Serum vitamin D status in a cohort of infants with food protein-induced gastrointestinal disease

MENG-YAO ZHOU[1*], XIN LI[2*], JING YANG[1], XIAO-JUAN ZHOU[3], LI-JING XIONG[1], XIAO-QING HE[1] and XIAO-LI XIE[1]

[1]Department of Pediatric Infection and Gastroenterology, Chengdu Women and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology, Chengdu, Sichuan 611731; [2]Department of Pediatric, University of Electronic Science and Technology, Chengdu, Sichuan 610000; [3]Department of Pediatric Healthcare, Chengdu Women and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology, Chengdu, Sichuan 611731, P.R. China

Received May 15, 2023; Accepted August 08, 2023

DOI: 10.3892/br.2023.1653

Abstract. Increases in the prevalence of food allergy and vitamin D deficiency have been observed in recent years. The association between vitamin D levels and food allergy remains to be fully elucidated, and research focused on the prevalence of vitamin D insufficiency in infants with food protein-induced gastrointestinal disease in Chengdu, Sichuan is lacking. Thus, the present study aimed to determine the prevalence and clinical characteristics of serum 25 hydroxyvitamin D [25-(OH)D] insufficiency and sufficiency in infants with food protein-induced gastrointestinal disease. The present study also aimed to identify the potential predisposing factors of 25-(OH)D insufficiency. The present retrospective study analyzed data obtained from Chengdu Women's and Children's Central Hospital spanning between June 2021 and February 2022. Children with a confirmed diagnosis of food protein-induced gastrointestinal disease were enrolled in the present study. Blood indicators, including serum 25-(OH)D, serum total immunoglobulin E (IgE), specific IgE against allergens, and hemoglobin were measured during the course of the disease. Clinical characteristics of patients and blood examination results were obtained from the hospital electronic database. A total of 361 patients were included in the study group and 45 healthy individuals were included in the control group. The results of the present study demonstrated that serum 25-(OH)D levels of infants with protein-induced gastrointestinal disease were significantly lower compared with the control group. Notably, female participants with higher serum total IgE levels exhibited insufficient serum 25-(OH)D levels. However, the results of the logistic regression analysis revealed no predisposing factors associated with serum 25-(OH)D insufficiency. In conclusion, infants with food protein-induced gastrointestinal disease may exhibit a higher risk of low serum 25-(OH)D levels and this risk may be greater in females with higher total IgE.

Correspondence to: Dr Xiao-Li Xie, Department of Pediatric Infection and Gastroenterology, Chengdu Women and Children's Central Hospital, School of Medicine, University of Electronic Science and Technology, 1,617 Riyue Road, Qingyang, Chengdu, Sichuan 611731, P.R. China
E-mail: xxlilye@qq.com

*Contributed equally

Key words: gastrointestinal food allergy, vitamin D, 25 hydroxyvitamin D, pediatrics, immunoglobulin E

Introduction

In both developed and developing countries, the prevalence of pediatric food allergy has increased in recent years (1). Food protein-induced gastrointestinal disease is characterized by adverse reactions to a food protein that may lead to various dysfunctions of the digestive system (2). To date, three etiological models, including the vitamin D, hygiene hypothesis and dual allergen exposure hypothesis have been proposed to determine the mechanisms underlying food allergy (3).

Vitamin D is a fat-soluble vitamin obtained from relatively few dietary sources, such as oily fish and egg yolks. It is also produced following skin exposure to sunlight (UVB). Serum 25-hydroxyvitamin D [25-(OH)D] is the major metabolic form of vitamin D that acts as a reliable indicator for monitoring vitamin D levels (4). The results of previous studies demonstrated that vitamin D is active throughout the immune system, and vitamin D deficiency is present in numerous extra-skeletal diseases, including food allergies (5-7). Notably, vitamin D prevents food allergies by reducing the immune response, promoting immune tolerance, and maintaining intestinal barrier function (8).

The association between vitamin D and food allergy may be attributed to several factors. Notably, multiple factors may impact the levels of vitamin D, such as sun exposure, season of birth, race, lifestyle, place of residence, ethnicity, age, and use of vitamin D supplementation (9). Moreover, there is a

lack of consensus among academics and government agencies regarding the optimal vitamin D levels required for optimal health (10). Additionally, an individual's genetic background may also impact the individual levels of vitamin D (11). Reduced levels of vitamin D-binding protein leads to higher vitamin D bioavailability and the genotype of vitamin D-binding protein can be stratified into low (GT/TT genotype) and high (GG genotype). The results of a previous study demonstrated that children with the GG genotype exhibited higher vitamin D insufficiency polymorphisms when compared with children with the GT/TT genotype. Pre-pregnancy vitamin D supplementation may have a protective effect against food allergy, particularly in infants with the GT/TT genotype (12). However, the definition of food allergy may vary, and this may be determined via the diagnosis of a physician, observed food sensitization, or test-proven food allergy (13-15).

The present study aimed to investigate the levels of vitamin D in infants with a protein-induced gastrointestinal disease that was diagnosed in the Chengdu Women's and Children's Central Hospital (Chengdu, China). The present study also aimed to determine differences in the clinical features of infants with different vitamin D levels, and the potential predisposing factors for food protein-induced gastrointestinal disease.

Materials and methods

Research participants. The present retrospective study was performed at the Chengdu Women and Children's Central Hospital between June 2021 and February 2022. Infants with food allergies were initially diagnosed by a pediatric gastroenterologist based on their medical history, clinical symptoms, and physical examinations, and diagnoses were confirmed via an oral food test. Children with no gastrointestinal symptoms, concomitant non-atopic comorbidities (such as chronic kidney or liver disease, cerebral palsy, or a history of bowel surgery combined with severe cardiopulmonary disease) or a lack of response to the oral food test were excluded from the present study. Gastrointestinal symptoms included vomiting, diarrhea, gastrointestinal bleeding, reflux, feeding difficulties, food refusal, abdominal pain, bloating, and constipation. A total of 361 infants with food protein-induced gastrointestinal disease were recruited as the study group. 44% (159/361) of the cohort were female and the median age was 7 months and 16 days [interquartile range (IQR), 5-13 months]. A total of 45 healthy individuals were recruited as age-matched controls. These children received routine childcare without any underlying disease.

Serum 25-(OH)D levels, total immunoglobulin E (IgE), specific IgE (sIgE) against allergens, white blood cell counts, hemoglobin levels, and peripheral blood eosinophil counts were measured. Vitamin D levels at ≥75 nmol/l were indicative of sufficiency, vitamin D levels at <75 nmol/l were indicative of insufficiency, and vitamin D levels at <50 nmol/l were indicative of deficiency. Inpatients underwent a face-to-face survey during hospitalization. The survey included the following terms: i) Infant feeding, including feeding methods after birth and the potential introduction of solid foods at 6 months of age; ii) vitamins, including vitamin D supplementation in mothers during pregnancy and lactation, vitamin D supplementation in infants after birth, and vitamin D dosage and frequency; and iii) family history, including a history of allergic diseases in family members that were diagnosed by healthcare professionals.

Measurement of serum sIgE levels. Total IgE and sIgE levels targeting a panel of food allergens, including milk, egg, soybean, wheat flour, peanut, cashew nuts, shrimp, lobster/scallop, shellfish, cod, salmon, crab, lamb, beef, and mango were measured. Infants with sIgE values of ≥0.35 IU/ml and total IgE values based on age (newborn, >1.5 IU/ml; 1 month-1 year of age, >15 IU/ml; 1-5 years of age, >60 IU/ml; 6-9 years of age, >90 IU/ml; 10-15 years of age, >200 U/ml; and ≥15 years of age, >100 IU/ml) were classified as increased.

Statistical analysis. Categorical variables are presented as frequencies and percentages, and continuous variables are presented as the mean ± standard deviation. An unpaired Student's t-test was used for comparisons between age and serum 25-(OH)D levels. A χ^2 test was used for comparisons between sex and clinical characteristics. Logistic regression analysis was used to analyze the potential association between 25-(OH)D levels and food allergy. Types of allergens, number of allergens, age, and sex were considered as potential confounders. Potential predisposing factors, including vitamin D supplementation during pregnancy and lactation, vitamin D supplementation after birth, infant feeding after birth, and the introduction of solid food at 6 months of age were analyzed using logistic regression analysis, and age, sex, family history and number of siblings were set as potential confounders. A forward stepwise method was used to remove variables that were not significant. Variables with a P-value <0.10 in the univariate analysis were entered into the logistic regression model. All statistical analyses were performed using SPSS version 27 (IBM Corp.). P<0.05 was considered to indicate a statistically significant difference.

Results

A total of 361 infants with food protein-induced gastrointestinal disease were included in the present study. Of these, 298 infants were outpatients, and 63 infants were inpatients. Serum 25-(OH)D levels ranged from 17.40-150.19 nmol/l with a mean value of 83.31 nmol/l. In total, 38.22% (138/361) of the infants exhibited low serum 25-(OH)D levels at <75 nmol/l. A total of 5.54% (20/361) of infants exhibited vitamin D deficiency with levels of <50 nmol/l and 32.69% (118/361) of infants were vitamin D insufficient, with levels of 50-75 nmol/l. Notably, serum 25-(OH)D levels were significantly lower in patients than in healthy controls, and there were no significant differences in age or sex (Table I).

Patients with sufficient and insufficient serum 25-(OH)D levels were compared to determine the potential associations between patient demographics and clinical characteristics with vitamin D (Table II). The results of the present study demonstrated that the concentration of serum 25-(OH)D varied in infants with food protein-induced gastrointestinal disease. Mean serum 25-(OH)D levels in infants with low serum 25-(OH)] levels were significantly lower than in infants with normal serum 25-(OH)D levels. The results of

Table I. Comparison of 25(OH)-D levels between children affected by food protein-induced gastrointestinal diseases and healthy children.

Parameter	Patients, n=361	Healthy group, n=45	χ^2	P-value
Age, months[b]	9.50±6.5	8.22±6.04	-	0.2
Sex, n (%)			0.67	0.41
Male	202 (56)	18 (40)		
Female	159 (44)	27 (60)		
25-(OH)D, nmol/l[b]	83.31±22.50	103.04±47.30	-	0.005[a]

[a]P<0.01. [b]Mean ± standard deviation. 25-(OH)D, 25 hydroxyvitamin D.

Table II. Demographics and clinical characteristics between children affected by food protein-induced gastrointestinal diseases based on serum 25-(OH)D levels.

Characteristic	<75 nmol/l, n=138	≥75 nmol/l, n=223	χ^2	P-value
25-(OH)D, nmol/l	61.68±12.31	96.70±16.03	-	<0.001[c]
Age, months	9.89±7.80	9.26±5.59	-	0.414
Sex, n (%)			9.62	0.002[b]
Male	63 (45.65)	139 (62.33)		
Female	75 (54.35)	84 (37.67)		
Clinical characteristics, n (%)				
Gastrointestinal bleeding	55 (39.86)	83 (37.22)	0.03[a]	0.87
Diarrhea	58 (42.03)	80 (35.88)	0.04[a]	0.85
Vomiting/reflex	14 (10.10)	17 (7.62)	0.70	0.41
Constipation	12 (8.70)	19 (8.52)	0.003[b]	0.95
Food difficulty/bloating	17 (9.30)	31 (13.90)	0.19	0.67
Atopic dermatitis	10 (7.25)	15 (6.73)	0.04[a]	0.85

[a]P<0.05, [b]P<0.01, [c]P<0.001. 25-(OH)D, 25 hydroxyvitamin D.

the present study demonstrated that females exhibited higher levels of insufficient serum 25-(OH)D than males; however, there was no significant association between the levels of serum 25-(OH)D and age. Moreover, there were no significant differences in white blood cell count, hemoglobin levels, and eosinophil ratios between infants with insufficient 25-(OH)D and sufficient 25-(OH)D levels.

The results of the logistic regression analysis indicated that patients with higher total IgE levels exhibited insufficient serum 25-(OH)D levels. Notably, this result remained significant when adjusted for sex (Table III). However, there were no predisposing factors associated with insufficient serum 25-(OH)D levels in infants with food protein-induced gastrointestinal disease.

Discussion

Clinical studies have yielded conflicting results regarding the potential association between vitamin D levels and the development of food allergies or sensitization (16). The results of a previous study demonstrated that pre-school-aged children with high 25(OH)D levels (≥75 nmol/l) exhibited a two-fold increased risk for food allergy development compared with infants with low 25(OH)D levels (50-74.9 nmol/l) (17). By contrast, Foong *et al* (18) demonstrated that infants with non-IgE-mediated gastrointestinal food allergy were at risk of low vitamin D levels. Moreover, a previous study also demonstrated that infants with food allergies exhibited significantly lower vitamin D levels than controls (19). However, no significant difference was observed in the levels of vitamin D between infants with cow's milk protein allergy and controls (20).

At present, the optimal levels of vitamin D for preventing food allergy remain to be established. Levels of vitamin D sufficiency at >50 nmol/l are required for maintaining healthy bone mineralization, and calcium and phosphorus metabolism (21). The results of the present study demonstrated notable differences in vitamin D levels between infants with gastrointestinal food allergy and healthy controls and determined that vitamin D levels may play an important role in gastrointestinal food allergy. Although vitamin D levels were lower in children with food protein-induced gastrointestinal disease when compared with healthy controls, only 5.54% (20/361) of infants exhibited vitamin D levels <50 nmol/l. Therefore, vitamin D supplementation is recommended in infants with food protein-induced gastrointestinal disease, and excessive vitamin D supplementation in

Table III. Logistic regression analysis of sufficient vs. insufficient levels of 25-(OH)D.

	Unadjusted			Adjusted[c]		
Variable	OR	95% CI	P-value	OR	95% CI	P-value
Sex	0.468	0.295~0.742	0.001[b]	0.429	0.266~0.690	<0.001[b]
Total IgE	0.996	0.994~0.999	0.004[a]	0.996	0.994~0.998	0.001[b]

[a]P<0.01, [b]P<0.001. [c]Adjusted for sex. IgE, immunoglobulin E; 25-(OH)D, 25 hydroxyvitamin D; CI, confidence interval; OR, odds ratio.

infants without disease is not required. However, the appropriate supplemental dose needs to be further studied.

Clinical characteristics, such as age, sex, allergen type, and clinical symptoms may be associated with vitamin D insufficiency. The results of a previous study demonstrated that patients with eosinophilic esophagitis with insufficient vitamin D levels were older, and the proportion of patients with food impaction was larger, compared with patients with sufficient vitamin D levels (22). Moreover, the results of previous studies demonstrated that females had lower vitamin D levels and a lower incidence of gastrointestinal food allergies, and patients with lower vitamin D levels were older (18,23). The results of the present study were consistent with those of previous studies, demonstrating that females were at a high risk of developing insufficient vitamin D levels; however, a higher number of males presented with food allergies. Slack *et al* (22) revealed that a positive skin prick test reaction to peanuts was more common in patients with insufficient vitamin D levels, and Kostara *et al* (19) revealed that multiple-sensitized children exhibited significantly lower vitamin D levels. However, the results of the present study demonstrated no significant differences in allergen type or number between children with sufficient and insufficient vitamin D levels.

Mechanistically, vitamin D contributes to immune tolerance through the induction of tolerogenic dendritic cells and regulatory T cells, and the inhibition of IgE production in B cells (8). The results of a previous animal study demonstrated that vitamin D receptors, directly and indirectly, regulated IgE production in B cells, and vitamin D acts as an environmental factor that contributes to the maintenance of a low serum IgE response through vitamin D receptors (24). Similar to the results of previous studies (23,25), the results of the present study revealed that total IgE levels were associated with low vitamin D status in allergic diseases. However, further investigations into the precise mechanisms underlying the development of this inflammatory condition are required.

Research into vitamin D supplementation for primary allergy prevention is lacking. A randomized controlled and double-blinded study investigated the effects of vitamin D supplementation in early infancy on the allergy outcomes of high-risk infants with sufficient vitamin D levels at birth. The results revealed no statistically significant differences between the vitamin D-supplemented and placebo groups in the incidence of allergic disease outcomes or allergen sensitization rates at 1 or 2.5 years of age (26). Moreover, the results of an *in vivo* study demonstrated that high levels of vitamin D did not alleviate allergic symptoms in mice (27,28).

Allergic diseases pose a serious threat to human health. Prevention strategies implemented during early childhood, pregnancy, and lactation remain the subject of numerous studies, despite the lack of a gold standard of diagnosis and treatment options. However, multiple previous studies demonstrated that there was no association between maternal vitamin D levels and food allergy in offspring (15,29,30). Moreover, the present study demonstrated that there were no significant risk factors associated with vitamin D insufficiency. Thus, additional vitamin D supplementation during pregnancy or lactation may not be beneficial and may even increase the risk of early childhood food allergy (13,14,25).

However, the present study has some limitations. For example, the results of the present study were obtained from a single center, and further investigations including data obtained from centers nationwide are required to verify the vitamin D levels of infants with gastrointestinal food allergies. In addition, the present study highlighted significantly different serum 25-(OH)D levels between patients and healthy individuals; however, a causal association between low serum 25-(OH)D levels and food protein-induced gastrointestinal disease was not determined. Moreover, further investigations into the specific mechanisms underlying the effects of serum 25-(OH)D in patients with food protein-induced gastrointestinal diseases are required.

In conclusion, patients with food protein-induced gastrointestinal disease may be at risk of low 25-(OH)D levels, and this risk may be greater in females and individuals with higher total IgE. However, the optimal levels of vitamin D for the prevention of food allergy remain unknown; thus, supplementation in infants with food protein-induced gastrointestinal disease may not be required. In addition, a few patients in the present study demonstrated serum 25-(OH)D levels <50 nmol/l.

Acknowledgements

Not applicable.

Funding

The present study was supported by The Health Commission of Chengdu City (grant no. 2021227).

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

MYZ, XL, and XLX were involved in the study design, data collection, data analysis, and drafting of the manuscript. JY and LJX were involved in reviewing multiple drafts of the manuscript and data collection. JXZ and XQH were involved in data collection. MYZ, XL, and XLX confirm the authenticity of all the raw data. All authors have read and approved the final manuscript.

Ethics approval and consent to participant

Oral informed consent was obtained from the parents or guardians of infants involved in the present study. The present study was registered and approved by the Ethics Committee of Chengdu Women and Children's Central Hospital [approval no. (2021)55].

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

References

1. Sampath V, Abrams EM, Adlou B, Akdis C, Akdis M, Brough HA, Chan S, Chatchatee P, Chinthrajah RS, Cocco RR, *et al*: Food allergy across the globe. J Allergy Clin Immunol 148: 1347-1364, 2021.
2. Group of Gastroenterology SoP, Chinese Medical Association: Diagnosis of food allergy related gastrointestinal diseases: Consensus with management experts. Chin J Pediatr 55: 487-492, 2017.
3. Heine RG: Food allergy prevention and treatment by targeted nutrition. Ann Nutr Metab 72 (Suppl 3): S33-S45, 2018.
4. Ismailova A and White JH: Vitamin D, infections and immunity. Rev Endocr Metab Disord 23: 265-277, 2022.
5. Ao T, Kikuta J and Ishii M: The effects of vitamin D on immune system and inflammatory diseases. Biomolecules 11: 1624, 2021.
6. Rudders SA and Camargo CA Jr: Sunlight, vitamin D and food allergy. Curr Opin Allergy Clin Immunol 15: 350-357, 2015.
7. Di T and Chen L: A narrative review of vitamin D and food allergy in infants and children. Transl Pediatr 10: 2614-2620, 2021.
8. Suaini NH, Zhang Y, Vuillermin PJ, Allen KJ and Harrison LC: Immune modulation by vitamin D and Its relevance to food allergy. Nutrients 7: 6088-6108, 2015.
9. Brough HA, Lanser BJ, Sindher SB, Teng JMC, Leung DYM, Venter C, Chan SM, Santos AF, Bahnson HT, Guttman-Yassky E, *et al*: Early intervention and prevention of allergic diseases. Allergy 77: 416-441, 2022.
10. Linden MA, Freitas RGBON, Hessel G, Marmo DB and Bellomo-Brandão MÂ: Definition of vitamin D deficiency in schoolchildren: Systematic review with meta-analysis. Arq Gastroenterol 56: 425-430, 2019.
11. Matsui T, Tanaka K, Yamashita H, Saneyasu KI, Tanaka H, Takasato Y, Sugiura S, Inagaki N and Ito K: Food allergy is linked to season of birth, sun exposure, and vitamin D deficiency. Allergol Int 68: 172-177, 2019.
12. Koplin JJ, Suaini NH, Vuillermin P, Ellis JA, Panjari M, Ponsonby AL, Peters RL, Matheson MC, Martino D, Dang T, *et al*: Polymorphisms affecting vitamin D-binding protein modify the relationship between serum vitamin D [25(OH)D3] and food allergy. J Allergy Clin Immunol 137: 500-506.e4, 2016.
13. Wang NR, Liu SJ, Xiao GY, Zhang H, Huang YJ, Wang L and He CY: Cord blood 25(OH)D_3, cord blood total immunoglobulin E levels, and food allergies in infancy: A birth cohort study in Chongqing, China. World Allergy Organ J 15: 100645, 2022.
14. Rosendahl J, Pelkonen AS, Helve O, Hauta-Alus H, Holmlund-Suila E, Valkama S, Enlund-Cerullo M, Viljakainen H, Hytinantti T, Mäkitie O, *et al*: High-dose vitamin D supplementation does not prevent allergic sensitization of infants. J Pediatr 209: 139-145.e1, 2019.
15. Molloy J, Koplin JJ, Allen KJ, Tang MLK, Collier F, Carlin JB, Saffery R, Burgner D, Ranganathan S, Dwyer T, *et al*: Vitamin D insufficiency in the first 6 months of infancy and challenge-proven IgE-mediated food allergy at 1 year of age: A case-cohort study. Allergy 72: 1222-1231, 2017.
16. Chan AW, Chan JK, Tam AY, Leung TF and Lee TH: Guidelines for allergy prevention in Hong Kong. Hong Kong Med J 22: 279-285, 2016.
17. Cairncross C, Grant C, Stonehouse W, Conlon C, McDonald B, Houghton L, Eyles D, Camargo CA, Coad J and von Hurst P: The relationship between vitamin D status and allergic diseases in New Zealand preschool children. Nutrients 8: 326, 2016.
18. Foong RX, Meyer R, Dziubak R, Lozinsky AC, Godwin H, Reeve K, Hussain ST, Nourzaie R and Shah N: Establishing the prevalence of low vitamin D in non-immunoglobulin-E mediated gastrointestinal food allergic children in a tertiary centre. World Allergy Organ J 10: 4, 2017.
19. Kostara M, Giapros V, Serbis A, Siomou E, Cholevas V, Rallis D and Tsabouri S: Food allergy in children is associated with vitamin D deficiency: A case-control study. Acta Paediatr 111: 644-645, 2022.
20. Ercan N, Bostanci İB, Ozmen S and Tekindal MA: Is there an association between vitamin D levels and cow's milk protein allergy at infancy? Arch Argent Pediatr 117: 306-313, 2019 (In English, Spanish).
21. Subspecialty Group of Child Health Care SoP, Chinese Medical Association, Editorial Board of Chinese Journal of Pediatrics: Clinical issues related to vitamin D nutrition in Chinese children practice guidelines. Chin J Pediatr 60: 387-3, 2022.
22. Slack MA, Ogbogu PU, Phillips G, Platts-Mills TA and Erwin EA: Serum vitamin D levels in a cohort of adult and pediatric patients with eosinophilic esophagitis. Ann Allergy Asthma Immunol 115: 45-50, 2015.
23. Guo H, Zheng Y, Cai X, Yang H, Zhang Y, Hao L, Jin Y and Yang G: Correlation between serum vitamin D status and immunological changes in children affected by gastrointestinal food allergy. Allergol Immunopathol (Madr) 46: 39-44, 2018.
24. James J, Weaver V and Cantorna MT: Control of circulating IgE by the vitamin D receptor in vivo involves B cell wintrinsic and extrinsic mechanisms. J Immunol 198: 1164-1171, 2017.
25. Wu J, Zhong Y, Shen X, Yang K and Cai W: Maternal and early-life vitamin D deficiency enhances allergic reaction in an ovalbumin-sensitized BALB/c mouse model. Food Nutr Res 62, 2018.
26. Rueter K, Jones AP, Siafarikas A, Lim EM, Prescott SL and Palmer DJ: In 'high-risk' infants with sufficient vitamin D status at birth, infant vitamin D supplementation had no effect on allergy outcomes: A randomized controlled trial. Nutrients 12: 1747, 2020.
27. Kerperien J, Veening-Griffioen D, Oja A, Wehkamp T, Jeurink PV, Garssen J, Knippels LMJ and Willemsen LEM: Dietary vitamin D supplementation is ineffective in preventing murine cow's milk allergy, irrespective of the presence of nondigestible oligosaccharides. Int Arch Allergy Immunol 181: 908-918, 2020.
28. Fang Y and Zhang Q: Effect of 1,23-dihydroxyvitamin D3 on food allergy mice. Chin J Appl Clin Pediatr 34: 693-697, 2019.
29. Hennessy Á, Hourihane JO, Malvisi L, Irvine AD, Kenny LC, Murray DM and Kiely ME: Antenatal vitamin D exposure and childhood eczema, food allergy, asthma and allergic rhinitis at 2 and 5 years of age in the atopic disease-specific Cork BASELINE birth cohort study. Allergy 73: 2182-2191, 2018.
30. Woon FC, Chin YS, Ismail IH, Abdul Latiff AH, Batterham M and Chan YM; On Behalf Of The Micos Research Group: Maternal vitamin D levels during late pregnancy and risk of allergic diseases and sensitization during the first year of life-A birth cohort study. Nutrients 12: 2418, 2020.