

Patterns of Acetaminophen Use at a Tertiary Care Center: Exposures Exceeding 4 Grams Daily

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Introduction

Unintentional hepatotoxicity due to acetaminophen use at the recommended daily dose of up to four grams daily has increasingly been recognized as a significant problem. The phrase “therapeutic misadventure” has been coined in the literature, in reference to biochemical evidence of hepatocellular injury associated with acetaminophen use at recommended doses. Previous studies have documented a 25% to 40% incidence of two- to three-fold alanine aminotransferase (ALT) elevation, in healthy volunteers administered one gram of acetaminophen every six hours.

The recognition of this problem is reflected in part by recent changes in FDA recommendations, including more stringent controls on the amount of acetaminophen which may be contained per tablet in combination formulations together with narcotics. Furthermore, an advisory panel to the FDA recommended that the currently widely accepted maximum daily dose of up to four grams daily may be too high.

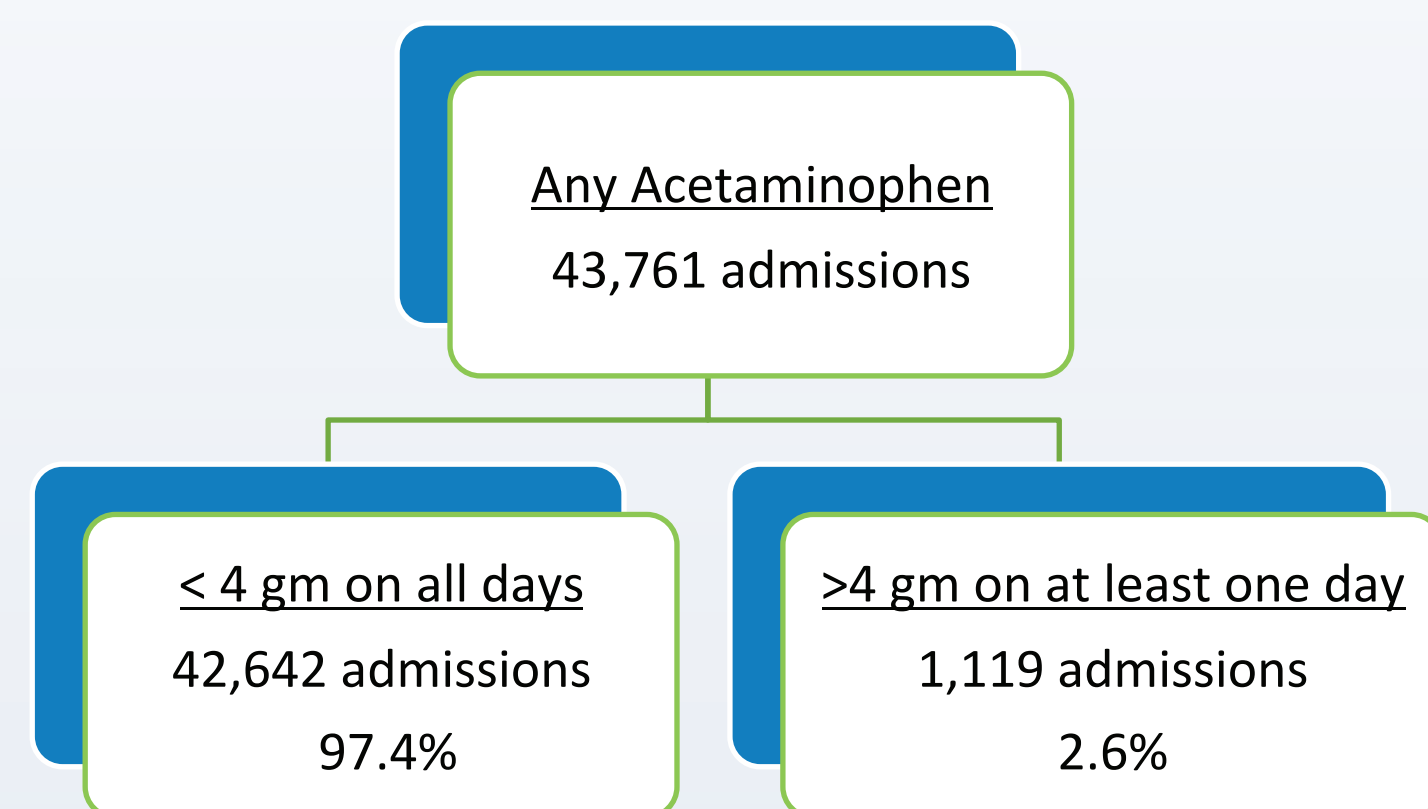
Aims

- To quantify the frequency at which acetaminophen is administered at doses in excess of four grams daily in an inpatient population, on a per-admission basis
- To quantify the number of acetaminophen-containing medications administered to this population
- To quantify the frequency of ALT monitoring in patients administered doses of acetaminophen in excess of four grams per day

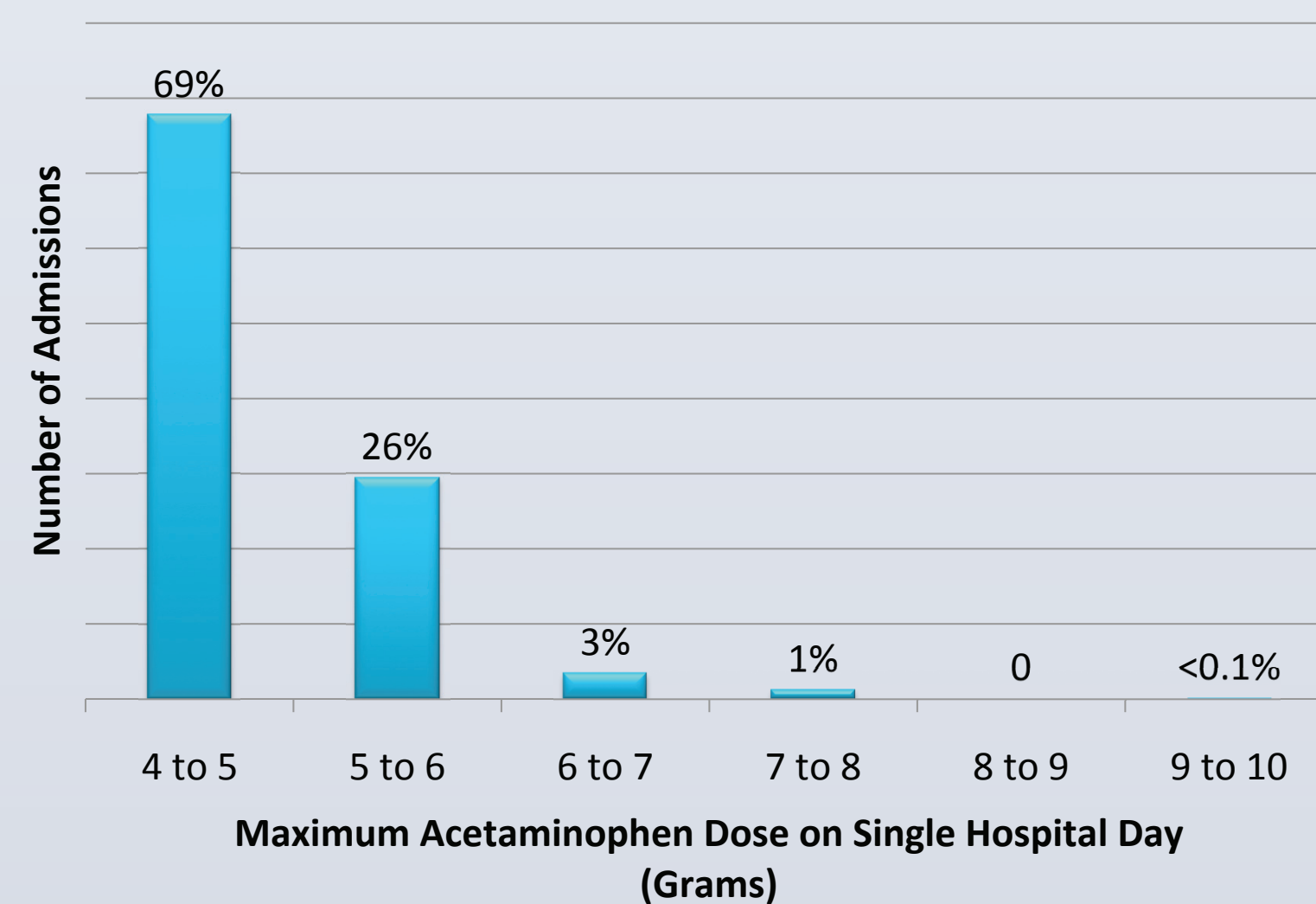
Methods

- Retrospective cohort study
- Single center - large tertiary care academic hospital
- Utilizing inpatient electronic medical record, performed database query to generate list of all hospital admissions involving administration of at least one dose of acetaminophen
- Data for all admissions to hospital with discharge date between January 1, 2008 and December 31, 2010 were analyzed
- For each admission, the cumulative daily dose of acetaminophen was calculated, including all acetaminophen-containing medication formulations
- Identified all ALT measurements performed during hospital admission within fourteen day period following each exposure in excess of four grams per day

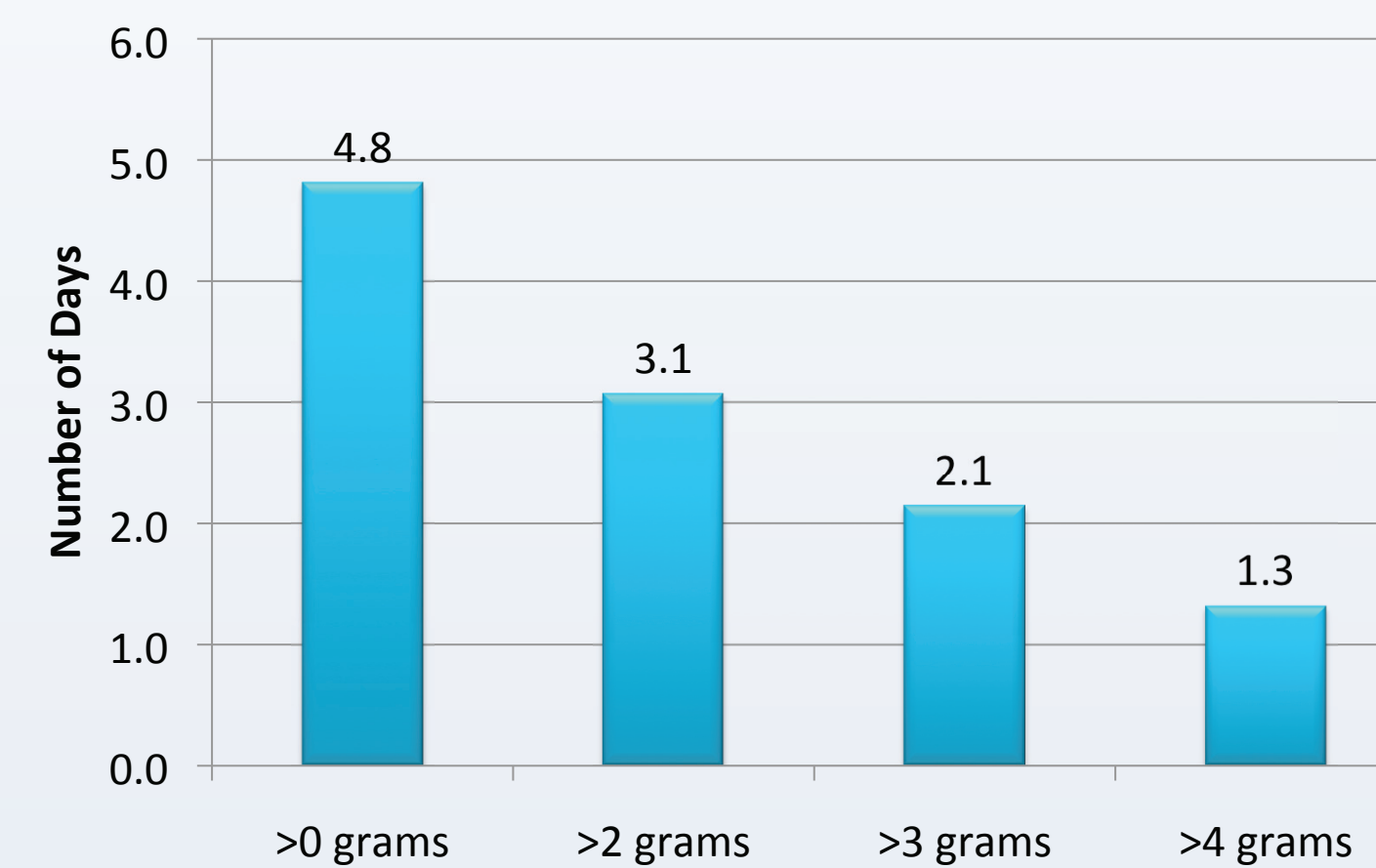
Results: Number of Admissions Involving Administration of Acetaminophen In Excess of Four Grams Daily



Results: Distribution of Maximum Dose on Any Calendar Day During Admission For 1,119 Admissions Involving Dosing In Excess of Four Grams



Results: Average Duration of Exposure To Specific Daily Doses of Acetaminophen for 1,119 Admissions Involving Dosing In Excess of Four Grams

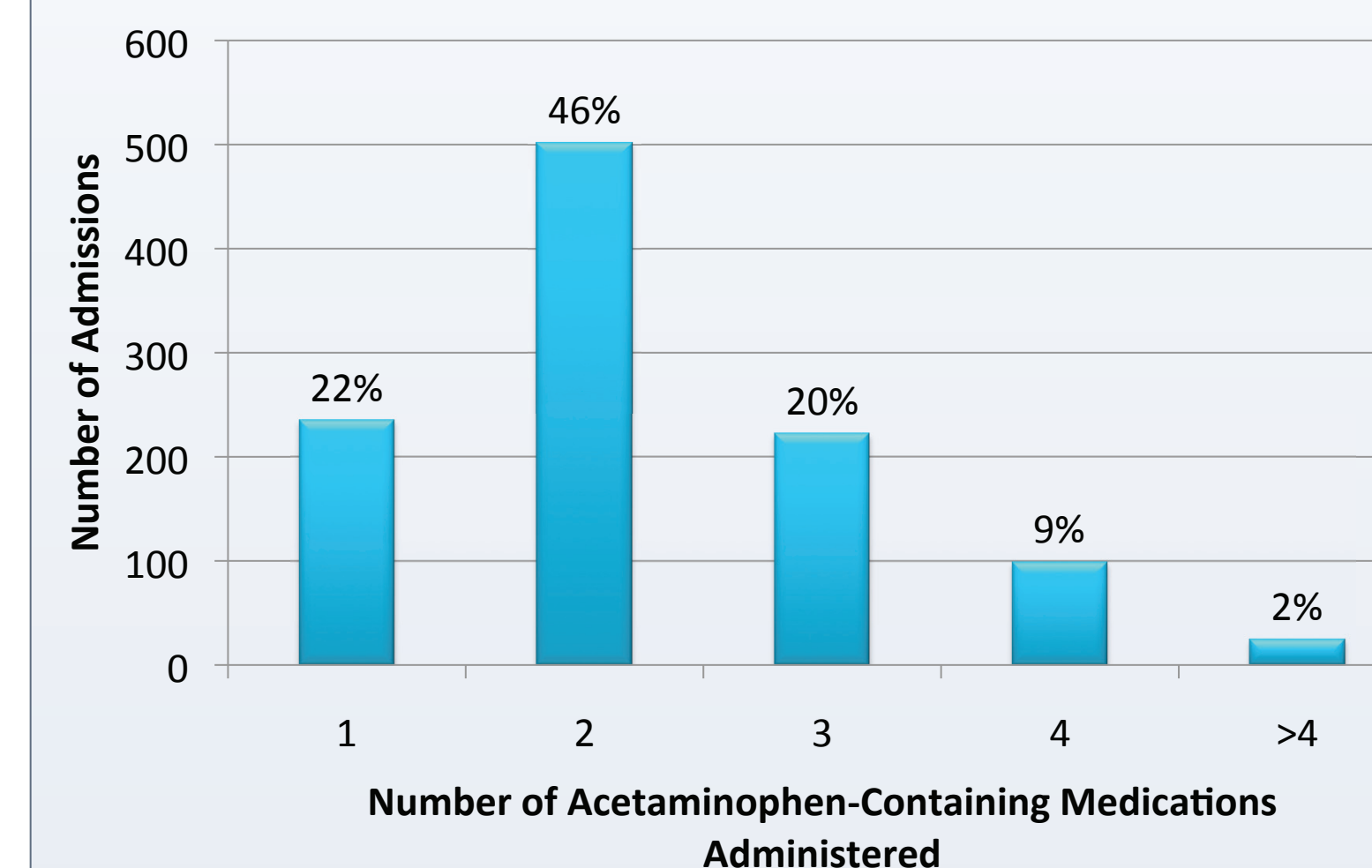


Note: average length of stay for this cohort was 6.2 days

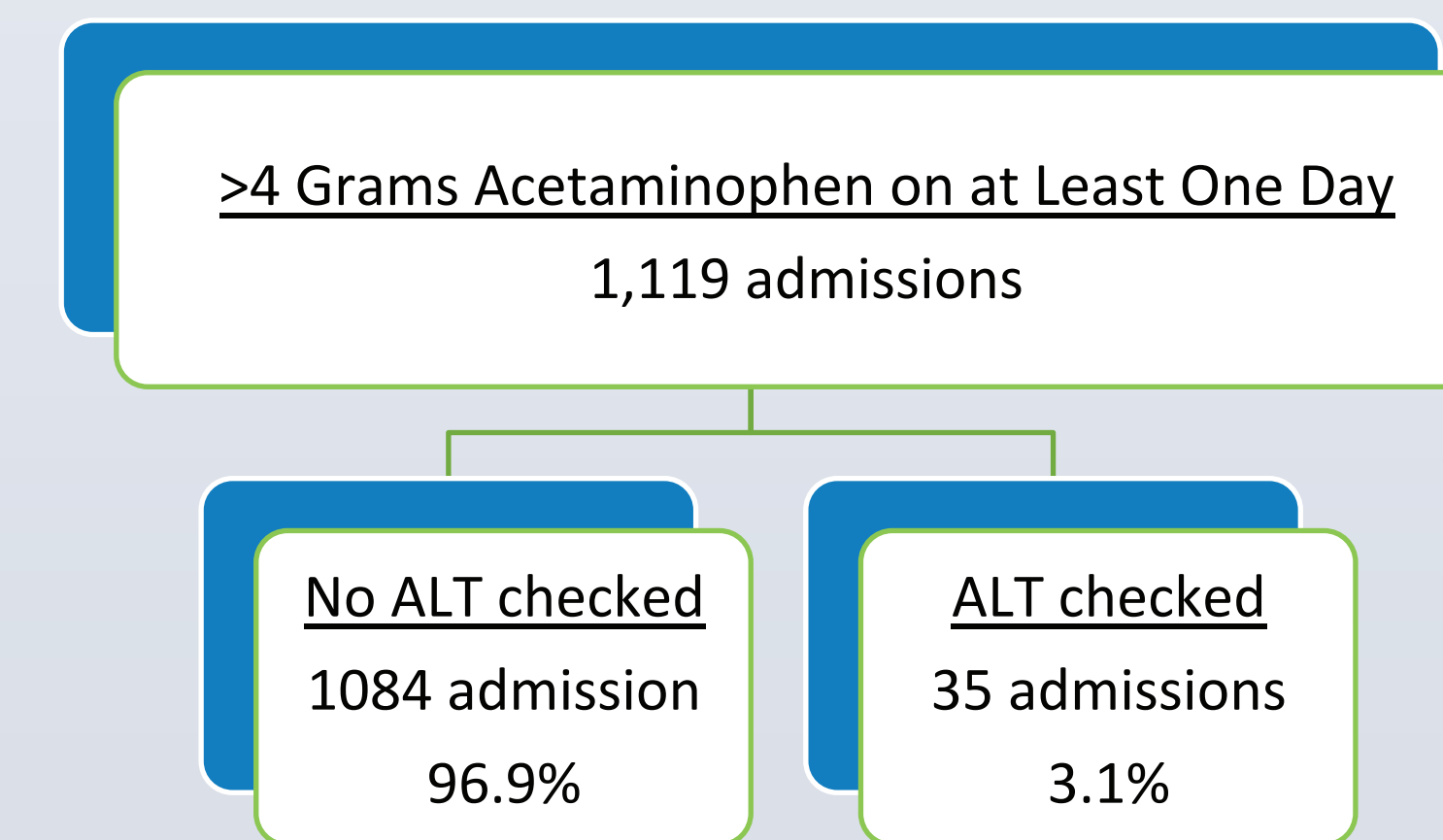
Results: Attributes of Admissions Associated with Exposure to Acetaminophen in Excess of Four Grams

Variable	> 4 Grams N = 1,119	< 4 Grams N = 42,642	p-Value
Age	57.0 ± 13.4 Years	54.3 ± 18.0 Years	< 0.001
Male	475 (42.4%)	18,037 (42.3%)	0.902
Caucasian	895 (80.1%)	27,305 (64.0%)	< 0.001
Length of Stay	6.2 ± 4.8 Days	7.0 ± 9.4 Days	< 0.001
Admitted to Orthopedic Surgery Service	904 (80.6%)	7355 (17.3%)	< 0.001
Number of acetaminophen-containing medications	2.27 ± 1.03	1.50 ± 0.78	< 0.001

Results: Number of Acetaminophen-Containing Medications Administered in Cohort of 1,119 Admissions Involving Dosing in Excess of Four Grams



Results: Number of Admissions With ALT Checked Within Fourteen Days of Acetaminophen Exposure in Excess of Four Grams



Results: Attributes of Admissions Associated with Frequency of ALT Monitoring

Variable	ALT Checked N = 35	ALT Not Checked N = 1084	p-Value
Ages	59.3 ± 15.2	60.0 ± 13.3	0.79
Male	17 (48.6%)	458 (42.2%)	0.49
Caucasian	26 (74.3%)	869 (80.2%)	0.39
Length of Stay	16.7 ± 10.9 Days	5.9 ± 4.1 Days	<0.001
Admitted to Orthopedic Surgery Service	14 (40.0%)	888 (82.0%)	<0.001
Number of acetaminophen-containing medications	2.17	2.25	0.39

Conclusions

- At a large tertiary care center, 2.6% of hospitalized patients were administered acetaminophen at doses exceeding recommended maximum of four grams daily
- Administration of multiple acetaminophen-containing medications contributed to cumulative dosing in excess of four grams daily
- ALT monitoring in patients administered doses in excess of four grams daily was infrequent
- Therefore, safeguards are needed to prevent excessive acetaminophen dosing of hospitalized patients.

References

- Watkins et al. Aminotransferase elevations in healthy adults receiving 4 grams of acetaminophen daily: a randomized controlled trial. *JAMA*. 2006; 296: 87-93.
- Winnike et al. Use of pharmaco-metabonomics for early prediction of acetaminophen-induced hepatotoxicity in humans. *Clinical Pharmacology & Therapeutics*. 2010; 88(1): 45-51.