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ORIGINAL ARTICLE

Nutrition

Protein intake and insulin-like growth factor-1 at 12 months and associations with growth, body composition, and metabolic syndrome at 8 years

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Abstract

Objectives: Metabolic programming may occur during early life and have long-lasting effects on metabolic health. This study examined what impact early protein intake and levels of insulin-like growth factor (IGF-1) at 1 year of age had on growth, body composition and risk factors for metabolic syndrome at 8 years of age.

Methods: This was a prospective, observational, population-based study of 551 healthy, Swedish children. We used food diaries handed in at 1 year of age, and IGF-1 was measured at the same age. At 8 years of age, the children attended a clinical visit, where they underwent a dual X-ray absorptiometry scan, blood sampling, and anthropometry measurements.

Results: Protein intake at 1 year of age was associated with high waist circumference and insulin resistance measured as homeostatic model assessment for insulin resistance, at 8 years of age.

Conclusions: Protein intake at 1 year of age may have an impact on later metabolic health, mainly in form of insulin resistance and waist circumference.

KEYWORDS

macro nutrients, metabolism, nutrition, obesity

1 | INTRODUCTION

Obesity is an increasing global health issue for both children and adults. The World Health Organization (WHO) estimates that 37 million children under 5 years of age had obesity in 2019.[1] Obesity is associated with increased risk of metabolic disease through high blood pressure, insulin resistance and dyslipidemia, called the metabolic syndrome, and may lead to type 2 diabetes, atherosclerosis and premature death if left untreated.[2–4]

There is increasing evidence that a child's nutritional status during fetal life and the first years of life (1000 days) are crucial for later weight gain, body composition, and health.[5] One dietary factor that may play a role in this type of metabolic programming is protein intake.[6–9] The early protein hypothesis was introduced by Rolland-Cachera et al., and stipulates that higher protein content in the infant's and toddler's food causes a more rapid growth.[10] The mechanism for this is thought to be increased insulin secretion stimulating hepatic growth hormone sensitivity. This increases levels of insulin-like growth factor (IGF)-1, which then stimulates growth.[11] Emerging knowledge about early life programming shows that several environmental factors may play a role in metabolic health during childhood, adolescence, and adulthood. This type of programming of health later in life is mediated by epigenetic regulation through DNA methylation and histone modification.[12,13]

The aim of this study was to investigate whether protein intake and levels of IGF-1 had any impact on growth, body composition, and the risk factors associated with the metabolic syndrome at 8 years of age. It

also explored the correlation between protein intake and IGF-1-levels at 1 year of age.

What is Known

- Current evidence suggests that protein intake during early childhood has an influence on later metabolic health, however, results are ambiguous, and the relationships remain unclear.
- Average protein intake in many studies exceeds the recommended daily intake.

What is New

- This study supports the hypothesis that early protein intake has an impact on later cardiometabolic health.
- Higher protein intake was associated with impaired metabolic health in form of higher insulin resistance and higher waist circumference.
- Higher protein intake was associated with lower blood lipids (cholesterol and low-density lipoprotein cholesterol).

2 | METHODS

2.1 | Ethics statement

The parents received written information about the study at their visit to the maternal health care unit and were recruited before delivery, when the mothers registered at the maternity ward. The study complied with the declaration of Helsinki, and was approved by the ethical committee in Lund (number 44/2008, 531/2014, 442/2016). Written and verbal informed consent was obtained from all families upon enrollment.

2.2 | Subjects

This study was part of the ongoing longitudinal birth cohort Halland Health and Growth Study (H2GS) in southwest Sweden.[14] The children were recruited at Halmstad Hospital, Halland between April 2008 to June 2009, and June 2010 to August 2011.

2.3 | Study design

2.3.1 | Clinical visits

Study participants were measured (weight, height, and waist circumference) by the same two trained pediatric nurses, and blood samples collected at clinical visits during their first week of life, at 1 year and 8 years of age.

All children were weighed naked, or in their underwear, by the research nurses at onsite visits on electronic scales, and their height was measured using a stadiometer. Weight was measured on baby scales in the supine position as infants, and in a sitting position at 1 year of age and thereafter on a step scale. Height was measured in the supine position until 1 year of age and in standing position at 8 years. Waist circumference was measured midway between the iliac crest and the lowest rib. For each child, standard deviation score (SDS) were produced for weight, height and body mass index (BMI), based on Swedish reference curves.[15] BMI and the lean and fat mass indexes were calculated as kg/m^2. Study participants were classified as normal weight, overweight or obese according to the international obesity task force (IOTF) cut offs.[16] Blood samples were obtained after local anesthesia with Emla® (lidokain/prilokain).

At the age of 8 years, a dual X-ray absorptiometry (DXA)-scan and blood sampling were performed, after overnight fasting. Homeostatic model assessment for insulin resistance (HOMA-IR) was calculated using the formula (fasting insulin × fasting blood glucose)/22.5. Blood pressure was measured by a Welch Allyn Spot Vital Signs digital monitor (Welch Allyn) on the right arm, after resting for at least 10 min. Cuffs were chosen in line with the manufacturer's instructions.

2.3.2 | Food diaries

Parents completed food diaries for 3 consecutive days before the 1-year visit. They were instructed to provide the exact measures for food and drinks. Brands and contents were requested. These records were analyzed by trained dieticians and entered into the DietistXP digital nutrient database. This is based on the Swedish Food Agency's database and provides information about the macronutrients and micronutrients of more than 2000 common Swedish foods and dishes. Mean intakes of energy (kJ/day) and protein (g/day) were calculated, the latter was used when calculating protein intake. Total energy intake per kilogram of body weight was used as a surrogate marker for the quality of the dietary records. We excluded 22 children whose mean energy intake was less than 50% of recommended daily intake (RDI) kJ/kg based on the Nordic nutrition recommendations. Five children with 1 day of poor-quality intake were included and their data were based on the remaining 2 days.

There were good quality dietary records for 431 of the 551 children in the cohort, and 223 participated in the 8-year follow-up (51.7%). Five children had missing

or failed blood samples, leaving 218 participants remaining at 8 years of age. However, those five children were still included in the calculations on growth and body composition. There were no significant differences in mean gestational age, birthweight, birth length or BMI at 1 year of age when those 223 participants were compared with the 328 children who were excluded due to loss to follow up.

2.4 | Laboratory methods

All blood samples were centrifuged and frozen to −80 degrees Centigrade within 1 h of sampling. Plasma glucose and insulin were analyzed immediately, using a Cobas 6000 analyzer (Roche Diagnostics). Triglycerides, total cholesterol, high density lipoprotein (HDL) and low-density lipoprotein (LDL) cholesterol were analyzed using an enzymatic colorimetric assay on a Cobas 6000 analyzer (Roche, see previous description).

IGF-1was analyzed using IDS-iSYS. All samples were analyzed in the same batch, and the intra-assay coefficient of variation for IGF-1 was 2.8%.[17]

2.5 | Statistics

Categorical variables were described as frequencies and percentages, normally distributed continuous variables as means and standard deviations and non-normal continuous variables as medians and quartiles. Correlations were analyzed accordingly with Pearson's correlations, and the Student's *t*-test was used to compare groups. All statistical analyses were performed using SPSS version 29.0.0.0 (IBM Corp).

The all-components model was used to study the effect of protein, independent of energy content and other macronutrients.[18] Multivariable linear regression examined associations between protein intake and growth outcomes (weight, weight-SDS, height, height-SDS, BMI, and BMI-SDS), body composition (fat mass, fat mass index, lean mass, lean mass index, and body fat percentage), and metabolic factors (systolic and diastolic blood pressure, waist circumference, HOMA-IR, HDL, LDL, triglycerides, and cholesterol). The model was adjusted for height-SDS at 1 year of age when examining height and height-SDS at 8 years of age, and weight-SDS at 1 year of age when examining weight and weight-SDS at 8 years of age. When examining BMI and all factors for body composition, the model was adjusted for BMI-SDS at 1 year of age, to evaluate whether protein intake at 1 year of age could predict body composition independent of baseline BMI.[19] The model examining associations between protein intake at 1 year of age and metabolic syndrome factors at 8 years of age was adjusted for adiposity, namely body fat percentage, at 8 years of age.[19] We further used backwards regression to determine what factors to adjust for. Based on theory and previous literature, the following factors were considered but not included since they didn't have an impact on the effect estimates: gestational age, mode of delivery, maternal age, maternal education, child's age at follow-up. In the final model adjustments were made for birth weight-SDS and maternal BMI.

To study the effects of IGF-1 at 1 year of age on growth, we first performed a simple linear regression between IGF-1 and growth outcomes; weight, weight-SDS, height, height-SDS, BMI, and BMI-SDS. The model was then adjusted for height-SDS at 1 year of age when examining height and height-SDS at 8 years of age and adjusted for weight-SDS at 1 year of age when examining weight and weight-SDS at 8 years of age. When examining BMI and BMI-SDS, the model was adjusted for BMI-SDS at 1 year of age. In a similar manner, we performed simple linear regression between IGF-1 and measures of body composition examined by DXA. To evaluate whether IGF-1 at 1 year of age could predict body composition at 8 years of age independent of baseline BMI, the model was adjusted for BMI-SDS at 1 year of age. The model that examined the association between IGF-1 at 1 year of age and metabolic syndrome factors at 8 years of age was adjusted for adiposity at 8 years of age, in the form of body fat percentage. We further used backwards regression to determine what factors to adjust for. Based on theory and previous literature, the following factors were considered but not included since they didn't have an impact on the effect estimates: gestational age, mode of delivery, maternal age, maternal education, child's age at follow-up. In the final model adjustments were made for birth weight-SDS and maternal BMI.

3 | RESULTS

3.1 | Subject characteristics

Two-thirds of the 223 children (65.5%) were born vaginally, and the rest were born by c-section. We found that 6.7% were born small for gestational age (SGA) and 2.7% were born large for gestational age (LGA). The IOTF cut offs indicated that 3.5% ($n = 8$) had obesity and 16.5% ($n = 37$) were overweight at the 8-year follow-up.[16] See Table 1.

3.2 | Protein intake

Mean total protein intake at 1 year of age was 2.9 g/kg/day, which gives an energy percentage of almost 14 E %. The children had a mean energy intake of 351 kJ/kg,

TABLE 1 Characteristics of the participating children and their mothers.

	All ($n = 223$) (SD)	Boys ($n = 114$) (SD)	Girls ($n = 109$) (SD)	p value
Maternal characteristics				
Maternal age at enrollment (years)	31.4 (4.8)	31.1 (5.2)	31.6 (4.3)	0.515
Maternal BMI at enrollment (kg/m^2)	24.5 (4.7)	24.4 (4.2)	24.7 (5.0)	0.625
Child characteristics at birth				
Gestational age at birth (days)	278 (11)	279 (11)	277 (12)	0.445
Birth weight (g)	**3560 (603)**	**3658 (585)**	**3457 (607)**	**0.012**
Birth length (cm)	**50.6 (2.6)**	**51.1 (2.6)**	**50.1 (2.5)**	**0.004**
Child characteristics from dietary records				
Age at time of dietary records (days)	366 (9)	367 (7)	367 (10)	0.412
Total energy intake (kJ/day)	**3565 (699)**	**3674 (703)**	**3456 (678)**	**0.02**
Total energy intake (kcal/day)	**852 (167)**	**878 (168)**	**826 (162)**	**0.02**
Protein intake (g/day)	**29.4 (7.6)**	**31.0 (8.0)**	**27.9 (6.8)**	**0.002**
Protein intake (E%)	13.8 (2.4)	14.1 (2.7)	13.5 (2.0)	0.051
Fat intake (g/day)	29.7 (7.8)	30.5 (7.5)	29.0 (8.0)	0.154
Fat intake (E%)	31.3 (5.0)	31.2 (4.6)	31.5 (5.4)	0.447
Carbohydrate intake (g/day)	109.3 (24.3)	112.0 (24.0)	116.6 (24.0)	0.099
Carbohydrate intake (E%)	51.3 (5.4)	51.1 (5.3)	51.6 (5.5)	0.669
IGF-1 (μg/l)	**55.9 (25.6)**	**50.7 (20.9)**	**61.2 (28.7)**	**0.003**
Child characteristics at 8-year visit				
Age (years)	8.4 (0.3)	8.4 (0.3)	8.0 (0.3)	0.67
Weight (kg)	29.6 (5.6)	30.1 (5.4)	29.0 (5.9)	0.074
Height (cm)	**133.2 (5.8)**	**134.4 (5.6)**	**132.0 (5.7)**	**0.001**
Waist circumference (cm)	**57.7 (5.8)**	**58.7 (5.2)**	**56.7 (6.1)**	**0.009**
BMI (kg/m^2)	16.6 (2.4)	16.6 (2.2)	16.6 (2.6)	0.948
Body fat percentage (%)	**27.1 (6.5)**	**25.0 (6.2)**	**29.3 (6.0)**	**<0.001**
Lean mass (kg)	**20.7 (2.8)**	**21.9 (2.7)**	**19.6 (2.5)**	**<0.001**
Fat mass (kg)	8.0 (3.3)	7.6 (3.3)	8.5 (3.3)	0.054
Systolic blood pressure (mm Hg)	100 (7)	101 (7)	100 (8)	0.235
Diastolic blood pressure (mm Hg)	63 (5)	63 (5)	63 (6)	0.643
HDL cholesterol (mmol/l)	1.6 (0.3)	1.7 (0.3)	1.6 (0.3)	0.055
LDL cholesterol (mmol/l)	**2.4 (0.6)**	**2.4 (0.6)**	**2.5 (0.6)**	**0.027**
Cholesterol (mmol/l)	4.1 (0.6)	4.0 (0.7)	4.2 (0.7)	0.139
Triglyceride levels (mmol/l)	**0.6 (0.2)**	**0.6 (0.2)**	**0.7 (0.2)**	**0.003**

TABLE 1 (Continued)

	All ($n = 223$) (SD)	Boys ($n = 114$) (SD)	Girls ($n = 109$) (SD)	p value
HOMA-IR	1.5 (1.2)	1.6 (1.6)	1.4 (0.7)	0.478
HbA1c (mmol/mol)	34.5 (2.5)	34.3 (2.8)	34.7 (2.3)	0.349
Insulin levels (mU/l)	6.5 (5.1)	6.7 (6.5)	6.3 (3.0)	0.632
Glucose levels (mmol/l)	4.8 (0.5)	4.9 (0.5)	4.8 (0.4)	0.181

Note: Data given as mean and SD. Bold values indicate statistical significance.

Abbreviations: BMI, body mass index; E%, percentage of total energy intake; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; IGF, insulin-like growth factor; LDL, low-density lipoprotein; SD, standard deviation.

and the range of energy intake was wide, 185–657 kJ/kg/day.

3.2.1 | Protein intake versus IGF-1 at 1 year of age

There was a weak but significant correlation between IGF-1 and protein intake ($r = 0.184$, $p = 0.007$) and carbohydrate intake ($r = 0.153$, $p = 0.025$) but not fat intake at 1 year of age. The associations were not significant when analyzed with univariate linear regression.

3.2.2 | Protein intake versus growth

There was an association between protein intake at 1 year of age and height-SDS at 8 years of age ($p = 0.008$), which disappeared when adjusting for height-SDS at 1 year in the whole group. This association was significant for boys ($p = 0.041$) also after adjustments.

There were no associations between protein intake at 1 year and weight, weight-SDS, BMI, and BMI-SDS at 8 years. All models were adjusted for fat intake and carbohydrate intake, as well as birth weight-SDS and maternal BMI. Weight and weight-SDS at 8 years were adjusted for weight-SDS at 1 year of age, and BMI and BMI-SDS were adjusted for BMI-SDS at 1 year of age.

3.2.3 | Protein intake versus body composition

There was an association between protein intake at 1 year of age and lean mass at 8 years of age ($p = 0.04$) for the whole group. This association disappeared when adjusting for BMI-SDS at 1 year of age ($p = 0.065$). All other measures (lean mass index, fat mass, fat mass index, and body fat percentage) were not significant. All factors were adjusted for fat intake, carbohydrate intake, birth weight-SDS, maternal BMI, and child BMI-SDS at 1 year of age.

3.2.4 | Protein intake versus metabolic syndrome

Table 2 shows the associations between protein intake and metabolic syndrome. There was a significant association between protein intake at 1 year of age and HOMA-IR at 8 years of age, which was significant for boys, but not for girls when dividing by sex. This association remained when adjusting for birth weight-SDS and maternal BMI.

There was a significant association between protein intake and waist circumference for the whole group, which remained unchanged after adjustment. This association was not significant when the sexes were analyzed separately. There was an association between protein intake and systolic blood pressure for boys, but not for girls or the whole group.

Negative associations were found between protein intake and LDL cholesterol and total cholesterol for the whole group. Boys also showed a negative association between LDL cholesterol and cholesterol and protein intake.

All models were adjusted for fat intake, carbohydrate intake at 1 year and body fat percentage at 8 years of age. We then stepwise adjusted for birth weight-SDS and maternal BMI, as can be seen in Table 2.

3.3 | IGF-1

3.3.1 | IGF-1 versus growth

Simple linear regression showed a significant association between IGF-1 at 1 year of age and BMI at 8 years. This association remained significant when adjusted for BMI-SDS at 1 year, and birth weight-SDS. It was also significant for girls, but not for boys using the same method. This association disappeared when adjusted for maternal BMI.

There was no association between IGF-1 at 1 year and height, height-SDS (adjusted for height-SDS at

TABLE 2 Multivariable regression models showing associations between protein intake and factors of metabolic syndrome.

Predicting variable: Protein intake (g/day)							
		Adjusted for factors described below		Adjusted for birth weight-SDS and factors described below		Adjusted for birth weight-SDS, maternal BMI and factors described below	
	Dependent variables	Beta	*p* value	Beta	*p* value	Beta	*p* value
All	HOMA-IR	0.045	**0.005**	0.046	**0.004**	0.049	**0.003**
	Waist circumference (cm)	0.148	**0.006**	0.137	**0.009**	0.147	**0.007**
	Triglycerides (mmol/L)	−0.005	0.103	−0.004	0.128	−0.005	0.072
	Cholesterol (mmol/L)	−0.019	**0.027**	−0.019	**0.033**	−0.02	**0.03**
	LDL (mmol/L)	−0.02	**0.013**	−0.02	**0.015**	−0.02	**0.13**
	HDL (mmol/L)	−0.001	0.781	−0.001	0.82	−0.001	0.824
	SBP (mmHg)	0.183	0.057	0.174	0.071	0.167	0.097
	DBP (mmHg)	0.099	0.159	0.096	0.174	0.099	0.18
Boys	HOMA-IR	0.054	**0.027**	0.054	**0.028**	0.056	**0.033**
	Waist circumference (cm)	0.086	0.099	0.089	0.82	0.078	0.144
	Triglycerides (mmol/L)	−0.005	0.163	−0.005	0.167	−0.005	0.163
	Cholesterol (mmol/L)	−0.021	0.056	−0.021	0.051	−0.022	**0.043**
	LDL (mmol/L)	−0.023	**0.018**	−0.023	**0.016**	−0.024	**0.015**
	HDL (mmol/L)	−0.003	0.538	−0.003	0.519	−0.004	0.5
	SBP (mmHg)	0.215	**0.048**	0.212	**0.05**	0.226	**0.048**
	DBP (mmHg)	0.106	0.199	0.104	0.207	0.111	0.202
Girls	HOMA-IR	0.005	0.752	0.009	0.567	0.013	0.419
	Waist circumference (cm)	0.000	0.996	−0.026	0.72	−0.003	0.97
	Triglycerides (mmol/L)	−0.004	0.533	−0.002	0.737	−0.004	0.45
	Cholesterol (mmol/L)	−0.013	0.441	−0.012	0.459	−0.015	0.381
	LDL (mmol/L)	−0.009	0.566	−0.009	0.548	−0.011	0.476
	HDL (mmol/L)	0.003	0.75	0.002	0.769	0.001	0.935
	SBP (mmHg)	−0.034	0.85	−0.09	0.62	−0.163	0.394
	DBP (mmHg)	0.053	0.687	0.022	0.866	0.006	0.964

Note: Protein intake measured at 1 year of age. Each variable adjusted for fat intake (g/day), carbohydrate intake (g/day) and body fat percentage (BF%). Stepwise adjusted for birth weight-SDS and maternal BMI. β-estimate refers to the unstandardized coefficient of the linear regression. Bold values indicate statistical significance.

Abbreviations: BMI, body mass index; DBP, diastolic blood pressure; HDL, high density lipoprotein; HOMA-IR, homeostatic model assessment for insulin resistance; LDL, low-density lipoprotein; SBP, systolic blood pressure; SDS, standard deviation score.

1 year), weight, weight-SDS (adjusted for weight-SDS at 1 year) and BMI-SDS at 8 years (adjusted for BMI-SDS at 1 year). All factors were also stepwise adjusted for birth weight-SDS and maternal BMI.

3.3.2 | IGF-1 versus body composition

Table 3 shows the association between IGF-1 and body composition. IGF-1 at 1 year of age was associated with all adiposity measures of body composition examined by DXA. Fat mass, fat mass index and body fat percentage all correlated significantly, for all measures using both univariate correlation and linear regression. Associations persisted when adjusted for BMI-SDS at 1 year, and birth weight-SDS. When adjusted for maternal BMI all associations lost significance. There was a weak association for girls but not for boys regarding IGF-1 and fat mass, and IGF-1 and fat mass index when performing linear regression and adjusting for BMI-SDS at 1 year. These associations persisted when adjusted for birth weight-SDS, but disappeared when adjusted for maternal BMI, as can be seen in Table 3.

3.3.3 | IGF-1 versus the metabolic syndrome

There were no significant associations between IGF-1 at 1 year of age and any factors for the metabolic syndrome at 8 years of age when performing linear regression. All factors were adjusted for body fat percentage at 8 years, birth weight-SDS, and maternal BMI.

4 | DISCUSSION

In this longitudinal birth cohort, the main finding was that protein intake at 1 year of age was associated with increased risk for some signs of the metabolic syndrome at 8 years of age. There was an association between protein intake at 1 year of age and insulin resistance measured as HOMA-IR, which persisted when adjusted for body fat percentage at 8 years of age, birth weight-SDS and maternal BMI. This implies that early protein intake might exert metabolic imprinting, contributing to higher risk of impaired glucose tolerance later in life. Insulin resistance is known to be one of the strongest risk factors for later development of the metabolic syndrome.[20] One earlier study has shown that higher protein intake at 4 years of age leads to higher fasting insulin at 7 years of age,[21] and our finding is in line with that.

There was a strong association between protein intake and waist circumference, an indirect measure of subcutaneous and visceral fat. The latter is known to be more metabolically active, and might play an important role regarding risk of metabolic syndrome.[22,23] If this association can be proven to possess a causal relationship in future studies, increasing protein intake by 10 g/day at the age of one would increase waist circumference by almost 1.5 cm at the age of eight according to our measures (see Table 2).

On the other hand, a weak negative association with protein intake and cholesterol and LDL-cholesterol was found. This finding is in line with a meta analysis in an adult population showing that high protein intake can reduce cholesterol, LDL and triglycerides, although the mechanism remains unclear.[24] In a pediatric setting, a previous study has shown that higher protein intake among boys at the age of 1 year led to lower levels of triglycerides at 6 years of age.[19]

It is worth pointing out that these metabolic associations could be seen even though the children in this cohort did not exceed the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition recommendations of 15 E% of protein. These results need to be confirmed in larger studies.

Interestingly, IGF-1 displayed an association to body fat at 8 years of age. IGF-1 at 1 year of age was associated with all measures for fat mass from the DXA scan (fat mass, fat mass index and body fat percentage), which remained significant when adjusting for BMI-SDS at 1 year of age and birth weight-SDS, but disappeared when adjusting for maternal BMI, indicating a genetic or possibly intra uterine component involved in the association. Previous results from the same cohort showed that high levels of IGF-1 at 4 months were associated with high BMI at 6 years of age.[25] IGF-1 is a key regulator of growth, but also effects on metabolic processes such as glucose and lipid metabolism, and thereby body composition. IGF-1-levels are influenced primarily by nutrition in infancy, but regulated by growth hormone in childhood.[11,26,27] Increased weight gain in infancy is associated with increases in insulin and IGF-1 concentrations, which also stimulate linear growth. Mean total protein intake at 1 year of age was 2.9 g/kg/day, which gives an energy percentage of almost 14 E%. This can be compared to the figures from the Nordic nutrition recommendations from 2023, which recommend an energy percentage from protein of 10–15 E%, and recommended intake (RI) of 1.05 g/kg. The children in this cohort had a mean energy intake of 351 kJ/kg, slightly exceeding recommendations, 337 kJ/kg for boys, and 333 kJ/kg for girls. However, the range of energy intake was wide, 185–657 kJ/kg/day. Previous studies have shown that many young children exceed recommendations regarding protein intake.[9,28]

Previous studies have shown that a higher protein intake during early childhood can lead to higher IGF-1 later during adolescence or early adulthood.[21,29,30] In this study, we could not see any correlation between

TABLE 3 Multivariable regression models showing associations between body composition and IGF-1.

Predicting variable: IGF-1 (μg/L)							
		Adjusted for BMI-SDS at 1 year of age		Adjusted for BMI-SDS at 1 year of age and birth weight-SDS		Adjusted for BMI-SDS at 1 year of age, birth weight-SDS and maternal BMI	
	Dependent variables	Beta	*p* value	Beta	*p* value	Beta	*p* value
All	Body fat %	0.041	**0.012**	0.042	**0.011**	0.032	0.052
	Fat mass (g)	19.5	**0.016**	19.9	**0.014**	14.89	0.068
	Fat mass index (kg/m^2)	0.01	**0.016**	0.01	**0.015**	0.007	0.076
	Lean mass (g)	4.31	0.548	4.97	0.478	3.53	0.629
	Lean mass index (kg/m^2)	0.000	0.93	0	0.985	−0.001	0.766
	BMI (kg/m^2)	0.011	**0.049**	0.011	**0.043**	0.008	0.163
Boys	Body fat %	0.004	0.894	0.005	0.852	−0.006	0.809
	Fat mass (g)	9.75	0.510	10.71	0.467	4.88	0.718
	Fat mass index (kg/m^2)	0.002	0.753	0.003	0.711	0	0.966
	Lean mass (g)	21.45	0.077	22.76	0.054	19.67	0.098
	Lean mass index (kg/m^2)	0.005	0.229	0.005	0.192	0.004	0.31
	BMI (kg/m^2)	0.007	0.48	0.008	0.421	0.004	0.65
Girls	Body fat %	0.034	0.066	0.034	0.067	0.025	0.188
	Fat mass (g)	19.87	**0.04**	19.97	**0.039**	15.45	0.125
	Fat mass index (kg/m^2)	0.01	**0.042**	0.01	**0.042**	0.007	0.138
	Lean mass (g)	11.04	0.143	11.29	0.123	10.18	0.19
	Lean mass index (kg/m^2)	0.003	0.324	0.003	0.308	0.002	0.486
	BMI (kg/m^2)	0.014	**0.043**	0.014	**0.044**	0.01	0.139

Note: Each variable adjusted for BMI-SDS at one year of age. β-estimate refers to the unstandardized coefficient of the linear regression. Stepwise adjusted for birth weight-SDS and maternal BMI. Bold values indicate statistical significance.

Abbreviations: BMI, body mass index; IGF, insulin-like growth factor; SDS, standard deviation score.

these two, but the reason may be that IGF-1 only was measured at 1 year of age. We know from a previous article in a subgroup from the same cohort, that breast feeding correlated to lower IGF-1 levels at 4 months of age.[31] IGF-1 is strongly associated with nutritional status up to approximately 9 months of age, after which levels are mainly driven by a functioning growth hormone secretion. It is possible that if IGF-1 would have been measured earlier during infancy, IGF-1 would correlate stronger with the protein intake.

One previous study has shown that protein intake during childhood correlated to final height in females.[32] In our study there was an association between protein intake at 1 year of age and height-SDS at 8 years but only for boys. The lack of correlation in girls can be due to a lower range of protein intake or other more important unknown influential factors as girls are found here and in other publications to have higher IGF-1 levels.

The strength of this study is the prospective, longitudinal design from birth and also the population-based cohort of healthy, term children. A major limitation is the high drop-out percentage and relatively small number of participants, both concerning dietary records, and 8-year follow-up.

5 | CONCLUSIONS

To conclude, we showed that high protein intake at 1 year of age was associated with some risk factors for the metabolic syndrome, mainly insulin resistance and

increased waist circumference, during early school age. Why there is a negative association to cholesterol merits further evaluation, although some evidence from other studies supports this finding. Further studies are needed to confirm these findings in a larger cohort, and to explore whether these cardiometabolic changes persist in adolescence and adulthood.

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CONFLICT OF INTEREST STATEMENT

Jovanna Dahlgren, Stefan Bergman, Gerd Almquist Tangen and Josefine Roswall were all involved in starting this cohort. Gabriella Olander Seidal is the main author of the manuscript. All authors have been involved in the interpretation of data, and have made comments on drafts. The authors have no conflicts of interest to disclose.

DATA AVAILABILITY STATEMENT

The datasets generated in this study are not publicly available for ethical reasons and in line with Swedish legislation. Requests to make data available to reproduce the findings should be made to Josefine Roswall (josefine.roswall@regionhalland.se).

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