

IRB Study Protocol 2014

Ava Satnick PGY2

TITLE: Screening and Prevalence of Abnormal Metabolic Parameters in Overweight and Obese Pediatric Patients.

INVESTIGATORS: Ava Satnick, John Rausch

A. SPECIFIC AIMS: The goal of this study is to identify the prevalence of abnormalities in metabolic screens associated with overweight and obese status in children in the clinics associated with Columbia University.

#### B. STUDY PURPOSE AND RATIONALE

According to the Centers for Disease Control (CDC) and Prevention, 17% of all children

and adolescents in the United States are obese.<sup>1</sup> Obesity is a well-recognized risk factor for many pediatric and adult diseases including non-insulin dependent diabetes (NIDDM), dyslipidemia, and non-alcoholic fatty liver disease (NAFLD).<sup>2-3</sup>

Fasting glucose, insulin and insulin resistance are significantly increased in obese children.<sup>4-5</sup> A study by May et. al. reported the prevalence of abnormal cholesterol in all adolescents to be 20%. When participants in this study were further stratified by weight class of normal, overweight and obese, according to CDC guidelines, the prevalence were 18%, 28% and 32% respectively. <sup>2</sup> This study also found that the overall prevalence of pre-diabetes (fasting plasma glucose >99 to <126) or diabetes (fasting plasma glucose ≥126) in adolescents ages 12- 19 from 1998-2008 is 15%. Further stratified by normal, overweight and obese, the prevalence of pre-diabetes or diabetes was 13%, 16% and 20% respectively.<sup>2</sup> Obesity status (BMI >95th percentile) puts children at a higher risk of elevated fasting insulin than overweight children when compared to normal weight children.<sup>6</sup>

Fatty liver is the most common pediatric hepatic disease.<sup>7</sup> The gold standard of diagnosis of NAFLD or NASH is with liver biopsy.<sup>8</sup> Liver Biopsy proven NAFLD is prevalent in 5% of normal weight children, 16% in overweight children and 38% in obese children.<sup>9</sup> In order to avoid an invasive procedure, serum ALT values are often used as a surrogate marker for fatty liver. Consistently elevated ALT values in obese children are predictive of NAFLD in the setting of a negative infectious workup.<sup>3,10,11</sup>

NHANES data reviewed by Skinner and Skelton demonstrate that the prevalence of obesity classes 2 and 3 defined by >120 percent or >140 percent of the 95th percentile for gender and age continue to be on the rise.<sup>12</sup> Screening criteria as well as co-morbid consequences of metabolic syndrome are becoming elucidated based on the severity or class of obesity. A pilot study performed at Stony Brook University Children's Hospital suggests that the prevalence of abnormal laboratory values including ALT, TG, HDL and fasting insulin have a relationship with the severity of obesity.<sup>14</sup> Current screening recommendations as discussed by Fitch et. al. include screening based on risk factors such as BMI stratification, signs and symptoms associated with metabolic syndrome and family history.<sup>13,14</sup>

The Obesity Prevention Clinical Working Group had released guidelines for screening for dyslipidemia, diabetes and NAFLD in the pediatric population. These guidelines have been implemented in all pediatric clinics at MSCHONY-P as of March 2012. The goal of this study is to determine if the prevalence of abnormal metabolic parameters is statistically significant between obesity classes.

### C. STUDY DESIGN AND STATISTICAL ANALYSIS

1. Research Site: Columbia University Pediatric Clinics: Washington Heights, Audobon, Rangel, Broadway

3. Study sample: This will be a retrospective review of 1000 pediatric patients at Columbia University associated pediatric clinics between ages 4-18. The inclusion criteria for review is having a primary diagnosis of being overweight (278.02), obese (278.00) or morbidly obese (278.01), and having a screening metabolic panel performed soon after the time of diagnosis within six months. Further, within each group the children were stratified by gender, age (5-8; 9-12; 13-15; 16-18). Birth weight is also documented.. A control group of normal weight children is retrospectively not possible, as there was no indication for a metabolic screening panel. The demographics will include patient clinic, patient residential zip code, insurance, gender, age, race/ethnicity. Patient characteristics will also include parental reported juice intake, physical activity per week, milk consumed, alcohol intake if applicable. The laboratory data that will be collected includes: ALT/AST, HbA1C, random glucose, insulin, total cholesterol, HDL, LDL, Triglycerides (TG)

4. Screening: Children with BMI > 85% and received a weight screening panel within six months of diagnosis that includes chemistry metabolic panel and/or hepatic panel and/or thyroid function tests.

5. Methods: Once data is collected patient's with a BMI greater than 95% will be given a corrected BMI according to the formula: (Patients BMI/BMI for age and gender at 95%tile) x 100%. The laboratory data will have defined thresholds for what is considered abnormal. The exception will be ALT which will be based off a 3-tier system (30-35, 35-40, >40). A scatter plot will be created patients BMI vs. prevalence

of abnormal metabolic parameter. By creating a scatter plot the hope is to define obesity classes based off the prevalence of abnormal laboratory values that correlate with previously described classes.

Associations between obesity classes, patient characteristics, and clinical characteristics will be examined using the chi square test of independence. If appropriate, mean differences among the obesity class and continuous measures will be examined using one-way analysis of variance. All tests of significance are two-sided and evaluated at the level of  $p < 0.05$ . Frequency distributions of all study variables will be examined.

6. Procedures: None

F. FUNDING STATUS, DETAILS: not applicable

G. HUMAN SUBJECTS RESEARCH PROTECTION FROM RISK

Risk to Subjects: minimal risk

Adequacy of Protection Against Risks: A minimal risk as data collection is retrospective.

Potential Benefits of Proposed Research to the Subjects and Others: Benefits is to identify the prevalence of abnormal metabolic parameters in children so that the need for screening and early intervention can be evaluated.

Importance of the Knowledge to be gained: Identify patients who are overweight or obese to determine possible need for lab screening in order to evaluate their risk for co-morbidities.

H. DATA SAFETY MONITORING PLAN (for more than minimal risk studies)

I. LITERATURE CITED

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