

Patterns of Medication Use Among Adult Patients with Elevated Serum ALT Levels in Patients with NAFLD: TARGET-NASH



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INTRODUCTION

- Polypharmacy is common among patients with nonalcoholic fatty liver disease (NAFLD).
- Relationships among polypharmacy, potential drug induced liver injury (DILI), elevated liver enzymes, and severity of liver disease are unclear

OBJECTIVE

- This work evaluated patterns of medication use by liver disease severity and the association between medication use and serum ALT elevation

METHODS

Cohort

- TARGET-NASH is an ongoing longitudinal, observational cohort of >3,700 patients with NAFLD managed according to local practice standards at 55 academic and community sites in the United States
- Patient narratives, laboratory, pathology, and imaging data are extracted and stored in a secured database. Patient reported outcomes (PRO) measures as well as blood samples were collected annually

Study Population

- 3,284 patients ≥ 18 years enrolled in TARGET-NASH between August 2016 and October 2018 were included in the study

Variable Definitions

Patients were classified by

- Severity of liver disease (NAFLD Cirrhosis, NASH, NAFL)
- Serum ALT levels ≤50 U/L or >50 U/L at enrollment
- Medication use: Any use of medications by at least 10% of patients within one year of enrollment

Site Type
▲ Academic
▼ Community



Statistical Methods

- Patterns of medication use were estimated within severity of liver disease using hierarchical cluster analysis
- The odds of ALT elevation and 95% confidence intervals were estimated by medication class

RESULTS

Patient Characteristics at enrollment

- 3,284 patients ≥ 18 years
 - 39% NAFLD cirrhosis, 40% NASH, and 21% NAFL
 - Median age was 56.9 years, and median BMI was 33.2 kg/m²
 - 59% were female
 - 66% were receiving treatment at academic sites
 - 59% had private insurance, 32% had Medicare, and 13% had Medicaid
 - 74% were White, 5% were African American, and 12% were Hispanic
- Multiple medications were associated with a decrease in the odds of having an ALT>50 U/L (Figure 1)
 - Users of statins were 38% less likely to have an ALT >50 U/L
 - Vitamin D was also associated with a 27% decrease in the odds of higher ALT level

Figure 1. Odds of Having an ALT > 50 U/L Among All Patients with NAFLD Who Are Users of a Specific Medication Class Compared to Non-users

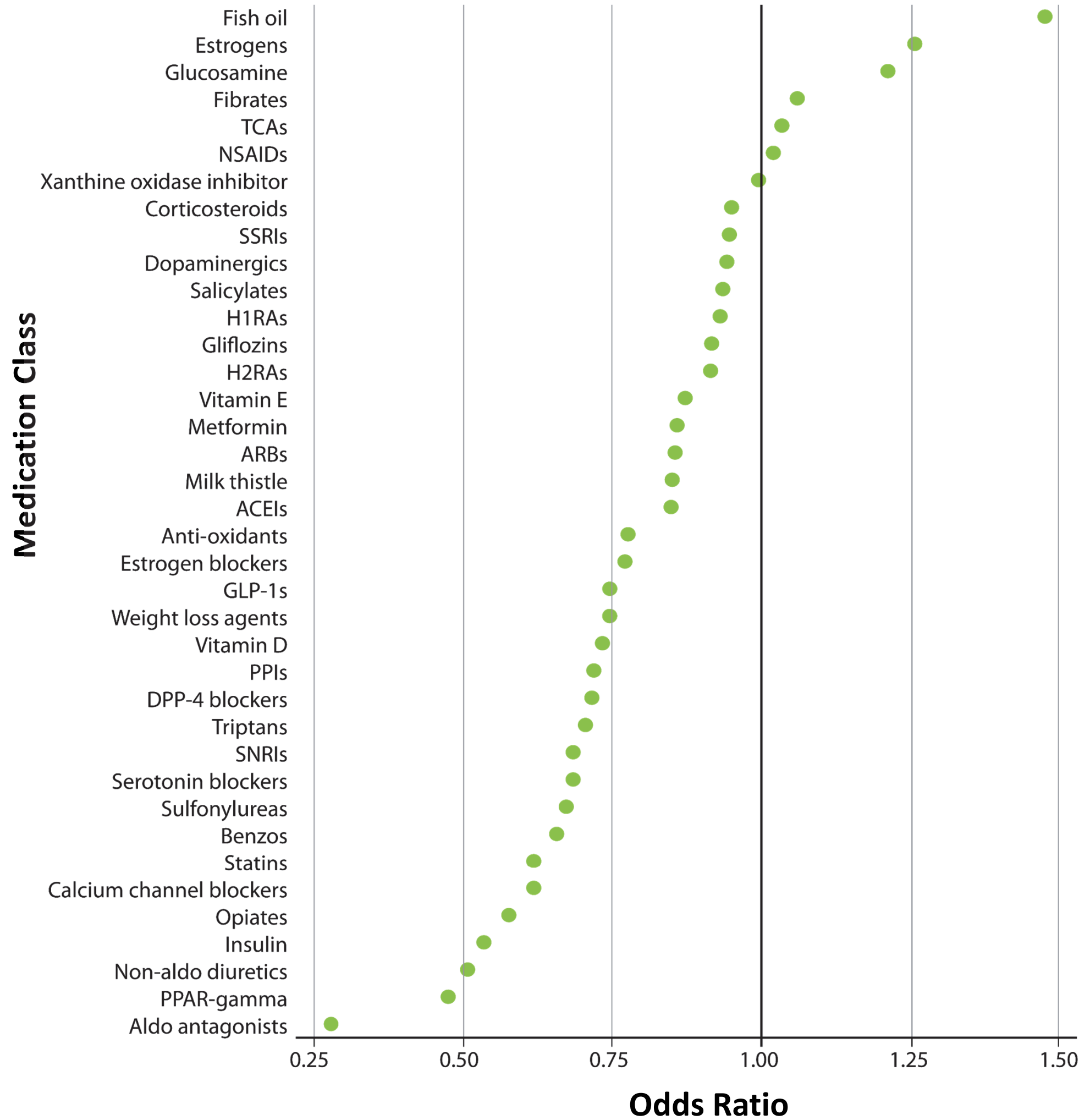
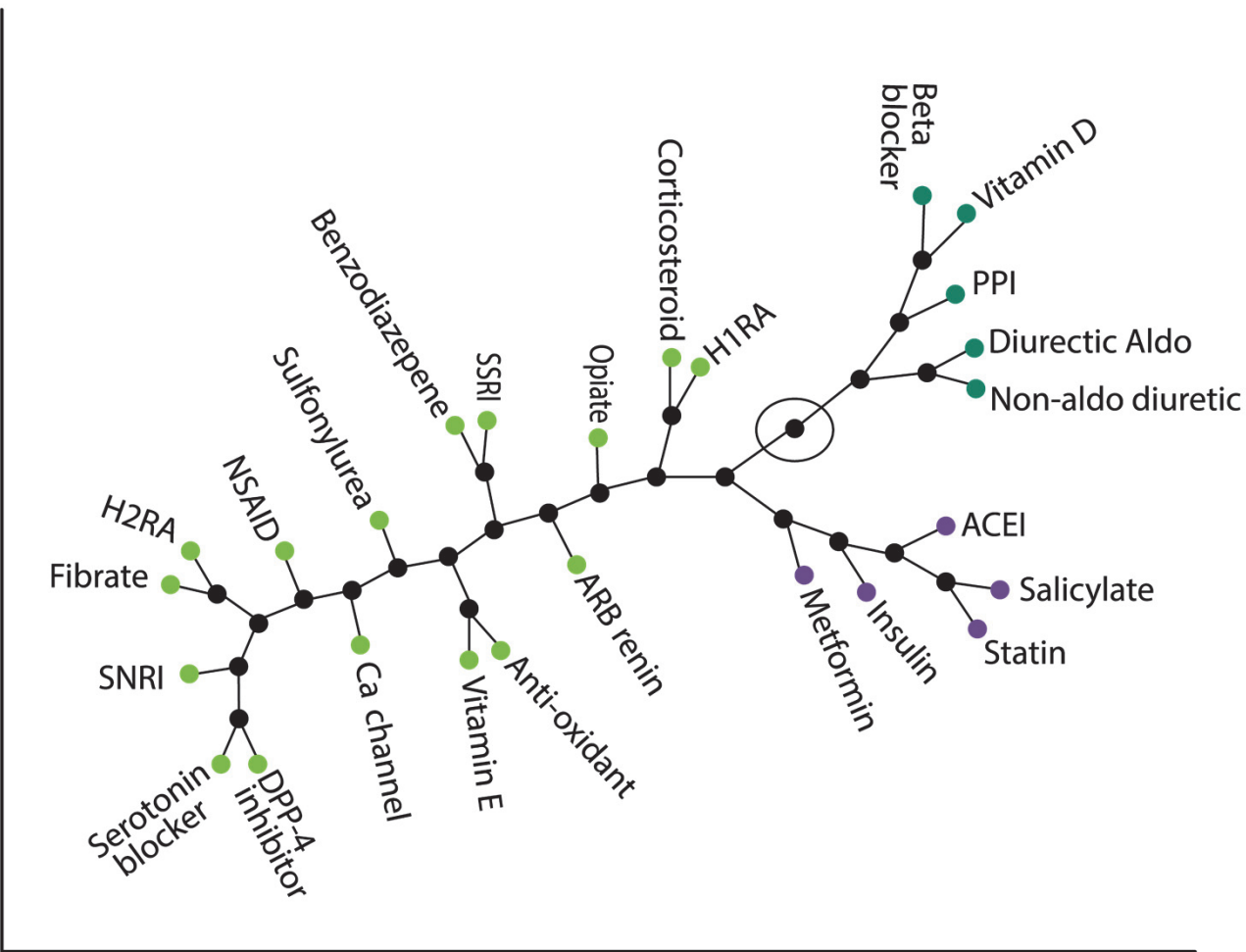


Figure 2: Hierarchical Clustering of Medication Use Among People with NAFLD Cirrhosis

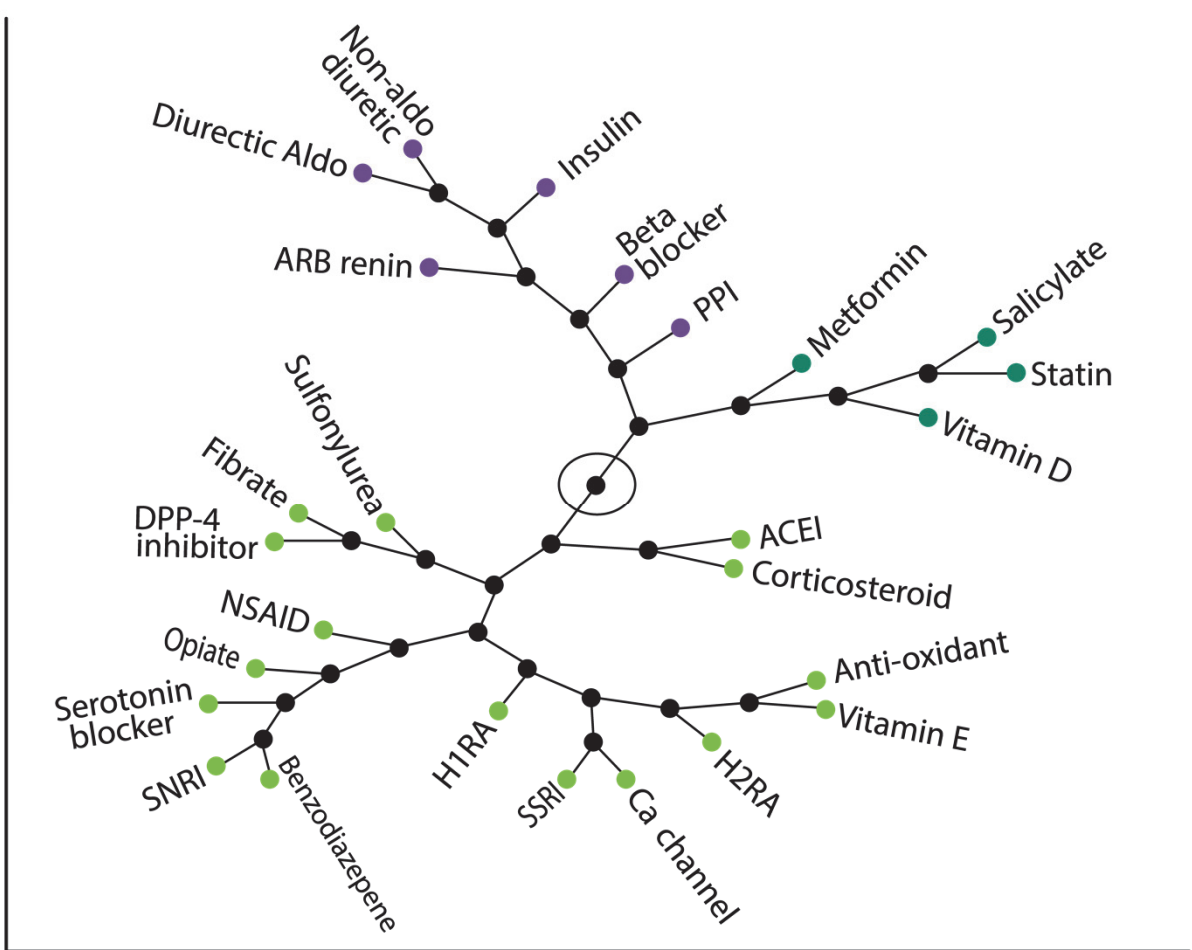
A) NAFLD Cirrhosis with ALT ≤50



Two distinct clusters:

- Beta blockers, vitamin D, PPI, aldosterone and non-aldosterone diuretics
- Ace inhibitors, salicylates, statins, insulin, and metformin

B) NAFLD Cirrhosis with ALT > 50



Four distinct clusters:

- Pain medications/mental health medications
- Medications for portal hypertension (beta-blockers and diuretics)
- Medications for the metabolic syndrome
- Anti-oxidants

Represents the spatial similarity of use among classes of medications.

CONCLUSIONS

- Understanding the association between medication use and ALT levels may allow the identification of subtle and otherwise unappreciated effects of medications on NAFLD
- Among patients with NAFLD, statins and anti-diabetic medications reduced the odds of having an ALT >50
- Further research is needed to determine causality and the direction of the associations among specific medications and ALT levels

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