Sugar-Sweetened Beverages, Physical Activity Independently Linked to Insulin Resistance

Sugar-sweetened beverage intake and physical activity levels are each independently linked to insulin resistance (IR) in adolescents, according to the results of a cross-sectional analysis of the National Health and Nutrition Examination Survey (NHANES) data, collected by the National Center for Health Statistics.

"Two lifestyle behaviours associated with obesity, IR, and metabolic syndrome (MS) are (1) high levels of sugar-sweetened beverage intake and (2) low levels of physical activity," reported Andrew Bremer et al from the University of California School of Medicine.

"Diet and consistent exercise are thus two recommendations given by paediatricians to children at risk for or diagnosed with these disorders. Studies support the hypothesis that sugar-sweetened beverages may increase energy intake and induce weight gain via their reduced satiety response, the promotion of a positive energy balance by liquid calories relative to isoenergetic solid calories and their dysregulation of energy homeostasis."

The study goal was to examine the association between IR–associated metabolic parameters and anthropometric measurements with sugar-sweetened beverage intake and physical activity levels. A nationally representative sample of 6967 US adolescents participating in NHANES during the years 1999 to 2004 was used. Age range was 12 to 19 years.

Sugar-sweetened beverages were defined as caloric soft drinks, colas, sugar-sweetened fruit drinks, and any other sugar-sweetened drinks.

The interest was sugar-sweetened beverage consumption and physical activity levels, and the main endpoints were glucose and insulin levels; HOMA-IR; total, HDL- and LDL-cholesterol; triglycerides; systolic and diastolic BP; waist circumference; and BMI percentile for age and sex.

Increased sugar-sweetened beverage intake was independently associated with increased HOMA-IR, systolic blood pressure, waist circumference, and BMI percentile for age and sex and decreased HDL-cholesterol, based on multivariate linear regression analyses. Increased physical activity levels were independently associated with reduced HOMA-IR, LDL-cholesterol, and triglycerides and increased HDL-cholesterol.

"Low sugar-sweetened beverage intake and high physical activity levels appear to modify each others’ effects of decreasing HOMA-IR and triglycerides and increasing HDL-cholesterol," the study authors write. "Sugar-sweetened beverage intake and physical activity levels are each independently associated with IR–associated metabolic parameters and anthropometric measurements in adolescents."

Limitations of this study include cross-sectional design precluding determination of causality, inability to adjust for the subjects’ degree of sexual maturation, and use of questionnaire data with inherent limitations.

"Although prospective studies are needed to directly test the effects of dietary modification and consistent exercise on the development of obesity, IR, and MS in the paediatric population, paediatricians should continue promoting these lifestyle modifications in efforts to improve overall health," the study authors conclude.
**Maturity-Onset Diabetes of the Young Seen in 5% of Antibody-Negative Children with Diabetes**

Approximately 5% of antibody-negative / C-peptide–positive children and adolescents diagnosed with diabetes in the USA may have Maturity-Onset Diabetes of the Young (MODY) rather than type 2 diabetes, Lisa Gilliam, University of Washington, Seattle, reported at the annual scientific sessions of the American Diabetes Association.

MODY, first described in the mid-1970s, is a clinically heterogeneous group of disorders characterised by non-ketotic diabetes, an autosomal dominant pattern of inheritance, and typical onset below the age of 25 years. It can arise from mutations in any one of at least six different genes associated with beta-cell function. The most common form, MODY3, arises from a mutation in the HNF [hepatocyte nuclear factor]-1 [alpha] gene (N Engl J Med. 2001;345:971-80).

New findings suggest that MODY is under-recognised and often inappropriately treated. Clinicians need to maintain a high level of suspicion for MODY in antibody-negative children who have residual beta-cell function, and certainly consider screening in individuals who meet the classic criteria for MODY.

The data come from SEARCH, a federally funded study of physician-diagnosed diabetes in individuals under 20 years of age in six U.S. centres located in Southern California, Colorado, Ohio, Washington state, and South Carolina.

Of 3,993 participants in whom diabetes-associated autoantibodies and fasting C-peptide were measured, 438 were autoantibody-negative. Direct sequencing for the HNF-1 [alpha] gene was performed in a subset of 266 patients who were autoantibody-negative and who had fasting C-peptide levels greater than 0.8 ng/ml. Among those, 13 patients had 14 gene mutations, including 7 that had not previously been described.

Only 1 of the 13 patients had been clinically diagnosed with MODY, while 5 had been misdiagnosed with type 1 diabetes and 7 with type 2 diabetes. Seven were currently being treated with insulin, and none were taking sulphonylureas, which is the recommended pharmacological treatment for MODY3. Not only are MODY patients “exquisitely sensitive” to sulphonylureas, but they also are cheaper and easier to take than multiple daily insulin injections.

Several clinical characteristics helped distinguish MODY3 from type 1 diabetes. Compared with those 3,484 individuals with type 1 diabetes in this study, the 13 MODY3 patients were less likely to have had weight loss (46% vs. 74%) or polyuria (54% vs. 93%) at diagnosis. The MODY group also tended to be older, heavier (body mass index z score 1.5 vs. 0.6), much more likely to have a parent with diabetes (62% vs. 14%), and much less likely to have medium- to high-risk HLA types (46% vs. 85%). Just 3 of the 13 were non-Hispanic white (23%), compared with 69% of the type 1 group.

In contrast, virtually no clinical or biochemical characteristic was identified that could help in distinguishing MODY3 from type 2 diabetes on an individual basis. Although the MODY group was somewhat younger and less obese than the type 2 patients, there was a great deal of overlap between the two groups. The type 2 patients were just as likely as the MODY group to have a positive family history for diabetes - including an autosomal dominant three-generation family history - and fasting C-peptide levels were similar.

“With the prevalence of obesity and type 2 diabetes increasing in the paediatric population, it’s becoming more challenging to distinguish MODY from type 2 diabetes.”

Because **genetic screening is very expensive**, at this point it’s not feasible to recommend it in every antibody-negative child or adolescent with residual fasting C-peptide. “However, particularly as costs come down for this type of screening, I predict that the screening cost will be outweighed by the benefit to the subset of patients who would be diagnosed appropriately with MODY,” Gilliam said in the interview.

Specifically, that benefit would include lower cost, less hassle, and greater treatment efficacy for patients who could be switched from insulin to a sulphonylureas, she noted.

Genetic testing for MODY is available at 11 clinical laboratories around the world, including two in the United States. Such facilities can be found by searching with the keyword “MODY” at www.genetests.org.
A 10-year follow-up study has cast doubt on the value of population screening for type 2 diabetes, after finding no differences in health outcomes between people with diabetes identified on screening and people with diabetes who were not screened.

Specialists from centres in London and Cambridge, UK, studied data from the Ely Study, involving screening by oral glucose tolerance test (OGTT) at a single general practice in the city of Ely. In 1990, one-third of registered patients aged 40-64 years without known diabetes were selected at random to be offered 5-yearly screening by OGTT (the screened group). A further one-third were randomly selected for OGTT testing plus outcome measurement 10 years later (the unscreened group).

About three-quarters of the patients with diabetes in each group attended for the 10-year assessment (99 in the screened group, with diabetes mainly screen-detected; 67 in the unscreened group, with diabetes mainly diagnosed clinically). The patients in the screened group were significantly older than those in the unscreened group (mean 68.4 years versus 66.1 years, respectively), but there were no significant differences in duration of diabetes (mean 6.2 years versus 5.1 years, respectively).

The 10-year assessment revealed no significant differences between the two groups in any of the parameters measured: BMI, HbA1c, systolic blood pressure, diastolic blood pressure, microalbuminuria, neuropathy, retinopathy, ischaemic heart disease, and scores for physical function, general health and mental health on the SF-36 questionnaire.

The researchers concluded that the differences in outcomes between the two groups “were small 10 years after commencement of screening.” They added: “This study cannot exclude the possibility that early detection may reduce the long-term risk of complications, but stronger evidence of net benefit is needed before population screening can be recommended.

A 20-year prospective study of more than 900 patients with type 1 diabetes confirms that elevated urinary albumin excretion, among other risk factors, predicts increased mortality.

The findings show “that microalbuminuria and macroalbuminuria are very strong risk factors,” Peter Rossing said at the Annual Meeting of the EASD 2008.

Rossing and associates at the Steno Diabetes Centre, Gentofte, Denmark, longitudinally followed 939 patients who had been diagnosed with type 1 diabetes. Patients were followed for at least 5 years and for a mean of 16 years. At baseline, 593 had normal urinary albumin excretion (less than 30 mg/24h), 181 had persistent microalbuminuria (between 30 and 300 mg/24h), and 165 had macroalbuminuria / overt diabetic nephropathy (more than 300 mg/24h).

After 20 years, 34% of the patients with baseline normal albuminuria had died, compared with 47% of those with microalbuminuria and 62% of those with overt nephropathy / macroalbuminuria. Median survival time after the onset of overt diabetic nephropathy was approximately 14 years.

A stepwise, multiple Cox regression analysis revealed the following predictors of all-cause mortality: male sex (relative risk 1.84), poor glycaemic control (RR 1.7), smoking (RR 1.67), and elevated urinary albumin excretion rate (RR 1.50). Higher social class was protective (RR 0.57).

It was noted that the study’s definition of a normal albuminuria rate, as less than 30 mg/24h, should not be considered an absolute cut-off. Elevated urinary albumin excretion is often considered a continuous variable. “Even urinary albumin excretion in the upper range of normal is considered higher risk than the lower range both for progression to renal disease or mortality,” he said.
Type 1 diabetes, traditionally considered a disease of wasting, is now frequently diagnosed in children who are overweight, according to a new study. That means determining which paediatric patient has type 1 diabetes and which has type 2 is getting harder, according to Ingrid M. Libman, assistant professor of paediatric endocrinology at the University of Pittsburgh. "The problem now is that the lines are blurred between what we thought was clearly type 1 and 2 diabetes. The distinction can no longer be made based on phenotype."

Data she presented at the annual meeting of the EASD showed that over 23 years of observation (1979-2002), the overall prevalence of overweight and obesity in children with newly diagnosed insulin-treated diabetes (traditionally considered type 1 disease) has more than tripled – doubling in African American children (from 30% to 62%) and quadrupling in white children (from 6% to 26%).

"In some cases we now have no clear way of distinguishing what kind of diabetes someone has based on how they look," she said, adding that acanthosis nigricans, traditionally associated with type 2 diabetes, is now commonly found in overweight patients with type 1 disease as well.

Subjects diagnosed in period I (1979-1989) and period II (1990-98) were tested for beta-cell autoimmunity. In those with autoimmune positivity (known as diabetes type 1a), there was a similar increase in the prevalence of obesity between periods I and II: 6% to 21% among whites and 22% to 43% among African Americans. For period III (1999-2002), autoimmune antibodies are still being measured, she said. Autoimmune-negative subjects in the study may have had type 2 diabetes or type 1b – an insulin-dependent, non-autoimmune form of the disorder.

Libman said physicians might frequently face a new presentation of diabetes in which patients may actually have a confusing combination of characteristics. "What we argue is that some kids may have characteristics of both type 1 and type 2 disease processes going on. If they are autoimmune positive, they have type 1a diabetes; however, if they are also overweight and have acanthosis nigricans, you could argue that they may also be insulin resistant."

While establishing a clear diagnosis may often seem essential to physicians, Libman said that in the end, it might not be so important. "If the child is really sick, does it matter if they have type 1 or 2? You will need to treat them with insulin. If they are overweight, not sick, and diagnosed randomly, you can likely control their blood sugars with lifestyle and metformin. If their antibodies come back positive, it doesn't mean you should start insulin-but you may need to monitor them more carefully and you may have a lower threshold for starting it."

Overweight in children may not only make them more susceptible to developing type 2 disease, but in those who are genetically susceptible, it may also increase their risk or accelerate the development of type 1 disease—the concept of "double diabetes."

"Genetically, they have the genes to develop diabetes at some point (or not), but if they become overweight, they may have more chance. Weight makes the beta cell work harder and may trigger an increased immune response – this is known as the 'accelerator hypothesis.'" First-degree relatives of patients with type 1 diabetes have a 1 in 20 chance of developing the disorder, making overweight particularly dangerous in this group, she commented...

---

**The Changing Phenotype of Paediatric Type 1 Diabetes**

Type 1 diabetes, traditionally considered a disease of wasting, is now frequently diagnosed in children who are overweight, according to a new study. That means determining which paediatric patient has type 1 diabetes and which has type 2 is getting harder, according to Ingrid M. Libman, assistant professor of paediatric endocrinology at the University of Pittsburgh. "The problem now is that the lines are blurred between what we thought was clearly type 1 and 2 diabetes. The distinction can no longer be made based on phenotype."

Data she presented at the annual meeting of the EASD showed that over 23 years of observation (1979-2002), the overall prevalence of overweight and obesity in children with newly diagnosed insulin-treated diabetes (traditionally considered type 1 disease) has more than tripled – doubling in African American children (from 30% to 62%) and quadrupling in white children (from 6% to 26%).

"In some cases we now have no clear way of distinguishing what kind of diabetes someone has based on how they look," she said, adding that acanthosis nigricans, traditionally associated with type 2 diabetes, is now commonly found in overweight patients with type 1 disease as well.

Subjects diagnosed in period I (1979-1989) and period II (1990-98) were tested for beta-cell autoimmunity. In those with autoimmune positivity (known as diabetes type 1a), there was a similar increase in the prevalence of obesity between periods I and II: 6% to 21% among whites and 22% to 43% among African Americans. For period III (1999-2002), autoimmune antibodies are still being measured, she said. Autoimmune-negative subjects in the study may have had type 2 diabetes or type 1b – an insulin-dependent, non-autoimmune form of the disorder.

Libman said physicians might frequently face a new presentation of diabetes in which patients may actually have a confusing combination of characteristics. "What we argue is that some kids may have characteristics of both type 1 and type 2 disease processes going on. If they are autoimmune positive, they have type 1a diabetes; however, if they are also overweight and have acanthosis nigricans, you could argue that they may also be insulin resistant."

While establishing a clear diagnosis may often seem essential to physicians, Libman said that in the end, it might not be so important. "If the child is really sick, does it matter if they have type 1 or 2? You will need to treat them with insulin. If they are overweight, not sick, and diagnosed randomly, you can likely control their blood sugars with lifestyle and metformin. If their antibodies come back positive, it doesn't mean you should start insulin—but you may need to monitor them more carefully and you may have a lower threshold for starting it."

Overweight in children may not only make them more susceptible to developing type 2 disease, but in those who are genetically susceptible, it may also increase their risk or accelerate the development of type 1 disease—the concept of "double diabetes."

"Genetically, they have the genes to develop diabetes at some point (or not), but if they become overweight, they may have more chance. Weight makes the beta cell work harder and may trigger an increased immune response – this is known as the 'accelerator hypothesis.'" First-degree relatives of patients with type 1 diabetes have a 1 in 20 chance of developing the disorder, making overweight particularly dangerous in this group, she commented...