Background
Adolescent obesity is a pressing health concern in Hawaii, where 15% of high-school students are obese, and another 14% are overweight.6 Excess body fat can cause liver production and uptake of fatty acids in excess of the liver’s capacity to oxidize them or release them with very-low density lipoproteins. The resultant accumulation of fat in the liver cells is known as nonalcoholic fatty liver disease (NAFLD). Gradual weight loss through diet and exercise is the standard treatment for pediatric NAFLD. Unfortunately, the majority of children with NAFLD fail to lose weight, and reverse their liver disease as indicated by improvements in alanine aminotransferase (ALT), a key enzyme in amino acid metabolism, may be noncausal or artificial, and the weight loss is generally short-lived.

Objectives
The purpose of this study was to investigate the epidemiology and management of pediatric NAFLD in Hawaii. In particular:
- What proportion of adolescents with liver disease have NAFLD?
- What are the demographic, biological, clinical and pathological characteristics of this population?
- What is the efficacy of diet and exercise in achieving weight loss and reducing liver disease severity?

Methods
A chart review of patients referred to the pediatric gastroenterology clinic at Kapiolani Medical Center for Women and Children with transaminasemia from January 2000 to December 2010 was conducted. Patients diagnosed with other forms of liver disease were excluded from analysis. This study was approved by the University of Hawaii Institutional Review Board Committee on Human Studies.

Height and weight were converted into body mass index (BMI) percentiles for age and sex according to the Pediatric Growth Charts using the US CDC method7. Systolic blood pressure and diastolic blood pressure were converted into percentiles for age, sex, and height as described previously.8 Baseline characteristics of patients with NAFLD were summarized using descriptive statistics. Response to treatment was assessed in overweight subjects by change in BMI percentile and in ALT. The relationship between these two variables was assessed by Pearson’s correlation coefficient. Chi-squared was used to determine if duration of follow up beyond five months affected change in BMI percentile and ALT.

Results

Table 1. Baseline Characteristics of Patients with NAFLD

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean ± SD</th>
<th>Abnormal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>13.9 (3.0)</td>
<td>68%</td>
</tr>
<tr>
<td>BMI (%ile)</td>
<td>93.6 (18.6)</td>
<td>68% 87%</td>
</tr>
<tr>
<td>P30 (%ile)</td>
<td>70.3 (10.)</td>
<td>10% 40%</td>
</tr>
<tr>
<td>Chol (mg/dL)</td>
<td>195 (52)</td>
<td>31 39%</td>
</tr>
<tr>
<td>TG (mg/dL)</td>
<td>183 (130)</td>
<td>20 55%</td>
</tr>
<tr>
<td>HDL-C (mg/dL)</td>
<td>44 (11)</td>
<td>25 44%</td>
</tr>
<tr>
<td>LDL-C (mg/dL)</td>
<td>118 (43)</td>
<td>24 54%</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>122 (67)</td>
<td>64 97%</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>123 (15)</td>
<td>65 22%</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>72 (13)</td>
<td>65 14%</td>
</tr>
</tbody>
</table>

Abbreviations: BMI 95th percentile = Body Mass Index Percentile (≥95th percentile for age and sex), FBG = Fasting Blood Glucose (>110mg/dL for age and sex), HDL-C = HDL cholesterol, LDL-C = LDL cholesterol, Mean ± SD = Mean ± Standard Deviation, ALT = Alanine Aminotransferase (>31U/L), SBP = Systolic Blood Pressure (>95th percentile for age, sex and height), DBP = Diastolic Blood Pressure (>95th percentile for age, sex and height).

There is no standard definition of metabolic syndrome in adolescents. The criteria used here were those of the International Diabetes Federation9, which defines the metabolic syndrome as six or more of the following: BMI ≥95th percentile for age and sex, fasting blood glucose ≥110mg/dL, triglycerides ≥150mg/dL, HDL cholesterol <45mg/dL for males or <50mg/dL females, and systolic or diastolic blood pressure ≥95th percentile for age, sex and height. The majority of patients had inflammation (92%) and/or fibrosis (67%). Only one patient was found to have simple steatosis.

Figure 1. Study Overview

Figure 2. Prevalence of Metabolic Syndrome Features in Patients with NAFLD

Figure 3. Relationship Between Change in Body Mass Index (BMI) Percentage and Change in Alanine Aminotransferase (ALT) in Patient with NAFLD

a) All Patients with Follow Up Data (n=44)

b) Patients with Follow Up Data for Six Months or Longer (n=20)

Discussion
As seen in Figure 1, most patients referred to the pediatric gastroenterologist with transaminasemia have NAFLD. Male accounted for the majority of cases, supporting previous findings of a gender-specific propensity to NAFLD. As expected, patients were predominantly overweight or obese, and many had childhood comorbidities (Table 1). Aside from obesity, dyslipidemia was the most common feature of metabolic syndrome, present in roughly half of patients, while hypertension and insulin resistance were seen in about one-quarter and one-third of patients, respectively. Most patients had multiple features of metabolic syndrome (Figure 2). This presents a challenge for pediatrics working with this population as several medications (e.g. statins for dyslipidemia, or thiazolidinediones for insulin resistance) cannot be used.

Twelve patients had liver biopsies performed to assess the liver for the presence of inflammation and fibrosis. Similar to other studies, the majority of patients had inflammation and fibrosis of the liver (Figure 4).

One novel finding was weight reduction was typically minimal, and appears not to result in a reduction in disease severity. As this is the only established treatment for pediatric NAFLD, adjunctive therapies are urgently needed to address the epidemic of pediatric NAFLD.

References

Figure 4. Proportion of NAFLD Patients with Inflammation and Fibrosis of the Liver (n=12)

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Inflammation No Inflammation

Fibrosis No Fibrosis

Twelve (18%) of the patients with NAFLD had a liver biopsy performed to assess severity of disease. The majority of patients had inflammation (92%) and/or fibrosis (87%). Only one patient was found to have simple steatosis.