

# Serum leptin, adiponectin and IGF-I during infancy were associated with markers of metabolic syndrome at six years of age

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Disclosure statement: This study was supported with unrestricted grants from the Medical Research Council.

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## Introduction and objectives:

Metabolic programming occurs during early life and nutritional factors are known to have long-lasting influences on metabolic health. We investigate associations between insulin-like growth factor I (IGF-I), leptin and adiponectin during infancy and metabolic markers in the same children at six years of age.

## Methods:

**Cohort:** The Swedish longitudinal Halland Health and Growth birth cohort study analyzed serum IGF-I, leptin and adiponectin in 188 infants at birth, four months of age and twelve months of age, and compared these data to body mass index (BMI), fasting insulin and cholesterol at six years of age. Data from six years of age has been published elsewhere (1). Six of the children were born small for gestational age (SGA).

**Infancy:** IGF-I was analyzed in duplicate using the IDS-iSYS-technique (25) at our laboratory at the Gothenburg Pediatric Growth Research Centre. All the samples were analysed in the same batch and the intra-assay coefficient of variation (CV) for IGF-I was 2.8% (5.8% for levels <28 ng/mL). Leptin concentrations were measured by RIA (Linco Research, St. Charles, USA), with an intra-assay CV of 7% at 2.4 µg/L and 4.9% at 14.0 µg/L. The inter-assay CVs were 12.5% at 1.4 µg/L and 5.6% at 15.1 µg/L. Adiponectin concentrations were measured by enzyme-linked immunosorbent assay (R&D System Inc., Minneapolis, MI, USA) and expressed as µg/mL. The intra-assay CV was 3.6% and the inter-assay CV was 6.9%.

**Age six years:** Total cholesterol, triglycerides and high-density lipoprotein (HDL) cholesterol were analysed at Hallands Hospital Halmstad. They were measured with an enzymatic colorimetric assay on a Cobas 6000 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The intra-assay coefficient of variation (CV) was 1.9%, 1.8%, and 1.0% for total cholesterol, triglycerides and HDL cholesterol, respectively. Glucose was measured with an enzymatic method with hexokinase and insulin was measured by an electrochemiluminescence immunoassay. Both procedures were carried out with a Cobas 6000 analyzer (Roche Diagnostics GmbH, Mannheim, Germany). The intra-assay CV was 2.2% for glucose and 2.0% for insulin. HOMA-IR was calculated as (fasting insulin x fasting glucose)/22.5.

## Results:

### BMI at six years of age

Those being obese or overweight at six years of age (n=35) had lower adiponectin (p = 0.002) in their serum already at four months of age, but higher IGF-I (p <0.001) and leptin (p = 0.04). A significant larger increase in BMI was seen in children born SGA (1.55 ± 1.33 versus 0.65 ± 0.47 and 0.89 ± 1.33, p = 0.02), and these had a significantly higher insulin level at 6 years of age (7.2 ± 2.1 versus 4.8 ± 2.4, p = 0.02).

### Correlations to infant IGF-I

A lower IGF-I at four months correlated with a larger change in body mass index (BMI) from infancy to six years of age (p <0.001). Despite adjusting for sex, birth weight and current BMI, infant IGF-I was still associated with fasting insulin (p = 0.04) at six years of age.

### Correlations to infant adiponectin and leptin

Adiponectin at four months of age was associated with high-density lipoprotein cholesterol (p = 0.01) at six years of age but not after Holm-Bonferroni adjustment, whereas leptin at four months of age was associated with triglyceride levels (p=0.01) at six years of age still after Holm-Bonferroni adjustment.

### Regression analyses:

Infant leptin accounted for 14% (β = 0.39, p <0.001) of triglyceride levels at 6 years of age.

## Conclusion:

**IGF-I and adipokines at four months of age were found to be associated with metabolic markers in 6-year-old children.**

**Despite adjusting for known influences such as fetal growth, sex and current body size there seems to be an early programming by growth factors probably correlated through nutrition.**

**Table:** Associations between IGF-I, leptin and adiponectin during the first year of life (at the age of 4 and 12 months) and metabolic risk factors at 6 years of age. Data is expressed as linear regressions with standardized coefficients.

	Insulin	HOMA-IR	TG	WC	BMI
<b>IGF-I</b>					
4 month	0.22*	0.23*	0.19*	0.28*	0.26*
12 month	0.19	0.20	0.06	0.20*	0.21*
<b>Leptin</b>					
4 month	0.06	0.08	0.30*	0.15	0.23*
<b>Adiponectin</b>					
4 month	0.05	-0.01	-0.04	-0.22*	-0.24*

IR=insulin resistance, TG=triglycerides, WC=waist circumference, BMI=body mass index.

\*significant p-value after Holm-Bonferroni adjustment.

## Reference:

1. **Kjellberg E**, Roswall J, Bergman S, Almqvist-Tangen G, Alm B, **Dahlgren J**. Longitudinal birth cohort study found that a significant proportion of children had abnormal metabolic profiles and insulin resistance at 6 years of age. Acta Paediatr. 2019 Mar;108(3):486-492.