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Original Study

The Prevalence of Abnormal Liver Enzymes and Metabolic Syndrome in Obese Adolescent Females with Polycystic Ovary Syndrome

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Abstract. *Objectives:* We sought to determine the prevalence of abnormal liver enzymes suggestive of nonalcoholic steatohepatitis and metabolic syndrome in obese adolescent females with polycystic ovary syndrome.

Design: A retrospective chart review

Participants: Patients included 39 obese (body mass index Z score ≥ 2) adolescent females with a diagnosis of polycystic ovary syndrome. Clinical and biochemical data in these patients were reviewed.

Main Outcome Measures: Aspartate and alanine aminotransferase levels, lipid panel, blood pressure, body mass index, and glucose intolerance were the main outcome measures of the study.

Results: The study showed that 15.4 % (6 of 39) of patients had elevated aminotransferase levels, suggestive of nonalcoholic steatohepatitis, and 43.6 % (17 of 39) of patients qualified as having metabolic syndrome. Finally, 10.2 % (4 of 39) of patients were found to have both liver dysfunction and metabolic syndrome.

Conclusion: Liver dysfunction consistent with nonalcoholic steatohepatitis and metabolic syndrome are prevalent in obese adolescent females with polycystic ovary syndrome. Therefore, early screening and further work-up for both disease states are warranted in cases of young adolescent females with polycystic ovary syndrome.

Key Words. Polycystic ovary syndrome—Nonalcoh olic steatohepatitis—Metabolic syndrome—Liver dysfunction

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Introduction

Polycystic Ovary Syndrome

Polycystic ovary syndrome (PCOS) is an endocrine disorder that is present in 5% to 11% of reproductive-age women.[1] The disorder consists of chronic anovulation (characterized by oligomenorrhea or amenorrhea); hyperandrogenism (manifested by hirsutism, acne, and male-pattern balding); and insulin resistance or hyperinsulinemia. The disorder is usually discernable around menarche; however, some girls develop PCOS prior to their first menses.[2] The majority of adolescent females with PCOS have insulin resistance, glucose intolerance, or both, especially individuals who are obese.[3]

Depending on the diagnostic criteria, the prevalence of PCOS in adolescents is between 8% and 26%.[4,5] Adolescent females with PCOS typically present with irregular menstrual cycles, making it difficult to distinguish PCOS from physiologic anovulatory cycles, often found in normal adolescent females during the early years after menarche. In general, a diagnosis of PCOS should be considered when an adolescent female presents with hirsutism, acne, menstrual irregularities, premature pubarche, and a positive family history.[5]

Nonalcoholic Steatohepatitis

Nonalcoholic steatohepatitis (NASH) is a type of liver disease that involves steatosis (fat accumulation in the liver), hepatitis (inflammation of the hepatocytes), and occasionally fibrosis (scarring). The inflammation is reflected by an elevation of the liver enzymes aspartate aminotransferase (AST) and alanine aminotransferase (ALT). NASH is also associated with a greater risk for cirrhosis and liver-related mortality.[1] It is

associated with various disease states, including obesity, diabetes, insulin resistance, and hypertriglyceridemia, each of which is a component of the metabolic syndrome.[6,7]

NASH is also prevalent in women with PCOS. Setji and colleagues found that 15% of the women with PCOS had elevated transaminase levels.[1] Both adult and pediatric patients with NASH are commonly asymptomatic.[6] However, rarely patients may present with persistent right upper quadrant pain or chronic pain in the umbilical region.[6] On physical examination, more than 90% of patients with NASH are found to be obese, and acanthosis nigricans has been reported in 36% to 49% of patients.[6] With regard to elevated transaminase levels, pediatric NASH typically involves elevated serum ALT with means of 103 to 208 U/L, while serum ALT levels can range from slightly above the upper limit of normal to 10 times the upper limit.[6] Unfortunately, there is no proven effective treatment for NASH in the pediatric population. Lifestyle modifications, including gradual weight loss and a reduced-fat diet, are beneficial. Several pharmacological agents have been suggested as possible treatments, including ursodeoxycholic acid, vitamin E, and metformin.[7] The efficacy of these treatments, however, has not been adequately studied at this point.

Metabolic Syndrome

Metabolic syndrome is characterized by decreased high-density lipoprotein (HDL) levels, hypertriglyceridemia, hypertension, hyperglycemia, and increased abdominal girth or body mass index (BMI). Tapia and colleagues conducted a study to determine the prevalence of metabolic syndrome among obese adolescents.[8] They evaluated 97 obese adolescents (BMI $> 95^{th}$ percentile) and found that 18.6% had metabolic syndrome, and that there was a higher rate among pubertal children (26.2 %) versus prepubertal children (12.7 %).

Several studies suggest that both adult and adolescent females with PCOS have increased risk for developing metabolic syndrome. Coviello and colleagues conducted a cross-sectional case-control study to examine the prevalence of metabolic syndrome in a population of adolescent females.[3] They found that adolescent girls with PCOS were 4.5 times more likely to have metabolic syndrome than age-matched controls.

Study Objectives

The primary objective of our study was to determine the prevalence of liver dysfunction suggestive of NASH and of metabolic syndrome in a population of obese adolescent females with PCOS in an urban clinical setting.

Subjects and Methods

The Institutional Review Board of New York University Medical Center approved this cross-sectional retrospective analytic study.

Subjects

The study population was composed of 39 adolescent females with a diagnosis of PCOS who were obese (BMI Z score ≥ 2) and were followed by the Pediatric Endocrinology service at either Bellevue Hospital Center or NYU Hospital Center, both in New York City. Subject exclusion criteria were pregnant females, those with diagnoses of secondary hypertension, and chronic liver disease other than NASH.

Methods

This was a cross-sectional retrospective analytic study consisting of a chart review that included patient visits and laboratory tests between the years 2002 and 2007. A database was created on the basis of several criteria, including patient demographics, family history, physical examination findings, and laboratory values. Physical findings included the patient's age, weight, height, BMI, ethnicity, systolic and diastolic blood pressure, and presence of acanthosis nigricans, acne, and hirsutism. Laboratory values included in the database were oral glucose tolerance test (OGTT), lipid panels (including total cholesterol, HDL, low-density lipoproteins [LDL], and triglycerides), liver function tests (including AST and ALT), and hormone levels (including follicle-stimulating hormone, luteinizing hormone, fasting plasma glucose, insulin, sex hormone binding globulin, and free and total testosterone). All patients were tested for all parameters listed in the methods section, including a 2-hour glucose challenge using 75 g glucose. There was more than one determinant on liver function tests but we chose the one at the time of OGTT or within 4 weeks of the OGTT, so we could know the association of insulin resistance during the same time. We routinely performed all the listed tests in obese adolescents and repeated them at 4-to 6-months interval or on an as-needed basis at our center.

In this study, we characterized liver dysfunction suggestive of NASH based on any elevations in one or both transaminase levels. Because we assessed patients in two locations (Bellevue Hospital Center and NYU Medical Center), our definition of abnormal aminotransferase activity was dependent upon normative data in each laboratory. In the Bellevue laboratory, the normative data were AST 11 to 39 U/L and ALT 11 to 35 U/L. In the NYU Medical Center laboratory, normal values were AST 15 to 46 and ALT 8 to 50 U/L; Quest diagnostic normal values were AST 12 to 32 and ALT 6 to 19 U/L. Normal