

ORIGINAL ARTICLE

Growth and micronutrient levels of 6–12 years-old children with food allergies, food sensitisation, and food restrictions

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Abstract

Aim: We investigated the association of food allergy, food sensitisation, and food restriction with growth and micronutrients levels in schoolchildren.**Methods:** A total of 195 schoolchildren (6–12 years old) from six elementary schools in Korea were enrolled, and questionnaires were administered to their parents during June and July 2015. Food allergy was defined by the presence of urticaria, skin rash, pruritus, throat tightness, gastrointestinal complaints, or respiratory difficulty after consumption of a food to which allergy was plausible during the past 12 months. Skin prick tests were performed and serum levels of haemoglobin and micronutrients were measured.**Results:** Among 195 participants (51.3% males) enrolled, 35 (17.9%) were reported to have food allergies, 17 (8.7%) were on food restriction, and 27 (14.0%) were sensitised to at least one food allergen. Food allergy and food restriction were associated with a lower height-for-age z-score (p for trend = 0.018, $p = 0.048$; p for trend = 0.076, $p = 0.008$). Food restriction was related to reduced serum calcium level (aOR: -0.094, 95% CI: -0.156 to -0.032).**Conclusion:** Signs and symptoms of food allergy and consequent food restrictions in children were related to lower height-for-age z-score and lower serum calcium levels.

KEYWORDS

allergic disease, children health and growth, food restriction, micronutrient

1 | INTRODUCTION

Food allergies and the imposition of food restrictions can have negative effects on the health of children.¹ Poor growth status is an important indicator of health problems in children^{2,3} and might be related to food avoidance and dietary interventions.^{4,5} Thus, researchers have devoted increasing attention to the effects of food allergies and dietary restrictions on childhood growth.

Several studies showed that children with food allergies weighed less and were shorter than their peers, possibly because these children use elimination diets, have decreased calorie consumption, unmet nutrient requirements, or intestinal inflammation due to food allergies.^{6–8} Among the many possible reasons for the poor growth status of these children, there is increasing interest in the effects of dietary changes due to parental beliefs about food allergies.

Abbreviations: aOR, adjusted odds risk; BMI, body mass index; CI, confidence interval; Der f., *Dermatophagoides farinae*; Der p., *Dermatophagoides pteronyssinus*; SPT, skin prick test.

Man Yong Han and Eun Kyo Ha supervised this paper equally.

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Despite the rising concerns about the poor growth status of some children, the relationship of this condition with food allergy and food restriction remains unclear. Available research yielded inconsistent results on this topic. In particular, some studies reported associations of poor childhood growth and nutritional problems with food allergies.⁹ Other studies suggested that the association of failure to thrive during childhood with allergic diseases and food allergies that were reported in some studies^{10,11} was due to the use of inappropriate exclusion diets and inadequate nutrition counselling. Additional studies suggested no clear association between allergic diseases or food restrictions with the growth or nutritional status of children.^{7,12} Furthermore, the effect of parent-reported food allergy, food restriction, and allergic sensitisation¹³ on serum micronutrient levels has not yet been determined.

In this study, we assessed the effect of parent-reported food allergy, food allergen sensitisation, and avoidance on child growth and health status. Parental beliefs that food allergies cause health problems in their children can lead to inappropriate restrictions or elimination of foods, leading to suboptimal growth and nutritional status of these children.¹³ Although the association between food allergies and faltered growth is widely acknowledged, we hypothesised that this link may be related to disruption of serum micronutrient levels.

2 | METHODS

2.1 | Study population

The prospective study was performed during June and July 2015. We asked parents if they agree to answer questionnaires and to have their children involved in additional investigations. Paediatricians and trained field technicians took part in prior to physical examination, skin prick tests (SPTs) and blood sampling at participating schools. We contacted 4111 elementary schoolchildren and considered children whose parents agreed to answer the questionnaire and gave written consent to additional examinations including blood sampling eligible ($n = 417$). This study was approved by the Institutional Review Board of the CHA Bundang Medical Centre (IRB no. 2015-05-075). All parents or guardians provided written informed consent for participation.

2.2 | Anthropometric measurements

A trained field technician measured height and weight, and calculated the body mass index (BMI) of all participants. The standardised score (z-score) by sex and age were obtained using the Lambda-Mu-Sigma method with the 2017 Korean National Growth Charts.¹⁴ To assess growth, BMI, and height-for-age z-score were each classified as below the 25th percentile, 25th to 75th percentile, and above the 75th percentile.

Key Notes

- Links between children's growth and food allergy have been reported, and interest in the effect of dietary restriction due to parental concerns about food allergies is increasing.
- This study shows reduced growth and lower levels of serum calcium of children with symptoms and signs of food allergy and food restriction.
- Our findings implicate the importance of diagnosis of food allergy and decisions regarding dietary restrictions in children.

2.3 | Data collection

Detailed questionnaires were used to collect demographic data and identify the prevalence of allergic diseases in children, and parents received detailed instructions prior to questionnaire administration. The information collected included age, sex, height, weight, and year of birth. Monthly household income (4-million or more Korean won vs. <4-million Korean won) and maternal education level were recorded as indicators of socio-economic status. The questionnaire also recorded information about food allergies, dietary restrictions, and current symptoms of asthma, atopic eczema, and allergic rhinitis.

2.4 | Parental reports of food allergy, sensitisation to food allergens, and food restrictions

Food allergy was assessed by asking the parent if the child had urticaria, skin rash, pruritus, throat tightness, gastrointestinal complaints, or respiratory difficulties after consumption of food to which an allergy was plausible.¹⁵ A parent-reported food allergy was defined as present if the child had these symptoms at any time during the past 12 months. Open questions were also used to identify specific foods that the parents thought caused the allergy.

Skin prick tests of each child's forearm were used to assess sensitisation to foods, and these were performed by an experienced technician according to international guidelines. Subjects were classified as having food allergen sensitisation if there was a positive reaction (wheal diameter ≥ 3 mm) in response to one or more allergens. Reactions to 16 common foods and six aero-allergens were tested using extracts and control solutions from Lofarma: Egg, milk, peanut, wheat, walnut, cod, pork, mussel, shrimp, apple, peach, kiwi, orange, tomato, strawberry, celery, *Dermatophagoides pteronyssinus* (*Der p.*), *D. farina* (*Der f.*), birch, oak, elm, and hop.¹⁶

The impact of elimination diets on child health and information regarding food restrictions were collected from answers to questions about foods that possibly caused allergy symptoms. The foods

selected in this analysis were based on the results of previous publications of Korean children.¹⁷ If the parents used an elimination diet, they were required to describe the specific types of food(s) that were restricted.

2.5 | Measurement of micronutrients

Serum micronutrient levels were measured in peripheral blood samples. Folic acid, and vitamin B12 were measured using a Electrochemiluminescent immunoassay (Modular Analytics, E170, Roche/Germany) and serum 25(OH) D level was measured using a direct competitive chemiluminescence assay (LIAISON system). Serum selenium was measured using Inductively Coupled Plasma - Mass Spectrometry (ICP-MS, DRCE, PerkinElmer/Germany).¹⁸ Serum zinc was measured using a spectrofluorophotometer (ICP-MS, ELAN DRCE, PerkinElmer/Germany). Eosinophil counts¹⁶ were measured using an automated analyser. Haemoglobin was measured using the principles of a variant of ion-exchange high performance liquid chromatography (Bio-Rad Variant analyzers).

2.6 | Statistics

Data were checked for range, extremes, and logical accuracy. Continuous values for micronutrients were presented as medians, interquartile ranges, and 95th percentiles. The chi-square test for trend was used to evaluate the association of food allergy, food sensitisation, and food restriction with anthropometric measurements (height-for-age z-score and BMI z-score). A generalised linear model procedure with a Gaussian function was used to identify the associations of serum micronutrient levels and independent variables (food allergy, food sensitisation, and food restriction). Data were analysed after adjustment for confounders: sex (male or female), age (continuous variable), BMI z-score (continuous variable), prematurity or low birth weight (no or yes), socio-economic status (low or high), maternal education level (low or high), and percentage of eosinophils ($\geq 4\%$ or $< 4\%$). Results were expressed as adjusted beta ($\alpha\beta$) with 95% confidence intervals (CIs). For all analyses, a *p* value below 0.05 was considered significant. Statistical analyses were performed using SPSS version 23.0 (IBM Co.).

3 | RESULTS

3.1 | Characteristics of participating children

A total of 417 participants gave consent to complete the questionnaire, examination, and further tests. Additional micronutrient test was performed in the case of participants with a sufficient amount of blood. The total sample for analysis consisted of 195 school children (Table 1). The mean age was 9.4 ± 1.7 years, there were 51.3% males ($n = 100$) and 48.7% females ($n = 95$), 57 children (29.2%) were below

TABLE 1 Demographic and clinical characteristics of participating children ($n = 195$)

Variable	N (%)
Gender	
Male	100 (51.3)
Female	95 (48.7)
Age	
6–8 years	62 (31.8)
9–10 years	56 (28.7)
11–12 years	77 (39.5)
Height-for-age z-score	
<25th percentile	57 (29.2)
25–75th percentile	107 (54.9)
>75th percentile	31 (15.9)
BMI z-score	
<25th percentile	65 (33.3)
25–75th percentile	97 (49.7)
>75th percentile	33 (16.9)
Prematurity and/or low birth weight	
No	174 (90.2)
Yes	19 (9.8)
Household income	
Low (<4 million Korean won/month)	59 (31.2)
High (≥ 4 million Korean won/month)	130 (68.8)
Maternal education	
High school graduate or less	70 (36.8)
Beyond high school	120 (63.2)
Parent-reported food allergy	
No	160 (82.1)
Yes	35 (17.9)
Food restriction	
No	178 (91.3)
Yes	17 (8.7)
Skin prick test results ^a	
Aeroallergen	102 (52.8)
Food allergen	27 (14.0)
Total eosinophil percentage	
<4%	119 (61.0)
$\geq 4\%$	76 (39.0)

Abbreviations: BMI, body mass index; SD, standard deviation.

^aA positive skin-prick test was based on positivity to at least 1 of 16 food allergens (egg, milk, cod, mussel, shrimp, pork, peanut, walnut, wheat, celery, kiwi, orange, tomato, strawberry, apple, and peach) and 1 of 6 aeroallergens (House-dust mites [*Dermatophagoides farinae*, *D. pteronyssinus*], oak, birch, elm, and Japanese Hop). Missing data: $n = 2$.

the 25th percentile of height-for-age z-score, and 65 children (33.3%) had BMI z-scores below the 25th percentile. The skin prick tests indicated 108 children (52.8%) were sensitised to at least one aeroallergen and 27 children (14.0%) were sensitised to at least one food allergen.

Thirty-five children (17.9%) had food allergies, 17 (8.7%) had food restrictions, and 27 (13.8%) were sensitised to food allergens. In detail, 10 (5.1%) of them were defined as food allergy and food sensitised. Three (1.5%) of these children were also restricting foods (Figure 1). Eleven children had 1 food restriction, two had 2 food restrictions, two had three food restrictions, one had four food restrictions, and one had five food restrictions (Figure S1).

3.2 | Associations of height-for-age z-score and BMI z-score with food allergy, food allergen sensitisation, and food restriction

Relative to children without parent-reported food allergies, more children with parent-reported food allergies were below the 25th percentile of height-for-age z-score ($p = 0.048$, p for trend = 0.018, Table 2). This pattern was also present in children who had restricted diets ($p = 0.076$, p for trend = 0.008). The results were consistent in the analysis excluding 9 children with current asthma (Table S1). Meaningful differences in height for age z-score, and BMI z-score were not found when children with current atopic dermatitis and allergic rhinitis were separately analysed, implicating minimal effects of these allergic conditions on growths (Data not shown). Notably, food allergen sensitisation determined by skin prick tests was unrelated to height-for-age z-score or BMI z-score. Meanwhile, BMI z-score was unrelated to parent-reported food allergy.

3.3 | Associations of serum micronutrients with parent-reported food allergy, food allergen sensitisation, and food restriction

Serum haemoglobin and micronutrient levels were unrelated to parent-reported food allergies or food allergen sensitisation (Table 3). However, there was a significant relationship between low

calcium level and food restriction ($a\beta$ [95% CI], -0.094 [-0.156 to -0.032]). We also measured median levels of serum haemoglobin and micronutrients and quartile categories relative to the reference ranges (Table S2).

4 | DISCUSSION

We investigated the associations of food allergy, food allergen sensitisation, and food restriction with the health of elementary schoolchildren based on their growth status and serum levels of haemoglobin and micronutrients. Children with food allergies and food restrictions were shorter (but not lighter) and had lower levels of serum calcium than other children. Several recent studies have highlighted nutritional problems in children with food allergies.¹⁹ However, data assessing serum micronutrient levels that are receiving attention in children with food allergy and food restriction are still limited. In this study, we provided information regarding growth and nutritional status in children with food allergies, food allergen sensitisation, and food restrictions using objective body measurements and serum assayed micronutrient concentrations.

A major strength of our study is that we sampled a paediatric population irrespective of pre-existing allergic conditions. In addition, we used detailed and structured questionnaires, anthropometric measurements, specific IgE tests, and laboratory studies to comprehensively assess the associations between food allergy and child health status. All examinations and measurements were conducted by physicians and trained health care providers. We also collected data on major factors that could potentially confound the relationship between food allergy and growth, which enabled the use of multiple exposure assessments. Specifically, we investigated socio-economic status and considered it in conjunction with food allergy and child health status. Our results indicated associations of signs and symptoms of allergic diseases with reduced child growth and a low level of serum calcium. A limitation of this study is its cross-sectional design, which prevented us from inferring causal relationships. In addition, we identified food allergy in children using questionnaires administered to the parents. We did not use objective methods for confirmation of these diagnoses, such as oral food challenge tests, so the true incidence of food allergy in this population remains uncertain. Moreover, among the initially contacted children only a small portion participated, and the positive allergen sensitisation rate was high, which implicates the possibility of selection bias. Considering the purpose of the survey, parents with concerns regarding allergies would have been more inclined to respond to our survey and interpretation and interpretation with caution is needed. Another limitation is that data on micronutrient levels was missing in some participants. Because this was a survey implemented as a health screening program for schoolchildren, additional sampling was not easy and some of the participants provided insufficient samples. Further examinations of large populations that use a longitudinal study design are needed to confirm our results.

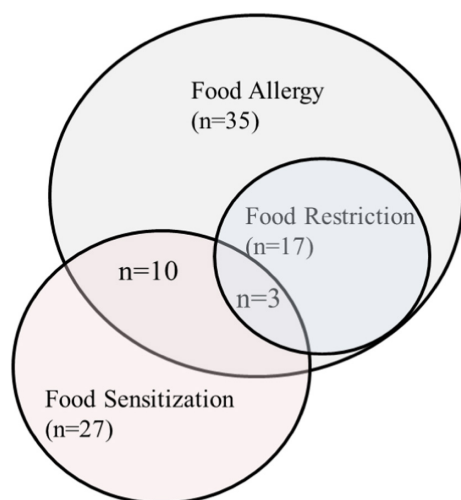


FIGURE 1 Venn diagram showing overlap of participants with food allergy, food allergen sensitisation, and food restriction

TABLE 2 Association of height-for-age z-score and BMI z-score with parent-reported food allergy, food allergen sensitisation, and food restriction ($n = 195$)

	Height-for-age z-score					BMI z-score				
	N (%)									
	<25th	25–75th	>75th	p Value	p for trend ^a	<25th	25–75th	>75th	p Value	p for trend ^a
Parent-reported food allergy										
No	41 (25.6)	91 (56.9)	28 (17.5)	0.048	0.018	56 (35.0)	83 (51.9)	21 (13.1)	0.802	0.541
Yes	16 (45.7)	16 (45.7)	3 (8.6)			11 (31.4)	18 (51.4)	6 (17.1)		
Food allergen sensitisation										
Non-	48 (28.9)	91 (54.8)	27 (16.3)	0.367	0.360	57 (34.3)	89 (53.6)	20 (12.0)	0.518	0.648
Mono-	4 (28.6)	6 (42.9)	4 (28.6)			4 (28.6)	6 (42.9)	4 (28.6)		
Poly-	5 (38.5)	8 (61.5)	0 (0.0)			5 (38.5)	6 (46.2)	2 (15.4)		
Food restriction										
0	47 (26.4)	101 (56.7)	30 (16.9)	0.076	0.008	62 (34.8)	92 (51.7)	24 (13.5)	0.069	0.472
1	6 (54.5)	4 (36.4)	1 (9.1)			5 (45.5)	3 (27.3)	3 (27.3)		
≥2	4 (66.7)	2 (33.3)	0 (0.0)			0 (0.0)	6 (100.0)	0 (0.0)		

^ap for trend: Linear-to-linear.Significant difference ($p < 0.05$) marked bold.**TABLE 3** Association of serum levels of haemoglobin and micronutrients with parent-reported food allergy, food allergen sensitisation, and food restriction^a

Independent variable	Dependent Variable					
	Parent-reported food allergy		Food allergen sensitisation		Food restriction	
	Adjusted beta (95% CI)	p Value	Adjusted beta (95% CI)	p Value	Adjusted beta (95% CI)	p Value
Haemoglobin	−0.022 (−0.285 to 0.241)	0.871	−0.053 (−0.121 to 0.016)	0.133	−0.101 (−0.265 to 0.063)	0.225
Folic acid	1.329 (−0.512 to 3.170)	0.157	−0.063 (−0.544 to 0.418)	0.798	−0.058 (−1.191 to 1.076)	0.921
Vitamin B12	81.45 (−9.949 to 172.8)	0.081	17.94 (−42.14 to 6.253)	0.146	10.35 (−47.22 to 67.92)	0.725
Vitamin D	1.033 (−0.720 to 2.786)	0.248	−0.173 (−0.633 to 0.288)	0.463	−0.499 (−1.596 to 0.598)	0.373
Calcium	−0.052 (−0.153 to 0.050)	0.317	0.006 (−0.033 to 0.021)	0.672	−0.094 (−0.156 to −0.032)	0.003
Selenium	1.907 (−4.154 to 7.968)	0.537	−2.802 (−5.635 to 0.030)	0.053	−1.691 (−5.365 to 1.982)	0.367
Zinc	−0.448 (−6.385 to 5.490)	0.883	−1.057 (−3.880 to 1.767)	0.463	0.065 (−3.544 to 3.673)	0.972

^aGeneralised linear regression with a Gaussian function and adjustment for gender, age, BMI z-score, prematurity and/or low birth weight, socio-economic status, maternal education level, and eosinophil percentage.Significant difference ($p < 0.05$) marked bold.

One of our main findings is that food allergy in schoolchildren was associated with decreased height-for-age z-score. This result is in accordance with previous studies that also reported reduced growth in children who had food allergies.^{20,21} A possible explanation for the reduced growth in these children is that the food restrictions or poor diets led to nutritional deficiencies. Previous research reported that food allergy combined with eczema led to reduced growth in children,^{19,21} and concluded this may be due to the presence of chronic inflammation and elevated metabolic demand. However, children with parents reported food allergy and food restrictions were not lighter than their controls according to our findings, suggesting a weak role for calorie consumption on the growth status in these children.

Most of the serum levels of micronutrients in our study population were in the normal range, despite self-reported food allergies that could have led to food restrictions. Only the serum level of calcium was significantly lower in children who had food allergies or restricted foods. This might be because important sources of calcium, such as milk, dairy, soy, seafood, and meat, are among the common foods avoided by children whose parents imposed dietary restrictions due to concerns of food allergy. Previous research reported that a low intake of calcium was associated with atopic dermatitis and food allergy.²² Regardless of the underlying mechanism, we found that the serum calcium level of our study population was influenced by parental concerns about food allergy.

In conclusion, our results support previous studies that food allergy and food restriction were related to low height-for-age z-score in children. We also provided evidence that a low serum calcium level was related to reduced growth in children with symptoms and signs of food allergy. Thus, the diagnosis of food allergies and decisions regarding dietary restrictions in children should be made carefully, and their possible negative effects on child growth should be considered. Parents in particular should be aware of the possibly adverse effects of unnecessary food restrictions.

AUTHOR CONTRIBUTIONS

EKH, JHK, HMJ, HSB, and MYH contributed to the study design. MYH, EKH, and JHK were involved in literature search and data analysis and interpretation. HMJ and MYH obtained funding. JYB, JOJ, EKH, YHS, and MYH were involved in manuscript preparation, writing and revision. All authors critically reviewed the manuscript for important intellectual contents and approved the final manuscript.

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CONFLICT OF INTEREST

The authors declare that no competing interests exist.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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