

Clinical features of children with coconut allergy and its sIgE profiling using immunoblot analysis

To the Editor,

Coconut is the edible fruit of the coconut palm (*Cocos nucifera*) in the palm family (Aracaceae). Coconut milk, extracted from the grated coconut meat, is a traditional food ingredient in South and Southeast Asia. In addition, the coconut oil is an ingredient in various skin care products. Based on the dual allergen exposure hypothesis, using coconut-based skincare products might cause sensitization through the skin before developing a coconut allergy.¹

Coconut, classified as a Drupe, is also considered a tree nut for food labeling purposes by the Food and Drug Administration (FDA).² Therefore, the patients that are allergic to coconut are advised to avoid all the nuts until further investigation. However, it is controversial whether cosensitization between coconut and tree nuts can occur. A study of 90 patients with positive coconut-sIgE reported a high co-sensitization to macadamia (71%) and almond (69%).² Whereas another study did not find a cross-relation between coconut and tree nut allergy.³ A recent case series of 26 pediatric patients with coconut allergy showed that 31% were sensitized to cashew.⁴ However, the number of patients with a cosensitization to coconut and tree nuts was similar to those with any food allergy.⁴

The incidence of coconut allergy is relatively rare. Most cases had immediate hypersensitivity reactions, including anaphylaxis.⁵⁻⁸ Due to limited data on coconut allergy in Asia, we aimed to review the clinical characteristics of Thai children with coconut allergy, cross-reactivity to other nuts, and profiles of IgE-binding coconut proteins.

We enrolled 11 patients between January and December 2021 at the Division of Allergy, Pediatric Department, Siriraj Hospital, Mahidol University. All the patients had an immediate reaction to coconut and positive skin prick test (SPT) and/or coconut-specific IgE (≥ 0.35 kUA/L). Prick-to-prick (PTP) tests were performed on coconut milk, coconut water, and coconut meat. The tree nuts (macadamia, cashew, and almond) and peanut extracts were prepared using tree nuts and peanut flour (Nuts.com, Cranford, New Jersey, USA) diluted in the Coca's solution (1:10 w/v). The positive and negative controls were histamine (10 mg/mL) and glycerinated saline solution. A mean wheal diameter (MWD) of ≥ 3 mm larger than the negative control was defined as positive. The specific IgE for coconut was measured using the ImmunoCAP system (Phadia, Uppsala, Sweden). The oral food challenge (OFC) test was performed only among participants who signed assent and consent from their parents and did

not have a recent reaction during the last six months. OFC was performed using coconut milk jelly with a cumulative dose of 3 g of coconut protein. The challenge step was 0.25, 0.5, 0.75, and 1.5 g of coconut protein with 30-minute intervals between each step.⁹

In total, three patients experienced anaphylaxis, while the other eight patients had only skin symptoms. The median age of the patients was 6.6 years (IQR 3–17), and the median age of onset was 12 months (IQR 6–132). Six out of 11 (54.5%) patients had the onset within the first year of life. Coconut milk was the most common source of exposure. No patient had previously used coconut lotion or oil before the onset of the allergy. The characteristics of the patients are summarized in Table 1 and Table S1.

When comparing the PTP test to three coconut components, coconut milk gave the largest MWD, followed by coconut meat and coconut water (Table 1). Only patients no. 10 and 11 underwent an OFC. Three patients (27.3%) had peanut sensitization and two patients (18.2%) had almond and macadamia sensitization. However, these five patients had no history of allergic reactions to peanuts and/or tree nuts. The correlation between coconut-sIgE and PTP in the different parts of the coconut is shown in Table 2. Coconut milk had the best correlation with coconut-sIgE, compared with the other components ($r = .72$, $p = .013$).

Serum IgE antibodies reactive against extracted coconut proteins were analyzed by immunoblotting using the 'Jess' fully automated system (ProteinSimple; Bio-Techne, USA). The IgE profiles of 10 patients showed sIgE bound multiple proteins with various intensities, indicating that, per patient, the amount of sIgE for each allergen was different (Figure 1). The 35 kDa allergen appears to be a major coconut allergen, as seven patients had high-intensity IgE bound. In total, 11 S globulin with a MW 35 kDa was identified as a coconut allergen and a cross-reactive allergen between coconut and tree nuts.^{5,6} However, all the patients in this study did not test positive for tree nuts or peanuts. Other strong IgE bound 66, and 21 kDa allergens were seen in the IgE profiles of patients no. 4–6 and 9; all had only skin manifestation (Figure 1). Based on the IgE profiles, patients with anaphylaxis history did not have a different profile than patients with skin manifestation. Interestingly, although we had positive results of coconut-sIgE and PTP using coconut meat, an IgE profile could not be detected using the serum of a patient (p3) with a history of anaphylaxis. This could be because this patient had outgrown the coconut allergy and had a low amount of sIgE.

Clinical characteristics	Total (n = 11)	Anaphylaxis (n = 3)	Only skin manifestation (n = 8)
Age (year)	6.6 (3–17)	9.42 (3–13.91)	6.45 (3.5–17)
Age of onset (month)	12 (6–132)	12 (12–101)	15 (6–132)
Sex: female, n (%)	6 (54.5)	2 (66.7)	4 (50)
Atopic diseases, n (%)			
Atopic dermatitis	7 (63.6)	1 (33.3)	6 (75)
Food allergy	10 (90.9)	3 (100)	7 (87.5)
Tree nut/peanut allergy	0	0	0
Asthma	2 (18.2)	2 (66.7)	0
Allergic rhinitis	7 (63.6)	2 (66.7)	5 (62.5)
Coconut sIgE (kUA/L), median (range)	3.83 (0.1–16.3)	3.83 (0.8–9.28)	2.72 (0.1–16.3)
PTP coconut water MWD (mm), median (range)	4 (0–12)	0 (0–8.5)	4 (0–12)
PTP coconut meat MWD (mm), median (range)	11.5 (2.5–20)	11.5 (8–15)	11.25 (2.5–20)
PTP coconut milk MWD (mm), median (range)	12.5 (0–19.5)	12.5 (8–16.5)	11 (0–19.5)

Abbreviations: MWD, Mean wheal diameter; PTP, Prick-to-prick; sIgE, specific IgE.

TABLE 1 Comparison of clinical characteristics of patients with coconut anaphylaxis and mild/moderate coconut allergy.

TABLE 2 Correlations between coconut sIgE and mean wheal diameter of prick-to-prick skin test of coconut (Spearman rank correlation coefficient; *r*)

Correlation	coconut sIgE (kUA/L)	PTP coconut water MWD (mm)	PTP coconut meat MWD (mm)	PTP coconut milk MWD (mm)
Coconut sIgE (kUA/L)	1.00	−0.037 (<i>p</i> = .914)	0.595 (<i>p</i> = .053)	0.72 (<i>p</i> = .013)
PTP coconut water MWD (mm)	−0.037 (<i>p</i> = .914)	1.00	0.35 (<i>p</i> = .292)	0.249 (<i>p</i> = .461)
PTP coconut meat MWD (mm)	0.595 (<i>p</i> = .053)	0.35 (<i>p</i> = .292)	1.00	0.823 (<i>p</i> = .002)
PTP coconut milk MWD (mm)	0.72 (<i>p</i> = .013)	0.249 (<i>p</i> = .461)	0.823 (<i>p</i> = .002)	1.00

Note: *p* < .05 indicates statistic significant.

Our study showed that coconut allergy occurred early in life, without any history of using coconut-based skin care products. This onset was earlier than the previous study, which reported onset at four years.⁴ Interestingly, 17.1% of the patients in that study used coconut-based skincare before the onset of the reaction. The earlier onset in our study may be caused by the early ingestion of coconut in the Thai population or proteins transferred to breast milk. As previously reported, two infants with eczema who were breastfed developed a coconut allergy at less than 6 months of age.¹⁰

Cosensitization between coconut and tree nuts, particularly, almond and macadamia, has been reported.^{2,3,5} We found that 18% of the patients were sensitized to peanut and tree nuts compared to an Australian study that showed peanut sensitization in 34% of coconut allergic patients.⁴ However, none of these patients had a history of allergic reactions to peanut or tree nuts. This could be because tree nuts and peanuts are not common causes of food allergy in the Thai children.¹¹

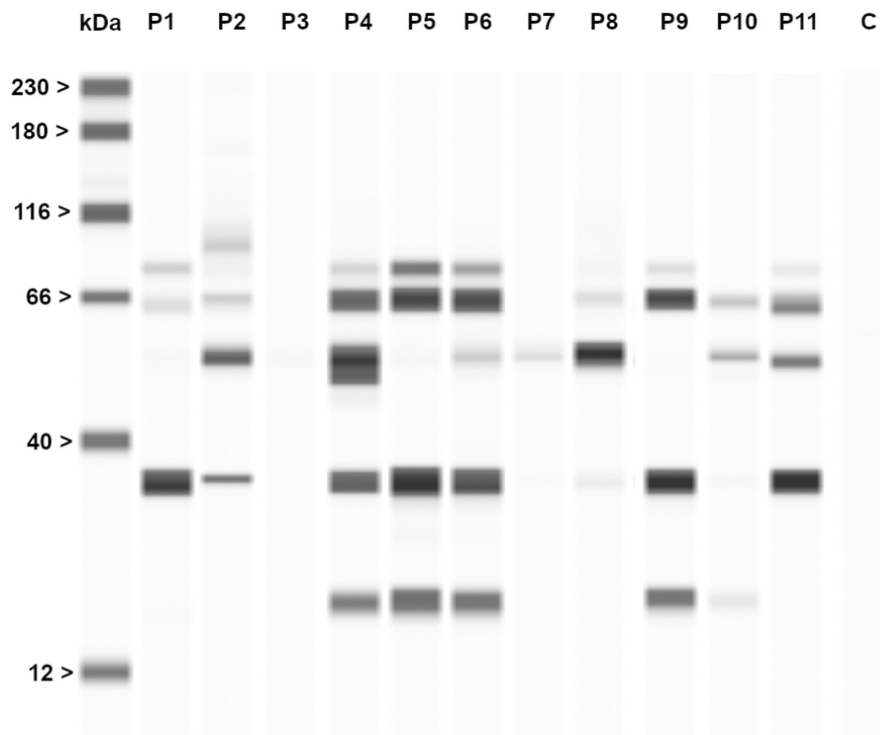
In Thailand, commercial coconut extract is not available. Thus, we used the PTP method with the three coconut components to

determine the best correlation with the coconut sIgE. Regarding the limited number of patients who underwent the OFC, we used the sIgE as a reference test. The correlation between the PTP test and sIgE to coconut was evaluated. The result showed that the median PTP to coconut meat and coconut milk had a larger MWD than coconut water. Using coconut water for the PTP test misdiagnosed 4 of 11 patients. Furthermore, coconut milk showed the best correlation with coconut-sIgE. From these results, we propose that PTP using coconut milk is the best test for coconut allergy.

The limitations of our study include a small sample size and that OFC was performed in only a few patients. However, coconut is not a common cause of food allergy in Thailand, and we recruited all the patients with positive PTP and/or sIgE to coconut together with their clinical history. Another limitation was that blood tests were obtained during the study period, but not at the onset of the coconut allergy. Thus, coconut-sIgE levels may have been lower than actual levels.

In conclusion, coconut allergy can occur very early in life and the use of coconut-based products is not mandatory to induce allergic

FIGURE 1 Profile of IgE bound coconut proteins from 11 patients. The automated immunoblotting was performed using serum of 11 patients (P) and 1 non-allergic individual (C).



reactions. PTP to coconut milk can be used to diagnose coconut allergy in limited-resource areas. Cross-sensitization to peanuts and tree nuts was not common in our study population.

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allergen, anaphylaxis, coconut, cross-reactivity, skin test

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SUPPORTING INFORMATION

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