

RESEARCH PAPER

Malnutrition in children with food allergies in the UKR. Meyer,* C. De Koker,* R. Dziubak,* C. Venter,† G. Dominguez-Ortega,* R. Cutts,‡ N. Yerlett,*
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doi:10.1111/jhn.12149**Abstract**

Background: The mainstay of dietary management of food allergies remains the elimination diet. However, the removal of major food groups may predispose children to an inadequate nutrient intake. We therefore set out to establish growth status in food allergic children receiving dietetic input in the UK.

Methods: Dietitians were approached via the Food Allergy and Intolerance Specialist Group from the British Dietetic Association and asked to submit anthropometrical data for children with food allergies. Data collected related to the systems involved and number of foods excluded. Malnutrition was defined according to World Health Organization standards.

Results: Data from 13 different centres yielded 97 patients (51 male and 46 female) of which 66 excluded ≤ 2 foods and 31 excluded ≥ 3 foods. Data indicated that 8.5% had a weight for age ≤ -2 Z-score and, conversely, 8.5% were ≥ 2 Z-score. For height for age, 11.1% were ≤ -2 Z-score and, for weight for height, 3.7% were ≤ -2 Z-score and 7.5% ≥ 2 Z-score. Type of allergy, system involved and specific food elimination did not impact on the level of malnutrition. However, the elimination of ≥ 3 foods significantly impacted on weight for age ($P = 0.044$).

Conclusions: The present study demonstrates that children with food allergies are more underweight than the general UK population, which appears to be linked to the number of foods excluded. However, the impact of the disease process itself should not be disregarded. Additionally, obesity can also occur in this population despite dietary elimination.

Introduction

It is considered that between 2.2–5.5% of young children in the UK suffer from a proven food allergy (Venter *et al.*, 2006). This prevalence may vary slightly between developed countries; nevertheless, treatment remains the same, which involves the complete elimination of the offending food allergen (Eigenmann *et al.*, 1998; Madsen, 2005; Burney *et al.*, 2010). The most common foods involved in allergic reactions in early childhood include cow's milk, hen's egg, soya bean, wheat, peanuts and tree nuts (Venter

& Meyer, 2010). Many of these foods, in particular cow's milk, contribute significant macro- and micronutrients that are essential for normal growth and development, especially during early childhood (Venter & Meyer, 2010). Most food allergy guidelines recommend including growth assessment as part of an allergy focussed history, and identify poor growth as one of the factors indicative of possible food allergy. However, a remarkably small number of multicentre studies have been published focusing only on growth of allergic children. Isolauri *et al.* (1998) highlighted poor growth, in particular stunting, as a problem

in Finnish children on a cow's milk exclusion diet in a single allergy centre. Vieira *et al.* (2010) performed a multicentre study in Brazilian children with non-immunoglobulin (Ig)E-mediated gastrointestinal allergy to cow's milk protein and found a very high percentage of both wasting (defined as a low weight for height) and stunting (defined as a low height for age) in children. More recently, Flammarion *et al.* (2011) reported data obtained from children with IgE-mediated allergy from Lille, France, and linked the number of foods excluded to a low weight for age and height for age. All previous studies were performed either on IgE- or non-IgE-mediated allergy alone, mostly in single centres, and some were also retrospective. Growth faltering has been shown to have a long-term impact on both longitudinal growth and cognitive skills (Emond *et al.*, 2007; Dewey & Begum, 2011). We therefore set out to prospectively establish the growth status of children with confirmed IgE- and/or non-IgE-mediated food allergies seen by dietitians in the UK, with the aim of enabling the development of future preventative and management strategies.

Materials and methods

Research dietitians at Great Ormond Street Hospital for Children NHS Foundation Trust in London coordinated the survey and obtained approval from the National Research and Ethics Services in the UK. Dietitians were approached through the Food Allergy and Intolerance Specialist Group (FAISG) of the British Dietetic Association in the UK via their mailing list. All FAISG dietitians working in primary, secondary or tertiary care were invited to partake in the study. Dietitians who were willing to participate were sent details of the survey, including the inclusion and exclusion criteria for the present study:

- Children (0–16 years) with either IgE or non-IgE-mediated food allergies, which were confirmed in the following way:
 - IgE-mediated: skin prick test and/or specific IgE together with an allergy focused history pointing towards a food allergy as per National Institute for Clinical Excellence (NICE) Guidelines on the diagnosis of food allergy in the UK (Sackeyfio *et al.*, 2011).
 - Non-IgE-mediated: elimination diet, followed by the reintroduction of offending food allergens with resolution and reappearance of clinical symptoms, in accordance with NICE guideline (Sackeyfio *et al.*, 2011).
- Children who have not had their diagnosis made according to above criteria were excluded from the survey.

Dietitians collected data prospectively, for 1 week, from all food allergic patients seen either as inpatients or in

their outpatient allergy clinics in September 2011, when schools would have resumed in the UK after the summer holidays. Dietitians were sent either a paper or electronic data collection sheet (Excel file; Microsoft Corp., Redmond, WA, USA) depending on their preference, which was faxed/e-mailed back to the survey coordinators. Table 1 summarises all of the data collected in the survey.

Statistical analysis

The standards for malnutrition provided by the World Health Organization (WHO) were used for data analysis. This defines normal growth as a weight for age (WA), weight for height (WH) and height for age (HA) of 0 to ± 2 Z-score, moderate undernutrition -2 to -3 Z-scores and severe undernutrition as < -3 Z-scores. Conversely, being overweight was defined as having a WA and WH of $> +2$ Z-scores and obesity as $> +3$ Z-scores (WHO, 2004; WHO & UNICEF, 2009). A low WH indicates wasting (< -2 Z-score), a low HA (< -2 Z-score) indicates stunting, and WA (< -2 Z-score) indicates a child just being underweight. Data were analysed with SPSS, version 19 (IBM Corp., Armonk, NY, USA) using statistical methods. Differences between groups were established using the Kruskal–Wallis test with post-hoc Kruskal–Wallis comparison using the Mann–Whitney *U*-test. The chi-squared test was used to assess differences in frequencies between groups. We compared the growth parameters of children excluding 1, 2 and 3 or more foods. $P < 0.05$ was considered statistically significant. Measures of central tendency are presented as the medians and means (SD).

Results

A total of 97 patients were recruited from 13 different dietitians across the UK working in a variety of care settings: two primary (12 patients), eight secondary

Table 1 Data submitted by dietitians taking part in the study

Data	Description
Clinical setting	Primary, secondary or tertiary care
Age of the child	Documented in months
Gender	Male/female
Type of food allergy	Immunoglobulin (Ig)E, non-IgE or mixed
System affected	Skin and/or gastrointestinal tract and/or respiratory tract
Food elimination diet	Milk, egg, soy, wheat, peanut, tree nut, shellfish, fish and other
Weight	Expressed in kg up to 1 decimal point
Height	Expressed in cm up to 1 decimal point
Head circumference	Expressed in cm up to 1 decimal point

(55 patients) and three tertiary (30 patients) (Fig. 1). No patient data were excluded from the data analysis. From these centres, we recruited 97 children (51 male and 46 female) with a median (range) age of 27 (0.5–149) months. Forty-five children were classified as having IgE-mediated, 29 had non-IgE-mediated and 23 had mixed IgE and non-IgE-mediated allergies. From this cohort, 67 excluded ≤ 2 foods (40 excluded one food and 27 excluded two foods) and 30 excluded ≥ 3 foods from their diet (Table 2). As expected, the most common food allergen was cow's milk, followed by hen's egg, tree nuts and then soy, wheat, peanut, sesame seed and fish (Fig. 2).

Forty-seven (48.5%) patients had gastrointestinal symptoms, 65 (67%) had skin symptoms and 19 (19.6%) had respiratory system symptoms. There was an expected

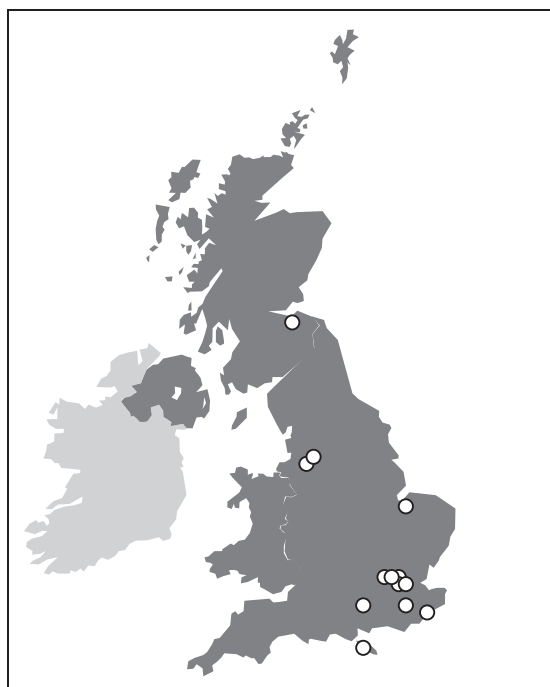


Figure 1 Geographical distribution of the participating centres.

Table 2 Number of foods excluded

Number of foods excluded	Number of patients	Percentage
1	39	40.2
2	27	27.8
3	11	11.3
4	9	9.3
5	8	8.2
6	1	1.0
7	2	2.1

overlap in symptoms, which we plotted against the foods excluded (Fig. 3). It was found that the main food allergen avoided in children with gastrointestinal symptoms was cow's milk (89.3%), whereas, in children with skin symptoms, the majority of children (60%) were required to exclude hen's egg, and, in 73.6% of children with respiratory symptoms, the main food allergen was tree nuts.

We investigated whether there were differences in growth parameters between primary, secondary or tertiary care centres. No differences were found in WA ($P = 0.625$), HA ($P = 0.752$) and WH ($P = 0.322$) if children saw a dietitian in a primary, secondary or tertiary care centre. Growth parameters WA, HA and WH were categorised by IgE-mediated, mixed IgE- and non-IgE-mediated, and non-IgE-mediated allergic reactions, and median Z-scores are illustrated in Table 3. We found no statistical difference between growth parameters in food allergies that were IgE-mediated, non-IgE-mediated or mixed (WA: $P = 0.818$; HA: $P = 0.690$; WH: $P = 0.899$). From the 97 children, 27 had a head circumference performed (age < 2 years), with a median Z-score of 0.19 (-1.67 to 2.49). Insufficient data were available on head circumference to enable further statistical analysis.

When we analysed HA and WH grouped by number of foods excluded (1, 2 and ≥ 3 of foods excluded), we found no significant differences between the groups. However, when the same analysis was performed for WA, a significant difference between groups (1, 2 and ≥ 3 of foods excluded from the diet) was found ($P = 0.044$). To identify where this difference lies, a post-hoc analysis showed a significant difference, particularly between 2 and ≥ 3 foods excluded ($P = 0.022$). Differences between 1 and 2 ($P = 0.066$) and 1 and ≥ 3 ($P = 0.292$) were not significant (Table 4). This difference was not attributed to the number of patients in the three groups. A relationship between being under- or overweight and particular foods excluded was also assessed, although no statistically significant impact of any specific food allergen exclusion was found on growth parameters.

Our data showed that 8.5% of children had a WA ≤ -2 Z-score indicating that they were underweight and, conversely, 8.5% had $\geq +2$ Z-score indicating that they were overweight. There was a greater proportion of children with low height for age (11.5%) compared to children tall for age (5.5%) in this sample. A mean of 3.7% of children met the criteria for moderate malnutrition with a WH ≤ -2 and 7.5% of children had a WH ≥ 2 Z-score, which indicated obesity (Table 4).

We also assessed whether allergic symptoms affecting the gastrointestinal tract, respiratory tract or skin were related to growth parameters and found no statistically significant association between gastrointestinal tract

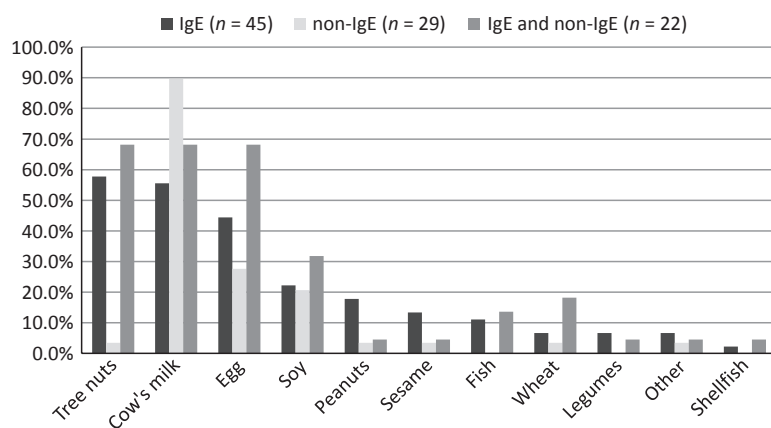


Figure 2 Summary of the most common food allergens excluded from the diet stratified by immunoglobulin (IgE), non-IgE and mixed IgE and non-IgE-mediated allergies.

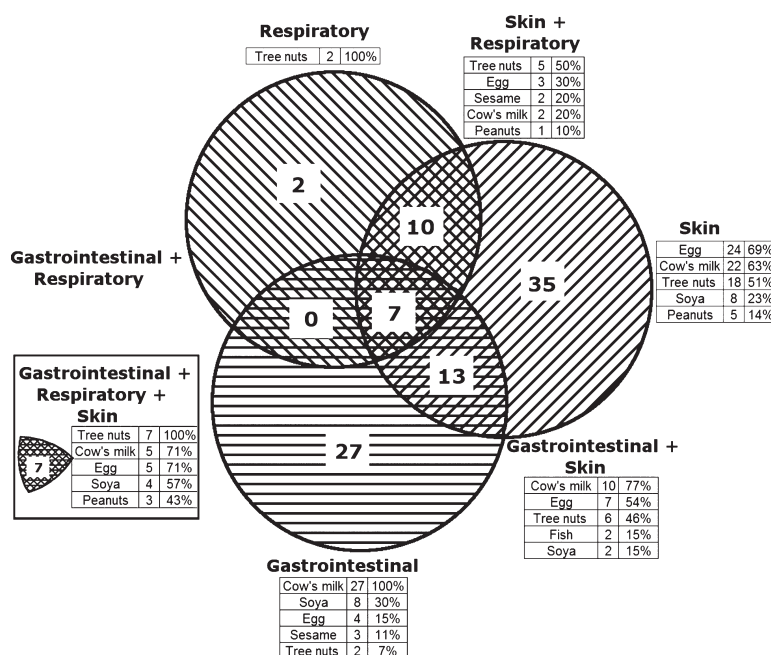


Figure 3 The overlap in gastrointestinal, skin and respiratory systems and the commonly avoided foods in each. In three patients, system involvement was not recorded by the dietitian collecting the data, explaining the 94 patients accounted for in the figure.

Table 3 Summary of median growth status of each category presented as Z-scores

	All children with FA	Children with IgE-mediated FA	Mixed IgE and non-IgE-mediated FA	Non-IgE-mediated FA
Number (n)	97	45	23	29
WA (range)	0.22 (−3.57 to 3.41)	0.19 (−3.58 to 3.41)	0.26 (−2.91 to 2.32)	0.37 (−2.99 to 2.11)
HA (range)	−0.06 (−5.03 to 3.12)	0.07 (−3.27 to 3.41)	0.33 (−5.03 to 2.56)	0.31 (−3.6 to 3.11)
WH (range)	0.51 (−2.58 to 2.58)	0.09 (−2.83 to 2.58)	0.57 (−0.96 to 2.48)	0.64 (−2.73 to 2.51)

FA, food allergy; HA, height for age; Ig, immunoglobulin; WA, weight for age; WH, weight for height.

symptoms and WA ($P = 0.461$), HA ($P = 0.202$) or WH ($P = 0.267$); skin symptoms and WA ($P = 0.156$), HA ($P = 0.470$) or WH ($P = 0.124$); and respiratory tract symptoms and WA ($P = 0.935$), HA ($P = 0.694$) or WH ($P = 0.515$). We were also interested in investigating

whether there was a difference in growth in children with IgE, non-IgE and mixed food allergies affecting the gastrointestinal tract, the respiratory tract and the skin. These results are summarised in Table 5. Because we did not have patients with both IgE and non-IgE-mediated

Table 4 Number of foods excluded categorised by weight and height

	≤2 Foods excluded [n = 66 (%)]	≥3 Foods excluded [n = 31 (%)]	All the children [n = 97 (%)]
WA			
≤ -2 Z-score	7.8	10*	8.5
≥2 Z-score	10.9	3.3	8.5
HA			
≤ -2 Z-score	10	14.2	11.5
≥2 Z-score	6.6	3.5	5.5
WH			
≤ -2 Z-score	4	3.5	3.7
≥2 Z-score	6	12	7.5

*P = 0.044.

HA, height for age; WA, weight for age; WH, weight for height.

allergies affecting the respiratory tract only, we are unable to present data for this parameter.

Discussion

To our knowledge, this is the first prospective multicentre study establishing the growth status of children with a variety of food allergic disorders seen by dietitians in primary, secondary and tertiary care centres in the UK. Growth faltering in early childhood has been shown to have long-term consequences, including effects on cognitive skills and IQ (Emond *et al.*, 2007; Ross *et al.*, 2009; Sawaya *et al.*, 2009; Dewey & Begum, 2011). Conversely, being overweight during early childhood may predispose children to adult obesity, cardiovascular disease and diabetes (Nadeau *et al.*, 2011). It is therefore important that growth impairment or excess is addressed early on, so that the risk of long-term consequences can be minimised.

In the present study, we found that 8.5% of all allergic children were underweight, with a WA < -2 Z-score, of which 7.8% and 10% had ≤2 food and ≥3 food exclusions, respectively. We also show an increased risk of being underweight with the exclusion of multiple foods, irrespective of system involvement. We were surprised to

find no statistical difference for between 1 and ≥3 food exclusions but between 2 and ≥3 food exclusions instead. This difference could not be explained by the type of food allergy, the age of children in each group, the system involvement or the foods excluded. This may be related to length of time that children have been diagnosed or dietary compliance, although the present survey did not collect such data, which may have provided some insight into these results.

The mean level of WA in the present study is considerably better than that reported by Vieira *et al.* (2010) where 15.1% of their children with suspected cow's milk allergy were underweight. The results from that study may be explained by the higher prevalence of children being underweight in Brazil per se (WHO, 2004). The percentage of children who were underweight in the present study was very similar to that reported by Flammariion *et al.* (2011), who found that 9.3% of their population had a malnutrition pattern ≤ -2 Z-scores. Similar to the present study, they also found that the elimination of ≥3 foods from the diet was linked to a poor WA. The WHO does not classify a low WA as being malnourished because it fails to distinguish between a short child of adequate body weight and a tall or thin children (WHO, 2012). However, studies have linked a low WA (i.e. being underweight) to increased morbidity and mortality. Thus, having a low WA should be addressed early on also in the allergic child (Arbor Clinical Nutrition Updates, 2005: 5 A.D.).

In the present study, 11.5% of all children enrolled had a height for age ≤ -2 Z-score, classified by the WHO as stunting. This was particularly high in children who excluded ≥3 foods from their diet (14.2%), although no statistically significant difference was found between the group excluding ≤2 and ≥3 foods. The study from Vieira *et al.* (2010) had a significantly higher level of stunting at 23.9%, whereas Flammariion *et al.* (2011) had a slightly lower level (7.3%) in their whole population and 12.1% in the group that excluded ≥3 foods. Laitinen and Isolauri (2007) estimated the prevalence of stunting in children on an exclusion diet to range between 2–15%, which matches the results reported in the present study. We note that the WHO estimated the prevalence of stunting in developed countries in 2010 at approximately 6%, whereas, in Latin America, the prevalence was estimated at 13.5%, which may explain the different finding between these studies (WHO, 2004). Although we did not find a statistically significant association between height growth and the elimination of ≥3 foods, many other studies have done so. Christie *et al.* (2002) found that children who avoided ≥3 foods had a height growth below the 25th centile and Flammariion *et al.* (2011) also correlated the number of foods avoided with height

Table 5 Growth comparison between immunoglobulin (Ig)E, non-IgE and mixed food allergic children presenting with gastrointestinal or skin symptoms*

	Gastrointestinal tract P-values	Skin P-values
WA	0.945	0.706
HA	0.155	0.983
WH	0.199	0.484

*No patients with IgE and non-IgE-mediated allergy with respiratory symptoms.

HA, height for age; WA, weight for age; WH, weight for height.

growth. Optimal growth is especially important in young children because growth velocity is particularly rapid within the first 2 years of life, when the prevalence of food allergy is also high (Meyer *et al.*, 2012), and stunting has been implicated in reduced economic productivity in adulthood and maternal reproductive outcomes (Dewey & Begum, 2011).

We also found that 3.7% of children had a WH below ≤ 2 Z-scores [< 2 nd centile on UK body mass index (BMI) growth charts], classified as moderate malnutrition (or wasting) by the WHO. Unlike Cho *et al.* (2011), who found a decrease in WH with the number of sensitised food allergens, there was no significant impact of number of food allergens on WH in the present study. A survey performed in the UK in 2003 showed that between 3–4.8% of preschool children malnourished, based on the BMI being below the 2nd centile (Armstrong *et al.*, 2003). Although these data were based on the BMI, it can be inferred that children with food allergies in the UK have a similar percentage of moderate malnutrition compared to the general UK population; however, they are shorter and more at risk of being underweight compared to healthy children.

We assessed whether the elimination of specific allergens, such as cow's milk, soy, egg or nuts, was associated with height growth, although a statistically significant impact of individual foods on growth could not be found. This is in contrast to Isolauri *et al.* (1998), who, in a study focusing on cow's milk protein allergy, showed that the elimination of cow's milk was linked to stunting. The difference in the results may be linked to the improved nutritional content and availability of alternatives (i.e. hypoallergenic feeds) ever since the publication

of their study in 1998, as well the dietetic support that patients received in this study. Irrespective of the type of food allergen, dietitians would provide appropriate advice and ensure nutritional adequacy.

An attempt was made to categorise allergic symptoms according to type of allergy and system involvement (gastrointestinal tract, skin and respiratory tract) and to link this to foods eliminated and anthropometrical parameters. We were, however, disappointed to find no significant impact of any of parameters on growth, despite a higher percentage of cow's milk avoidance in the group with gastrointestinal symptoms versus the group with skin or respiratory symptoms. Given that all of the children in the present study were being seen by a specialist paediatric dietitian, it is likely that advice on suitable nutritional alternatives to eliminated foods would have been given, therefore masking a potential difference in growth. Nonetheless, the level of being underweight and stunted despite dietetic support was still marked. Growth faltering in the allergic child has mainly been linked to dietary elimination in previous studies but common atopic comorbidities (i.e. asthma, severe eczema) are rarely considered in the aetiology (Fig. 4). Inflammatory cytokines, particularly interleukin-6 produced by macrophages and tumour necrosis factor- α , are considered to play a central role in the development of allergic inflammation common in atopic disorders (De Benedetti *et al.*, 1997; Theoharides *et al.*, 2012). The impact of these and other cytokines on growth has been well established in inflammatory bowel disease and other chronic illnesses (De Benedetti, 2009; Ezri *et al.*, 2012; Gerner *et al.*, 2012). In addition, other factors unique to the management of the food allergic child may also lead to poor growth. This includes a reduced appetite

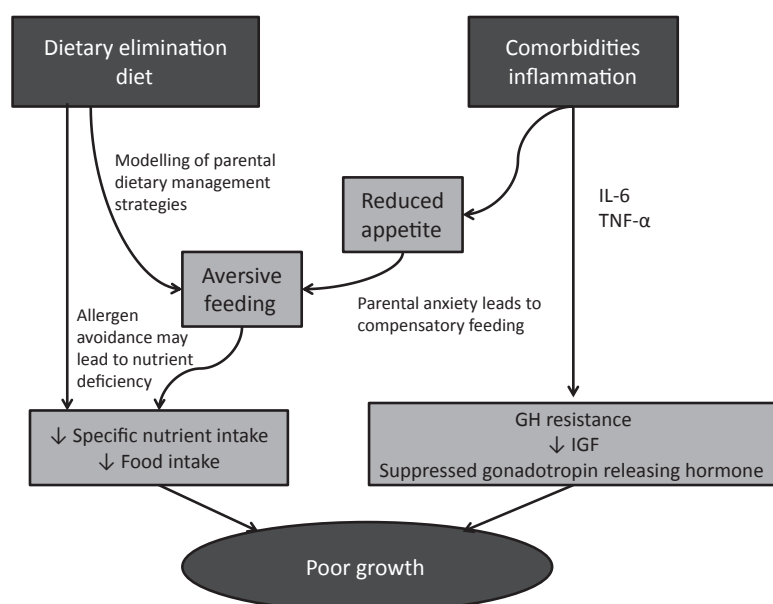


Figure 4 Proposed model for the development of malnutrition in the allergic child. IGF, insulin-like growth factor; IL, interleukin; TNF, tumour necrosis factor.

as a result of the inflammatory process and aversive feeding, which may result from parental strategies that have been adopted to overcome the poor appetite and the elimination diet itself (Wright *et al.*, 2006; Meyer *et al.*, 2010; Mukkada *et al.*, 2011).

We were surprised to find 8.5% of children with a WA ≥ 2 Z-scores and 7.5% with a WH ≥ 2 Z-scores, indicating a BMI >98th centile on UK growth charts; hence, these children would be classified as being obese. In particular, in children where ≥ 3 foods were avoided, WH was high, which is an interesting finding. In 2012, the Information Centre for Health and Social Care from the UK published levels for obesity, which were 15.3% and 13.9% for boys and girls between 2–10 years of age, respectively (The Information Centre for Health & Social Care, 2012). Although our levels of obesity were lower than those in the general paediatric population, a significant number of children who were avoiding ≥ 3 foods were obese. To our knowledge, this has not been reported before and whether parents compensate with more energy-dense foods in children with food allergies has never been investigated. This should remind clinicians that both low and excessive weight gain need to be addressed in this group. Food allergy management guidelines currently focus mainly on the management of undernutrition (Meyer *et al.*, 2012); however, the spectrum of overnutrition may also need to be considered in the dietary management of food allergic children. Clinicians should be also wary of dismissing the possibility of a food allergy, especially in non-IgE-mediated food allergies where symptoms are the key to diagnosis, if faltering growth is not present. According to our data, 91.5% of these children will not be underweight and 89% will not be stunted, although they still may have a food allergy.

Although the present survey collected data from almost 100 children with confirmed food allergies seen by dietitians from different areas of the UK, the main limitation remains the number of children recruited. Many of the subcategories related to foods avoided, the type of allergy and the systems involved had inadequate numbers to enable statistical analysis. Future surveys need to be adequately powered to establish the impact of type of food allergy and symptoms on nutritional status. Furthermore, the present study is based on children who have a diagnosis of food allergies based on the current NICE criteria in the UK and not based on double-blind food challenges, which remain the gold standard in the diagnosis of food allergy (Nowak-Węgrzyn *et al.*, 2009). This may be perceived as a limitation of the present study; however, we wanted to establish the nutritional status of children who are required to eliminate foods in accordance with NICE guidelines, which is reflective of current practice in a variety of care settings in the UK.

Another limitation of the present study is that we did not specify the time of diagnosis and therefore whether these are newly-diagnosed food allergic children or children who are well established on their elimination diet. This could have had a significant impact on the growth data collected and future studies should distinguish between newly-diagnosed and established patients and should attempt to follow-up patients to assess progression of growth. At the time of performing the present study, no competency-based allergy courses or national, peer-reviewed allergy diet sheets with dietary information were available for dietitians to provide to patients in the UK. Consequently, the level of dietary advice given to parents in the present study would have varied, which may have also impacted on the outcome. Future studies should therefore also include the level of dietetic competency and advice given when assessing nutritional status of children with food allergies.

In addition, single anthropometric measures (weight, height and head circumference) provide an indication of growth at one point in time, and do not reflect growth velocity. It was not possible to identify whether children with a low WH, HA and WA in the present study had changed or improved growth velocity since dietetic input. The present study also cannot establish the impact of dietetic care on growth because it is very difficult in the UK to find an allergic paediatric cohort that has not been seen by the dietitian, as a result of current NICE guidelines and those set out by the Royal College of Paediatric and Child Health recommending dietetic involvement in food allergic children.

Conclusions

In conclusion, the present study highlights that children with food allergies are more underweight than the general UK population, which appears to be linked to the number of foods excluded. However, we did not find a specific food allergen linked to growth and speculate that it is not only dependant on the adequacy of dietary intake, but also on the disease process itself. The present study also highlights that obesity can be a problem in children with food allergies, despite multiple food exclusions. Dietary interventions should aim to address both under and overnutrition, although it is important to be aware that dietary adequacy may not be the only factor involved in malnutrition, and that the disease process itself should not be disregarded.

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Conflict of interests, source of funding and authorship

The authors declare that there are no conflicts of interest.

No funding was received for the present study. All dietitians involved in the study are employed by the NHS.

RM and CDK organised the study, arranged the data collection and wrote up the publication. RD analysed the data and reviewed the publication. CV, NS and AF provided support for the conceptualising survey, interpreted the data and reviewed the publication. AKS, GO, NY and HG helped with interpreting the data, conceived possible explanations and reviewed the publication. All authors critically reviewed the manuscript and approved the final version submitted for publication.

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