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# Relationships Between Alanine Aminotransferase, Serum Triglycerides, Body Mass Index and Nonalcoholic Fatty Liver Disease in an Outpatient Pediatric Clinic Population[1,2]

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Nonalcoholic fatty liver disease (NAFLD) is the most prevalent chronic liver disease in children and adolescents. The goal of this study was to describe the demographic, anthropometric and biochemical data of children and adolescents diagnosed with NAFLD during a seven-year period in an outpatient pediatric clinic in the Southwest region of the US and to evaluate relationships between race, BMI, ALT, triglyceride levels, age and gender with a diagnosis of NAFLD. A retrospective medical record review of patients who attended an outpatient pediatric clinic with a billing diagnosis ICD-9 code of 571.8 was conducted. Forty-one patients met these criteria. The majority was male (74%) Hispanic (32%), Hispanic/Latino (68%) and obese. The small number of patients diagnosed with NAFLD in our study is consistent with previously reported results. Our results indicate that the population of this culturally diverse, high-risk population has significant clinical markers that are indicative of NAFLD.
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NONALCOHOLIC FATTY LIVER disease (NAFLD) is the most prevalent chronic liver disease in children and adolescents and is associated with overweight (body mass index [BMI] > 85th percentile) and obesity (> 95th percentile) in children and adolescents (Vajro et al., 2012). NAFLD encompasses a wide spectrum of disorders, ranging from simple benign hepatic steatosis to nonalcoholic steatohepatitis (NASH) with or without fibrosis in the absence of chronic alcohol consumption. Because hepatic steatosis can potentially progress to cirrhosis, end-stage liver diseases and hepatocellular carcinoma, there are significant long-term implications particularly when NAFLD is diagnosed in younger individuals (Feldstein et al., 2009).

There are many challenges associated with making a diagnosis of NAFLD in a pediatric patient. Liver biopsy is considered the "gold standard" for a definitive diagnosis, however, routine use is not practical in the clinical setting given the potential risks involved (Vajro et al., 2012). A liver biopsy is an invasive surgical procedure and the risks include pain, bleeding and death in small number of individuals (Nalbantoglu & Brunt, 2014). Physical discomfort of liver biopsy is a barrier to routine use in children. In addition, liver biopsy is expensive and many individuals may be uninsured or underinsured. Lack of standardized diagnostic criteria limits diagnostic capabilities and thus, many clinicians base their diagnosis on a combination

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of clinical, anthropometric and biochemical findings obtained during a medical examination.

Pediatric patients are screened for NAFLD using various imaging techniques, anthropometric and biochemical measurements. The liver can be assessed using imaging technologies however, limitations include cost (magnetic resonance imaging), exposure to ionizing radiation (computerized tomography) and low specificity and sensitivity (ultrasound). A waist circumference >90th percentile for age and gender (Fernandez, Redden, Pietrobelli, & Allison, 2004) and BMI >85th percentile are strongly associated with NAFLD risk in the pediatric population (Anwar et al., 2012). Insulin resistance measured using the homeostasis model assessment method (HOMA-IR = fasting insulin ($\mu$U/mL) $\times$ fasting glucose (mmol/L)/22.5) is also used to identify those at risk for NAFLD. Alanine aminotransferase (ALT) levels are most commonly used to screen for NAFLD. ALT levels are neither specific nor sensitive enough to make a diagnosis and many reference ranges are thought to be too high to be used as screening criteria for NAFLD in the pediatric population (Schwimmer et al., 2010). Recommendations regarding ALT levels include referral to a pediatric hepatologist or pediatric gastroenterologist for ALT levels that are twice the normal cutoff value (Barlow, 2007).

Screening children and adolescents for obesity and obesity related conditions appears to vary greatly among practitioners and institutions, primarily due to the lack of guidelines for pediatric obesity related comorbidities (Estrada et al., 2014). Among 25 US pediatric obesity centers, consensus statements were commonly used to guide treatment for hypertension, sleep apnea, dyslipidemia, fatty liver disease, diabetes and polycystic ovary syndrome, among others (Estrada et al., 2014). Metabolic syndrome in children and adolescents is being increasingly diagnosed and includes hypertension, abdominal obesity, type 2 diabetes and cardiovascular disease. Obese children with metabolic syndrome have a significantly increased risk of developing NAFLD compared to obese children without metabolic syndrome (Schwimmer, Pardee, Lavine, Blumkin, & Cook, 2008). Metabolic syndrome has significant long-term implications and thus, early screening and treatment is imperative. NAFLD has been deemed the hepatic manifestation of metabolic syndrome and is associated with insulin resistance in obesity.

In a study that included 396 children, Yang, Yi, and Choi (2014) found that the prevalence of metabolic syndrome and NAFLD was higher among those children who visited a pediatric obesity clinic compared to those children who visited a pediatric health promotion center that offered routine checkups for healthy children. This indicates that those children who attend a clinic whose specialty includes managing those children with obesity should consider adopting routine screening practices for NAFLD.

There also appears to be racial/ethnic differences in the relationship between ALT and insulin resistance. DeBoer, Wiener, Barnes, and Gurka (2013) found that non-Hispanic blacks showed a lower relationship between insulin resistance and elevated ALT in 4124 children and adolescents (age range 12– 19 years). In Hispanics, the presence of metabolic syndrome related indices, including elevated waist circumference, insulin resistance, and elevated triglycerides demonstrated increased odds ratio of elevated ALT (DeBoer, Wiener, Barnes, and Gurka, 2013).

A retrospective medical chart review by Hudson, Nunez, and Shaibi (2012) was conducted to assess the relationship between liver transaminases in 57 (n = 30 males, n = 27 females) adolescents with type 2 diabetes. Hispanic adolescents were more likely to have elevated AST, ALT levels compared to the African-American adolescents, however there were no significant differences between liver transaminases and non-Hispanic whites or between African Americans and non-Hispanic whites. The results of this study further demonstrate that Hispanic adolescents with type 2 diabetes may be at greater risk of developing NAFLD and that screening for NAFLD is important to prevent long-term complications associated with this disease. NAFLD has only recently been recognized as an increasingly common condition in young people. It has not been standard of care to screen for this condition in a pediatric setting; however, health care practitioners are becoming more aware of the risk factors for NAFLD. Hispanics ethnicity is identified as a risk factor for NAFLD and thus, screening for NAFLD in this population will help allow for early intervention and possibly minimize many adverse health outcomes in the future.

While several pediatric populations have been described to identify those at risk for NAFLD, to date the large pediatric outpatient clinic population at University of New Mexico Hospital (UNMH) has not been evaluated to determine the frequency of an NAFLD diagnosis.

According to the 2011 US Census Bureau, the state of New Mexico (NM) is comprised of a population which is 46.7% Hispanic or Latino in origin, 40.2% white, non-Hispanic, and 10.1% American Indian. The UNMH clinic system serves patients across the entire state of NM and therefore, offers medical care to a widely diverse and largely Hispanic and Latino population.

A retrospective study was conducted in order to determine the frequency of NAFLD diagnosis in the diverse population of pediatric patients receiving care at UNMH. The primary objective was to describe race, anthropometric and biochemical data of children and adolescents who have been diagnosed with NAFLD over a seven-year period and who were being followed by the health care professionals within the UNMH outpatient pediatric clinic system. Our secondary objective was to evaluate relationships between race, BMI, ALT, triglyceride levels and age with a diagnosis of NAFLD.

## Methods
### Design and Setting
A retrospective medical record review of patients who attended any outpatient pediatric clinic between January 2005 and September 2012 at UNMH was conducted. Approval for the study was obtained by the University of New Mexico (UNM) Human Research Protections Office Institutional Review Board (IRB). The UNM Health Sciences Center's Clinical and Translational Science Center (CTSC) provided