did not account for management of patients in conjunction with Department of Health providers

CONCLUSION

- The rate of DILI was 15.7% in our patient population.
- None of the patients that developed DILI had any prior history of hepatic disease, prior DILI, or alcohol use.
- A total of 76.4% of patients with DILI were receiving concomitant hepatotoxic agents.
- Management of DILI related to anti-tubercular medications can further be standardized in our institution (e.g., timing of and selection of agents to reinitiate).
- A review of concomitant hepatotoxic medications can also be performed to minimize the risk of DILI for those prescribed TB treatment.