

Childhood Obesity and Metabolic Syndrome in Preschool Children

Early markers and identification of individuals at risk in a longitudinal perspective

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentlig försvaras i föreläsningssal Tallen, Drottning Silvias Barn- och Ungdomssjukhus, 8 mars 2019, klockan 9.00.

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Avhandlingen baseras på följande delarbeten

- I. **E Kjellberg, J Roswall, S Bergman, G Almquist-Tangen, B Alm and J Dahlgren. Longitudinal birth cohort study found that a significant proportion of children had abnormal metabolic profiles and insulin resistance at 6 years of age. *Acta Paediatrica* 2018, Oct 17. DOI:10.1111/apa.14599**
- II. **E Kjellberg, J Roswall, J Andersson, S Bergman, AK Karlsson, PA Svensson, J Kullberg, J Dahlgren. Metabolic risk factors associate with visceral and subcutaneous adipose tissue in a sex-specific manner in seven-year-olds. *Accepted in Obesity* 2019**
- III. **E Kjellberg, J Roswall, S Bergman, B Strandvik, J Dahlgren. Serum n-6 and n-9 fatty acids correlate with serum IGF-1 and growth up to four months of age in healthy infants. *J Pediatric Gastroenterology and Nutrition* 2018; 66: 141-146**
- IV. **E Kjellberg, J Roswall, S Bergman, G Almquist-Tangen, B Alm and J Dahlgren. Serum adipokines and insulin-like growth factor 1 during infancy are associated with future markers of the metabolic syndrome. *Manuscript*.**

SAHLGRENKA AKADEMIN



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Abstract

Background: Overweight and obesity have increased worldwide and affect children at ever younger ages, resulting in cardiovascular disease and type 2 diabetes even in adolescents. This illustrates the importance of identifying children at risk at an early stage.

Aim: To study metabolic health in preschool children. Specific aims were to investigate (i) whether 6-year-olds show signs of metabolic syndrome, (ii) whether the fat distribution in 7-year-olds is associated with their metabolic profile and whether there are any related sex differences, (iii) the profile of fatty acids in infancy and their influence on growth, (iv) to study the risk of developing adiposity and an impaired metabolic profile at 6 years of age as a result of early nutrition.

Methods: This study is based on a longitudinal birth cohort (Halland Health and Growth Study) of 480 full-term infants, born at the regional hospital of Halmstad, Sweden, between 2008 and 2011. The children were monitored on regular visits for anthropometrics, blood tests, blood pressure, and food diaries. At 7 years of age, 81 children underwent magnetic resonance imaging to quantify visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT) volumes.

Results: One key measure showed that about one fourth (26%) of the children had one or more risk factors for metabolic syndrome requiring action at 6 years of age. Children with obesity (3%) and overweight (14%) were more likely to have insulin resistance (28% versus 5%, $p < 0.001$) and higher triglycerides (8% versus 0%, $p < 0.001$) than the normal-weight group. SAT showed a stronger correlation with metabolic risk factors than VAT. Girls in general showed a stronger correlation between adipose tissue and metabolic risk factors than boys. Feeding modality, i.e. breastfeeding versus formula feeding, had an impact on fatty acid profiles, with a higher linolenic acid level and n-6/n-3 ratio in formula-fed infants at 4 months of age. We found n-6 fatty acids to be associated with insulin-like growth factor I (IGF-I). IGF-I during infancy (0, 4, and 12 months) influenced body composition and fasting insulin at 6 years of age. The adipokines leptin and adiponectin at 4 months of age were also associated with BMI and waist circumference at 6 years of age (positively for leptin and negatively for adiponectin). In addition, early leptin was associated with triglycerides in 6-year-olds ($p > 0.001$) and early adiponectin was associated with high-density lipoprotein cholesterol in 6-year-olds ($p = 0.01$). This indicates an effect of early nutrition on metabolic programming.

Keywords: Adiponectin, childhood obesity, insulin resistance, leptin, metabolic syndrome, n-6 fatty acids, SAT, VAT, waist circumference.