Obesity and Insulin-resistance Dysregulate the Metabolome in Emirati Children. Monica J. Hubal[1], Evan P. Nadler[1], Nader Lessan[2], Zara Hannoun[2] and Maha T. Barakat[2]. [1]*Children's National Medical Center, Washington, DC.,* [2]*Imperial College of London Diabetes Centre, Abu Dhabi, United Arab Emirates.* Email: mhubal@cnmc.org

Emiratis have a high rate of Type 2 diabetes despite moderate obesity rates, suggesting an altered adiposity/diabetes relationship. This is particularly important to understand in youth with emerging cardiometabolic disease, during which targeted intervention would be most effective. This study identified the independent and dependent effects of obesity and insulin resistance on metabolite profiles in Emirati youth. Fasting serum samples were obtained from four groups: lean(L)/normoglycemic(N=7; 3 male/4 female; age 11.6 ± 3.4 yr), obese/normoglycemic (N=5; 2M/3F; 13.3 ± 3.4), lean/hyperglycemic(N=8; 4M/4F; 13.9 ± 1.6)), and Obese/hyperglycemic (N=10; 4M/6F; 13.1 ± 3.5). Global metabolites were assessed via mass spectrometry (Metabolon, Inc.), scaled, and analyzed using ANCOVA (obesity * insulin-resistance, age and gender covariates) and Pearson linear correlations (to body mass index (BMI) and fasting plasma glucose (FPG)). Group differences ($p<0.05$) were detected for obesity (31 metabolites) and insulin-resistance (14 metabolites), with little overlap. Thirty-nine metabolites showed a significant obesity*IFG interaction, dominated by amino acid-related metabolites (22/39). All three branched chain amino acids (BCAAs: leucine, isoleucine and valine) showed a significant obesity*IFG interaction. Metabolite correlates to FPG (24 total) were dominated by lysolipid species (16 species; r -0.38 to -0.58), in addition to caproate (r=-0.38; medium chain fatty acid) and ribitol (r=-0.45; pentose metabolism). BMI correlates (18 total) included several amino acid-related metabolites (including glycine; r=-0.4; p=0.01; but not BCAAs), cholesterol (r=0.4; p=0.01), and stearamide (r=0.51; p=0.001). Free phosphate was positively correlated to both FPG (r=0.4) and BMI (r=0.34). Most existing metabolite studies of insulin-resistance and obesity studied adults with established/progressive disease, making these data novel as they highlight early changes with developing disease, specifically the dependent nature of obesity and insulin dysregulation effects on altered amino-acid metabolism.