

# Early Factors Can Predict NAFLD in Adolescence

BY SUSAN LONDON

ANNUAL MEETING OF THE AMERICAN ASSOCIATION FOR THE STUDY OF LIVER DISEASES

SAN FRANCISCO – Factors that can be measured in the first few years of life can predict whether a child will develop nonalcoholic fatty liver disease (NAFLD) by adolescence, suggests a study presented at the meeting.

Investigators in Australia led by Dr. Oyekoya T. Ayonrinde prospectively followed more than 1,000 children from birth to adolescence, by which time one in eight had developed NAFLD, now the most common chronic liver disorder in pediatric and adult populations in many countries.

The data showed distinctly different trajectories for measures of adiposity and systolic blood pressure between the



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DR. AYONRINDE

children who did and did not develop NAFLD, Dr. Ayonrinde said.

Additionally, greater values for measures of adiposity at various ages in the first decade of life were among the independent positive predictors of NAFLD, whereas longer duration of breastfeeding and, among girls, larger head circumference were among the independent negative predictors.

“There seems to be a potential protective role of breastfeeding on NAFLD, which needs to be explored further,” Dr. Ayonrinde commented. “There [are] some data to show that breastfeeding is associated with lower insulin release and also less-rapid weight gain. And it has also been associated with larger head circumference as well, so that probably ties in to some degree.”

The study’s findings have implications for pediatric health assessments, he maintained. “Routine recording of childhood anthropometrics is recommended. The trajectory of systolic blood pressure and any adiposity measure during childhood identifies those at particular risk of NAFLD and associated metabolic disorders, who may benefit from further targeted assessment.”

Explaining the study’s rationale, Dr. Ayonrinde noted that little is known about the natural history of NAFLD, and the disease is underdiagnosed. “So it makes sense to consider that the identification of children at risk of NAFLD through longitudinal studies may provide improved understanding of the natural history and potential opportunities for prevention and therapy of NAFLD,” he said.

The investigators followed 1,170 children who were participating in the Raine Study, a birth cohort study that was conducted in western Australia ([www.rainestudy.org.au](http://www.rainestudy.org.au)). The children had serial anthropometric measurements between birth and the age of 17 years.

Liver ultrasound was performed when the participants were aged 17 years. Boys consuming at least two alcoholic drinks per day and girls consuming at least one alcoholic drink per day were excluded from the study to reduce that possible source of confounding, he noted.

Study results showed that by the age of 17 years, fully 13% of the children – 16% of girls and 10% of boys – had developed NAFLD, according to Dr. Ayonrinde, a gastroenterologist at the University of Western Australia in Perth.

A case-control analysis of the children who did and did not develop NAFLD showed that none of the anthropometric factors assessed at birth were associated with NAFLD, nor was weight gain in the first year of life. But breastfeeding was highly protective: Infants breastfed for more than 6 months were less than half as likely to have NAFLD as adolescents.

The earliest anthropometric measure to show an association with NAFLD was smaller head circumference (at the age of 1 year in girls), and the strongest predictor overall was suprailiac skinfold thickness, Dr. Ayonrinde reported.

In addition, the children who did and did not develop NAFLD had significantly different trajectories throughout childhood when it came to head circumference (in girls only), body weight, body mass index, various skinfold thicknesses, and systolic blood pressure.

In a multivariate analysis, boys were more likely to develop NAFLD if they had a greater suprailiac skinfold thickness at age 3 years, a greater chest circumference at age 5 years, a greater body mass index at age 8 years, or a greater suprailiac skinfold thickness at age 10 years (odds ratios ranged from 1.11 to 1.37). Boys were less likely to develop NAFLD if they were breastfed for longer as infants (OR, 0.91).

Girls were more likely to develop NAFLD if they had a higher body weight at age 3 years, a greater suprailiac skinfold thickness or chest circumference at age 5 years, a greater chest circumference at age 8 years, or a larger suprailiac skinfold thickness at age 10 years (OR, 1.08-1.44). Girls were less likely to develop NAFLD if they were breastfed for longer as infants or if they had a larger head circumference at age 3, 5, or 8 years (OR, 0.62-0.90).

Data on maternal factors, such as obesity and diabetes, and on socioeconomic factors, are available in the dataset but have not yet been analyzed, according to Dr. Ayonrinde.

Dr. Ayonrinde reported that he had no relevant conflicts of interest. ■

# Low-Protein Diet May Cause Less Weight Gain, More Fat

BY MARY ANN MOON

FROM JAMA

Overeating on a diet low in protein caused less weight gain than overeating on a normal- or high-protein diet – but most of the body mass gained was fat, rather than the leaner muscle mass created by high-protein overeating, according to a recent report.

The distinction is important, because the accumulation of excess fat is associated with obesity-related medical conditions, while accumulation of muscle mass is beneficial, noted Dr. George A. Bray of the Pennington Biomedical Research Center, Baton Rouge, La., and his associates (JAMA 2012;307:47-55).

Dr. Bray and his colleagues examined whether the level of dietary protein affected weight gain and body composition. Their randomized trial included 25 healthy, weight-stable adults (BMI 19-30 kg/m<sup>2</sup>) who lived under tightly controlled conditions in a metabolic unit for 10-12 weeks. During the first 2-4 weeks of the study – a weight stabilization period – the 16 men and 9 women (aged 18-35 years) consumed an isocaloric diet with 15% of energy from protein, 25% from fat, and 60% from carbohydrates.

During the final 8 weeks of the trial, subjects were deliberately overfed 40% more energy than was needed for weight maintenance, an excess of approximately 1,000 calories each day. During that overeating period, they were randomly assigned to diets containing 5% of energy from protein (the low-protein diet), 15% of energy from protein (the normal-protein diet), or 25% of energy from protein (the high-protein diet).

Body composition was measured by dual-energy x-ray absorptiometry. The

study subjects included 7 non-Hispanic whites, 16 blacks, and 2 Asians.

All the study subjects gained weight during the overeating period, and there were no significant differences in weight gain by subjects’ race or sex. That suggests that the data are generalizable to all races and both sexes.

Weight gain in the low-protein group was 3.16 kg, significantly less than the weight gain in the other two groups – 6.05 kg in the normal-protein group and 6.51 kg in the high-protein group.

In the low-protein group, more than



**In subjects overeating on a low-protein diet, more than 90% of the extra energy was stored as fat.**

90% of the extra energy was stored as fat. In contrast, in the normal- and high-protein groups, only about 50% of the extra energy was stored as fat, while the remaining 50% was lean body mass.

The findings imply that a low-protein diet is metabolically different from a normal- or high-protein diet, the investigators added.

The study was supported in part by the U.S. Department of Agriculture and Louisiana State University, New Orleans. Dr. Bray reported ties to Abbott Laboratories, Takeda Global Research Institute, Medifast, Herbalife, and Global Direction in Medicine. One of his associates reported ties to Bristol-Myers Squibb, Eli Lilly, Elcelyx, Merck, Philips, the International Life Sciences Institute, Catapult Health, and Domain & Associates. ■

## Focus on Fatness, Not Weight Gain

The findings of Bray and colleagues “suggest that overeating low-protein diets may increase fat deposition, leading to loss of lean body mass, despite lesser increases in body weight,” said Dr. Zhaoping Li and Dr. David Heber. “Clinicians should consider assessing a patient’s overall fatness rather than simply measuring body weight or body mass index, and concentrate on the potential complications of excess fat accumulation. The goals for obesity treatment should involve fat reduction rather than simply weight

loss, along with a better understanding of nutrition science,” they noted.

DR. LI and DR. HEBER are at the Center for Human Nutrition, University of California, Los Angeles. Dr. Heber reported ties to POM Wonderful, Herbalife, McCormick Spices, and the Obesity Society for Clinical Research. Dr. Li reported no financial conflicts of interest. These remarks were taken from their editorial accompanying Dr. Bray’s report (JAMA 2012;307:86-7).