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BRIEF REPORT | [Full Access](#)

Food allergy in children is associated with Vitamin D deficiency: A case-control study

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The association between food allergy (FA), vitamin D deficiency (VDD) and vitamin D binding protein (VDBP) is of special interest.¹ A previous study has shown that low serum vitamin D levels were associated with food allergy, particularly amongst infants with specific *VDBP* gene polymorphisms.² In addition, infants of Australian-born parents with inadequate vitamin D levels were more likely to be food allergic than were those with adequate vitamin D levels.³ In the United States, a significant association between VDD and the sensitisation to food allergens was detected.¹ On the contrary, a recent systematic review could not detect any difference in vitamin D levels in children with or without FA, indicating that the relationship between FA and vitamin D remains controversial.⁴

In this study, we aimed to evaluate the association of FA with VDD and the association of FA with vitamin D, after controlling for VDBP levels, parental smoking, breastfeeding and family history of atopy.

We conducted a case-control study in the Paediatric Allergy Department of the University Hospital of Ioannina, between 7/2018 and 1/2020, including children with definite IgE-mediated FA, and age and gender-matched controls with no history of food allergy. Food allergic children were recruited according to the following criteria, defined by EAACI: (1) the history of IgE-mediated allergic skin, respiratory or gastrointestinal reaction triggered by the consumption of a specific food; (2) positive specific IgEs and/or skin prick tests (SPTs); and (3) a diagnostic open oral food challenge.

The clinical characteristics were recorded, as depicted in Table [1](#). The serum 25-hydroxy-D (25OHD) concentration was measured at the first visit in the Paediatric Allergy Department (Abbott Analyzer i1000SR). A level of 25OHD <20 ng/ml was considered deficiency.

TABLE 1. Clinical and laboratory characteristics of children with food allergy and matched controls

	Children with food allergy (n = 51)	Controls (n = 28)	P value
Age, years	2.1 (1.0–4.2)	1.3 (1.0–3.5)	0.252
Gender, male	31 (61)	16 (57)	0.813
Parental smoking	18 (35)	12 (43)	0.629
Breastfeeding (yes/no)	35 (69)	20 (71)	0.806
Family history of atopy	16 (31)	1 (4)	0.004
Body weight, kg	12.5 (9.4–16.2)	10 (7–14.5)	0.114
Body height, m	0.86 (0.75–1.01)	0.78 (0.65–1.00)	0.102
Body mass index, kg/m ²	16.3 ± 1.6	16.7 ± 2.1	0.338
25-hydroxy-D, ng/ml	27.4 ± 11.1	30.1 ± 9.5	0.276
Vitamin D deficiency	16 (31)	3 (11)	0.049
Vitamin D binding protein, µg/ml	240 (190–298)	222 (196–268)	0.207

Note

Continuous variables expressed as mean±standard deviation or median (interquartile range). P of Student's t-test or Mann-Whitney test. Categorical variables expressed as n (%). P of chi-squared test or Fisher's exact test.

Continuous variables were expressed as mean±standard deviation or median (interquartile range) and compared with Student's t-test or Mann-Whitney test. Categorical variables were expressed as n (%) and compared with chi-squared or Fisher's exact test. Logistic regression analysis was used to evaluate the association of FA with VDD, after controlling for VDBP levels, parental smoking, breastfeeding and family history of atopy.

Sample analysis revealed that a size of 49 FA subjects and 24 controls could detect a difference of 20%, with a power of 0.8 and type-I error 0.05. The study was approved by the Ethical Committee of the Institution (No 1290).

We enrolled 51 subjects with IgE-mediated FA and 28 controls. No differences were recorded regarding body weight, body mass index, birth season, sun exposure duration, breastfeeding or parental smoking between cases and controls. Both groups received vitamin D supplementation up to six months of age. Cases differed significantly from

controls by family allergy (31% versus 4%).

Children with FA presented a significantly higher proportion of VDD in comparison with controls (31% versus 11%, $p = 0.049$). Amongst food allergic children, 27% were sensitised to egg, 25% to milk, 22% to nuts, 2% to fish and 24% to more than one food allergens. Multiple-sensitised children had significantly lower 25OHD levels (20.5 ± 11.1 ng/ml versus 29.5 ± 10.3 ng/ml, $p = 0.013$), and a higher ratio of VDD (58% versus 23%, $p = 0.033$), in comparison with mono-sensitised children. As per study design, controls had no history of food sensitisation.

FA was significantly associated with VDD (OR 5.11, 95%CI 1.02–25.51, $p = 0.047$), after controlling for VDBP levels, parental smoking, breastfeeding and family history of atopy. Also, a family history of atopy was significantly associated with FA (OR 16.13, 95%CI 1.82–142.46, $p = 0.012$).

Our findings support a strong association between FA and VDD. One of the largest studies in Australia suggested that infants with VDD levels were more likely to have FA in comparison with those with sufficient vitamin D status. According to the same study, vitamin D status was influenced by the parental country of birth, and this interaction was affected by various genetic, environmental or constitutional factors.³ The implication of genetics in the FA and vitamin D relation was supported by a subsequent study, showing that infants with FA had a similar *VDBP* genotypic polymorphism associated with lower vitamin D levels.² Moreover, infants with low vitamin D levels were more likely to suffer multiple food allergies.³ In addition, the National Health and Nutrition Examination Survey suggested an association between VDD and higher levels of specific IgEs, and thus sensitisation to several food allergens.¹ Our findings are also in line with previous studies, suggesting that most of the infants with cow's milk allergy had a positive history of atopy in the first-degree relatives.⁵

In conclusion, children with FA presented a higher proportion of VDD, whereas VDD was significantly associated with sensitisation to multiple food allergens. Moreover, the family history of atopy served as a unique positive marker of FA. Larger studies are warranted to draw firmer conclusions concerning the relationship of FA with vitamin D status.

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CONFLICTS OF INTEREST

None.

Consent to participate

Written informed consent form was provided by the parents.

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