

## CORRESPONDENCE

## Authors' reply to letter: vitamin D and atopic dermatitis: association, causation or confusion?

To the Editor,

We are glad to receive these interesting and constructive comments on our recent publication regarding a potential association between vitamin D deficiency and childhood atopic dermatitis (AD) (1). Whereas Lenko et al. made some valid points, they have not correctly perceived some of our messages. Firstly, we cannot agree with their criticism that the title of our article read 'vitamin D deficiency is *associated* with diagnosis and severity of childhood AD' was misleading. This title did not convey any message of strong correlation between vitamin D deficiency and severity of AD. We found that serum 25-hydroxyvitamin D [25(OH)D] levels were higher in controls than AD patients and that more patients were vitamin D deficient than controls. Serum 25(OH)D levels also showed inverse associations with both short-term and long-term AD severity. Thus, the title of our article did not imply that vitamin D deficiency *modifies the susceptibility* of AD in our children. We agree with the authors and have already stated clearly in our article that prospective cohort studies are needed to support such strong claim between vitamin D deficiency and childhood AD.

The authors commented that the aim of the study was not clearly defined. As what we stated, however, the article measured serum 25(OH)D levels in a case-control cohort of Chinese children to investigate the relationship between vitamin D and childhood AD. Again, such aim was correctly addressed by our findings that low 25(OH)D levels were *associated* with AD in Hong Kong Chinese children. They queried about our inclusion criteria to include children with mild AD. Intentionally, we did not set any minimum severity score of AD for our study. As one-third of our patients had mild disease, we believe that our results can be more generalizable to the entire AD population.

In addition, Lenko et al. doubted about the definition and criticized about the high rate (almost 50%) of atopy among our controls. We have clearly defined atopy as being positive for at

least one locally important aeroallergen by skin prick tests or serum-specific IgE assays. The high atopy rate in our non-allergic controls was also consistent with those reported in our published studies for asthma (2–4) and eczema (5, 6).

The authors also concerned that the large numbers of cases and controls being recruited might merely lead to statistical but not clinical significance for our study findings. We cannot agree with them about this issue. Our study found that AD patients had 15% lower mean serum 25(OH)D levels than controls, and the proportions of vitamin D deficiency among these two groups were 47.8% and 26.6%, respectively (1). Looking at these results, it would be unreasonable for us to dismiss such differences as being small or clinically insignificant.

Our group has recently reported a genetic association study in which 23 single-nucleotide polymorphisms (SNPs) of five vitamin D-related genes (*CYP27A1*, *CYP2R1*, *CYP27B1*, *GC* and *VDR*) were genotyped in 1442 AD children and 1231 controls (6). Atopic AD was associated with rs4674343 of *CYP27A1*. Two *CYP2R1* haplotypes increased and one *VDR* haplotype lowered the risk for AD. This alternative approach supported the importance of vitamin D pathway genes in modifying the susceptibility of childhood AD. Further study is being carried out to investigate whether the above SNPs alter the functionality of relevant vitamin D pathway genes.

In conclusion, we agree with Lenko et al. that our article (1) did not report any causation between AD and vitamin D deficiency. Prospective long-term studies are needed to truly determine whether vitamin D deficiency confers the risk for childhood AD. Importantly, our results showed high rate of vitamin D deficiency in Chinese children living in Hong Kong.

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DOI:10.1111/pai.12230

### References

1. Wang SS, Hon KL, Kong AP, et al. Vitamin D deficiency is associated with diagnosis and severity of childhood atopic dermatitis. *Pediatr Allergy Immunol* 2014; **25**: 30–5.
2. Leung TF, Tang NL, Li CY, Lam CW, Wong GW, Fok TF. Association between TARC C-431T and atopy and asthma in children. *J Allergy Clin Immunol* 2004; **114**: 199–202.
3. Leung TF, Tang NL, Sung YM, et al. Genetic association study between *mb12* and asthma phenotypes in Chinese children. *Pediatr Allergy Immunol* 2006; **17**: 501–7.
4. Leung TF, Sy HY, Ng MC, et al. Asthma and atopy are associated with chromosome 17q21 markers in Chinese children. *Allergy* 2009; **64**: 621–8.
5. Wang SS, Hon KL, Sy HY, et al. Interactions between genetic variants of *FLG* and chromosome 11q13 locus determine susceptibility for eczema phenotypes. *J Invest Dermatol* 2012; **132**: 1930–2.
6. Wang SS, Hon KL, Kong AP, et al. Eczema phenotypes are associated with multiple vitamin D pathway genes in Chinese children. *Allergy* 2014; **69**: 118–24.