Allergologia et immunopathologia
Sociedad Española de Inmunología Clínica, Alergología y Asma Pediátrica
www.all-imm.com

ORIGINAL ARTICLE

OPEN ACCESS

Clinical and laboratory characteristics of cashew nut allergy in Korean children: Findings from a tertiary hospital

Jaeeun Kim, Sanghwa Youm, Sooyoung Lee, Kyunguk Jeong*

Department of Pediatrics, Ajou University School of Medicine, Suwon, The Republic of Korea

Received 12 November 2024; Accepted 30 March 2025
Available online 1 May 2025

KEYWORDS
anaphylaxis;
cashew nut allergy;
children;
immediate type allergy;
tree nut allergy

Abstract
Objective: Cashew nut (CN) allergy is becoming increasingly prevalent and represents a major cause of tree nut-induced anaphylaxis in Korean children. This study investigated the clinical characteristics and laboratory findings of CN allergy in Korean children.
Patients and methods: Sixty-four children with a history of CN ingestion, who underwent serum CN-specific immunoglobulin E (CN-sIgE) measurements from January 2013 to February 2023, were enrolled through a retrospective medical record review. The demographic characteristics, clinical profiles, and laboratory findings were evaluated.
Result: Thirty-five patients had immediate-type reactions after exposure to CN (CN-allergic group), whereas 29 showed no symptoms after ingesting CN (CN-tolerant group). Over 60% of patients in the CN-allergic group were allergic to ≥ 1 other tree nuts and 17.1% had peanut allergies. In the CN-allergic group, cutaneous symptoms were most common (94.1%), followed by respiratory (35.3%), gastrointestinal (32.4%), and cardiovascular (2.9%) symptoms. Anaphylaxis due to CN exposure was observed in 51.4% of patients in the CN-allergic group. The median CN-sIgE level of the CN-allergic group was significantly higher than that of the CN-tolerant group (5.5 kUA/L vs. 0.06 kUA/L, $P < 0.001$). The optimal cutoff level for distinguishing the CN-allergic group from the CN-tolerant group was 0.55 kU_A/L (sensitivity 94.29%, specificity 93.10%).
Conclusion: Co-allergies to other tree nuts were common in children with CN allergy and more than 50% of patients with CN allergy experienced anaphylaxis. The optimal cutoff level for distinguishing between the CN-allergic and CN-tolerant groups was 0.55 kU_A/L.

***Corresponding author**: Kyunguk Jeong, MD, Department of Pediatrics, Ajou University School of Medicine, WorldCup-ro 164, Yeongtong-gu, Suwon, Republic of Korea. *Email address*: k.u.jeong@gmail.com

https://doi.org/10.15586/aei.v53i3.1289

Introduction

Food allergy is a common condition in children, with a prevalence of approximately 10%, and is gradually increasing worldwide.[1,2] The prevalence of food allergies among children in Korea varies depending on the age group and research design, ranging from 8.9 to 15.8%, with an increasing trend.[3,4]

Peanuts and tree nuts are common causes of food allergies in Western countries. The prevalence of tree nut allergy varies depending on country, region, age, and diagnostic criteria, ranging from 0.05 to 7.3%.[1,5] Tree nut allergies are increasing as nut consumption increases worldwide, particularly among children.[6] In addition, tree nut allergies are generally lifelong, often associated with severe symptoms, with increasing frequency of emergency department visits due to anaphylaxis.[7] According to multicenter studies in Korean children, tree nuts were the third leading cause of food allergies and food-induced anaphylaxis after milk and eggs.[8,9] Research on individual tree nut allergies is limited due to variations in their prevalence across countries, influenced by factors such as race, diet pattern, and living environment. Consequently, the characteristics of individual tree nut allergies remain underexplored.

Among tree nuts, cashew nut (CN) (*Anacardium occidentale*) is the most common cause of tree nut allergies in many countries, including Australia, the United States, and China.[10-12] In Canada, CN is the most common cause of nut-induced anaphylaxis,[13] and in Korea, CN is the fourth most common cause of tree nut allergies after walnut, pine nut, and almond, and the third most common cause of tree nut-induced anaphylaxis.[14,15] CN accounted for 5.1% of food-induced anaphylaxis in the European Anaphylaxis Registry and 1.4% of food-induced anaphylaxis in Korean children.[9,16] The major allergens of CN have been identified as Ana o 1, Ana o 2, and Ana o 3. All three are classified as seed storage proteins, which are recognized allergens in other tree nuts, legumes, and seeds. Among these, Ana o 3 is considered the most clinically relevant, with high diagnostic value for identifying true clinical allergy. Monosensitization to Ana o 3 has been reported to be associated with a high risk of severe anaphylaxis.[17,18]

CN allergy is typically diagnosed based on a convincing history and a positive skin prick test (SPT) or specific immunoglobulin E (sIgE). However, as sensitization does not always indicate clinical allergy—the oral food challenge (OFC) remains the gold standard. Given its risks and demands, OFC is rarely used first-line, and efforts have been made to replace it with SPT or sIgE testing. These tests have shown good diagnostic accuracy for CN allergy in a recent systematic review, with SPT demonstrating an area under the curve (AUC) of 0.81–0.94 and CN-sIgE showing similar performance (AUC 0.79–0.89).[19] McWilliam and Elizur reported a 95% positive predictive value (PPV) for diagnosing CN allergy with SPT wheal sizes of ≥ 14 mm and ≥ 12 mm, respectively.[20,21] A recent meta-analysis identified optimal cutoff values of 5 mm for SPT (93% sensitivity, 92% specificity), and 1.1 kU_A/L for CN-sIgE (94% sensitivity, 64% specificity).[22] However, studies assessing the diagnostic utility of SPT or CN-sIgE for CN allergy remain scarce in Asian populations.

Despite its prevalence and frequent association with anaphylaxis, CN allergy in Korean children has not been well studied. Hence, this study's aim was to investigate the clinical characteristics and laboratory findings of CN allergy in Korean children and identify the predictive value of CN-sIgE in pediatric patients with CN allergy.

Materials and Methods

From January 2013 to February 2023, 64 children with a history of CN ingestion who underwent a serum CN-sIgE assay at the Department of Pediatrics, Ajou University Hospital, Suwon, Korea, were enrolled. A retrospective medical record review was conducted, excluding cases with no history of CN exposure, no medical record of CN ingestion history or allergic reaction following CN ingestion, no CN-sIgE results, a time interval of > 1 year between ingestion and serum CN-sIgE assay, or simultaneous exposure to other tree nuts at the time of CN exposure. Patients were categorized into two groups: CN-allergic and CN-tolerant groups. The CN-allergic group consisted of 35 children who had immediate-type allergic reactions upon exposure to CN and the CN-tolerant group consisted of 29 atopic controls who were asymptomatic after the ingestion of CN. The CN-allergic group was further categorized into two subgroups according to their symptoms: anaphylaxis and nonanaphylaxis groups. Anaphylaxis was defined based on the clinical criteria of the National Institute of Allergy and Infectious Disease and the Food Allergy and Anaphylaxis Network.[23] Demographic profiles, clinical characteristics regarding CN allergy (clinical profiles, types of CN ingested, and time interval between CN exposure and symptom onset), and laboratory findings at the time of CN consumption were obtained and analyzed. Food allergies other than CN were defined as definite immediate allergic reactions that occurred after the ingestion of food through a medical record review. Tree pollen sensitization was defined as ≥ 1+ in multiple allergen simultaneous test (MAST) or ≥ 0.35 kU_A/L in ImmunoCAP (Thermo Fisher Scientific, Uppsala, Sweden). This study was approved by the Institutional Review Board of Ajou University Hospital (AJOUIRB-DB-2023-441).

Measurement of the total IgE and sIgE antibody levels

The serum total IgE and CN-sIgE levels for all participants were measured using ImmunoCAP. The lower limit of CN-sIgE using this assay was < 0.05 kU_A/L and the upper limit was > 100 kU_A/L, in accordance with the manufacturer's instructions. The values < 0.05 and > 100 kU_A/L were considered as 0.04 and 101 kU_A/L, respectively.

Statistical analysis

The Mann-Whitney *U* test was used to analyze continuous variables to compare characteristics and serologic parameters between the study groups. To compare categorical variables, chi-square and Fisher's exact tests were used. A *P*-value of < 0.05 was considered statistically significant. The AUC of the receiver operating characteristic (ROC)

curve was used to assess total IgE and CN-sIgE levels for diagnosing CN allergy and to obtain the cutoff values.

Results

A total of 64 children aged 12–152 months (median age: 48 months) were included in the study. Thirty-five patients had immediate-type reactions after CN exposure (CN-allergic group), whereas the remaining 29 showed no symptoms (CN-tolerant group). The median ages of the CN-allergic and CN-tolerant groups were 36 and 63 months, respectively. Over 60% of the CN-allergic group had allergy to ≥ 1 other tree nuts and 17.1% had peanut allergy.

Among the CN-allergic groups, 11.4% exhibited tree pollen sensitization. There was no significant difference in the demographic distribution between the CN-allergic and CN-tolerant groups, including sex, concurrent allergic diseases, other food allergies, tree pollen sensitization, and family history of allergic diseases, except for the median age (Table 1).

In the CN-allergic group, cutaneous symptoms were most common (94.1%), followed by respiratory (35.3%), gastrointestinal (32.4%), and cardiovascular (2.9%) symptoms. Anaphylaxis due to CN was observed in 51.4% patients in the CN-allergic group (Figure 1). There were no cases with oral symptoms alone. Among the symptoms observed in each organ system, urticaria (70.6%) was the most common cutaneous symptom, followed by dyspnea (26.5%) as the most frequent respiratory symptom and vomiting (29.4%) as the predominant gastrointestinal symptom. All the participants experienced allergic reactions following oral ingestion, with no cases resulting from skin contact or inhalation. More than two-thirds of the participants (69%) in the CN-allergic group experienced symptoms within 60 minutes of exposure to CN. All CN-allergic children experienced immediate-type reactions within 2 hours (Figure 2), except for cases in which the symptom onset time was not clearly documented. The most common form of CN ingested in the CN-allergic group was roasted CN (22.9%), followed by the extract (5.7%) and raw CN (2.9%) (Figure 3).

The median total IgE level was 310 kU/L in the CN-allergic group and 178 kU/L in the CN-tolerant group, and the difference between the two groups was statistically significant (P = 0.01). The median level of CN-sIgE was 5.5 kU_A/L (range 0.13–101.00 kU_A/L) in the CN-allergic group, which was significantly higher (P < 0.001) than that of the CN-tolerant group (0.06 kU_A/L; range 0.06–0.88 kU_A/L) (Table 2).

The ROC curve showed the diagnostic performance of total IgE and CN-sIgE in the diagnosis of clinical CN allergies. The AUC of CN-sIgE was 0.983 (95% CI, 0.913–0.999), and the CN-sIgE level was a good predictor for distinguishing the CN-allergic group from the CN-tolerant group compared to the total IgE level (AUC 0.688). The optimal cutoff level for distinguishing the CN-allergic group from the CN-tolerant group was 0.55 kU_A/L (sensitivity 94.29%, specificity 93.10%). The CN-sIgE level that could distinguish

Table 1 Demographic profiles of patients in CN-allergic or tolerant group.

	CN-allergic (n = 35)	CN-tolerant (n = 29)	Total (N = 64)
Age, months[a]	36 (12–106)	63 (12–152)	48 (12–152)
Sex			
Male	23 (65.7)	16 (55.2)	39 (60.9)
Female	12 (34.3)	13 (44.8)	25 (39.1)
Concurrent allergic diseases, ever			
Asthma	1 (2.9)	4 (13.8)	5 (7.8)
Allergic rhinitis	10 (28.6)	9 (31.0)	19 (29.7)
Atopic dermatitis	21 (60)	15 (51.7)	36 (56.3)
Chronic urticaria	0	0	0
Past anaphylaxis	16 (45.7)	12 (41.4)	28 (43.8)
Angioedema	4 (11.4)	5 (17.2)	9 (14.1)
Drug allergy	1(2.9)	0	1 (1.6)
Food allergy (other than CN)[b]	32 (91.4)	21 (72.4)	53 (82.8)
Food allergy to other tree nuts[c]	22 (62.9)	15 (51.7)	37 (57.8)
Food allergy to peanuts[c]	6 (17.1)	3 (10.3)	9 (14.1)
Tree pollen sensitization	4 (11.4)	4 (13.8)	8 (12.5)
Exclusive breastfeeding	22 (62.9)	15 (51.7)	37 (57.8)
Family history of allergic diseases	29 (82.9)	20 (69.0)	49 (76.5)

Values are expressed as median (range) or number (%).
[a]P value 0.008 (Mann-Whitney).
[b]Most subjects had food allergies other than CN.
[c]Convincing history of clinical symptoms to other tree nuts and peanuts.

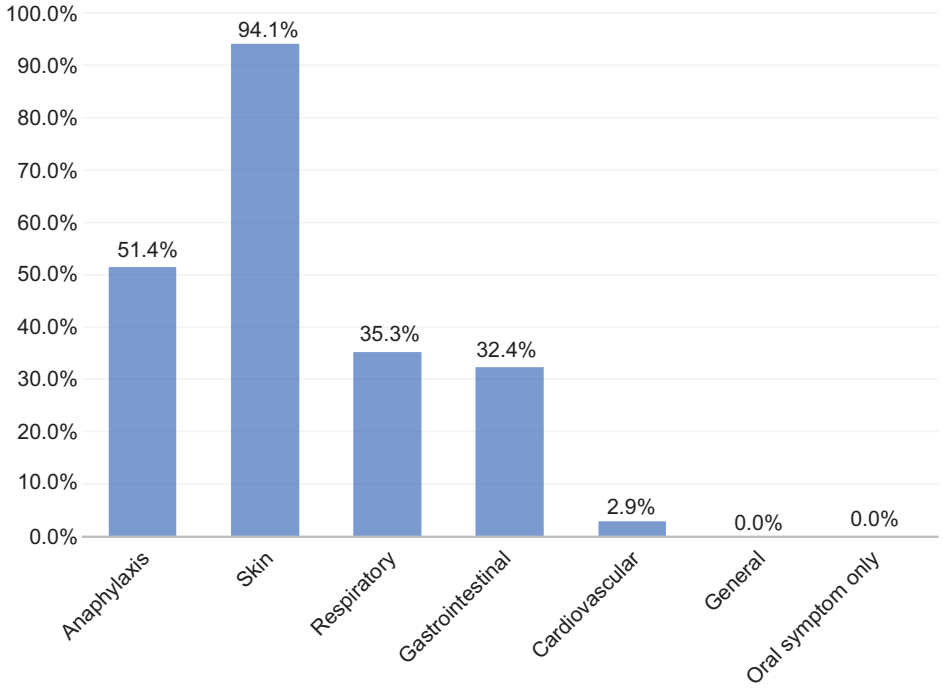


Figure 1 Clinical manifestations in CN-allergic group. Several subjects had more than one symptom. Patients with anaphylaxis were also counted in the respective categories of skin, respiratory, gastrointestinal, and/or cardiovascular symptoms according to their detailed symptom profiles.

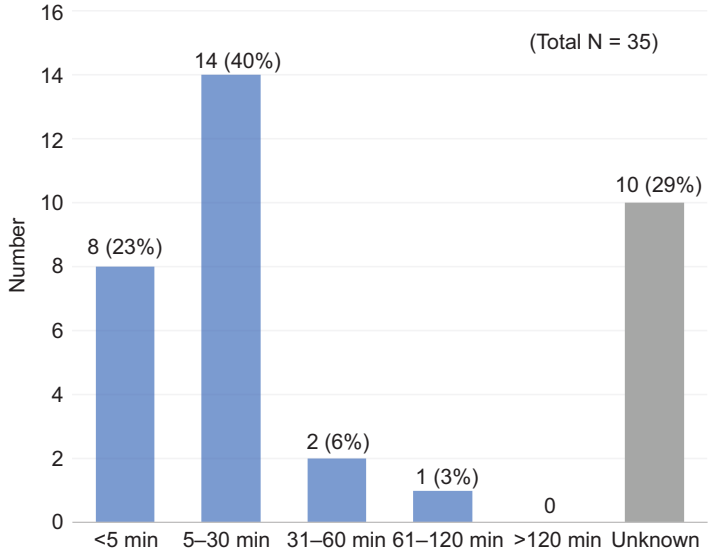


Figure 2 Time interval between CN exposure and symptom onset in CN-allergic group.

the allergic group from the tolerant group with a specificity of 100% was 0.88 kU_A/L (Figure 4).

A comparison between the anaphylactic and nonanaphylactic groups is summarized in Tables 3 and 4. There was no statistically significant difference in the median total IgE levels between the anaphylactic and nonanaphylactic groups (365 kU/L vs. 305 kU/L, $P = 0.338$). The median level of CN-sIgE was 17.35 kU_A/L (range 0.67–101.00 kU_A/L) in the anaphylaxis group, which was significantly higher ($P = 0.029$) than 4 kU_A/L for the nonanaphylaxis group (range 0.13–71.7 kU_A/L). The cutoff level of CN-sIgE for predicting anaphylaxis was 2.72 kU_A/L, with sensitivity of 88.89%, specificity of 47.06%, PPV of 23.5%, and negative predictive value of 93.4%. The amount of CN consumed ranged from less than 1–10 pieces with no significant difference ($P = 0.185$) between the anaphylactic and nonanaphylactic groups. The time interval from CN exposure to symptom

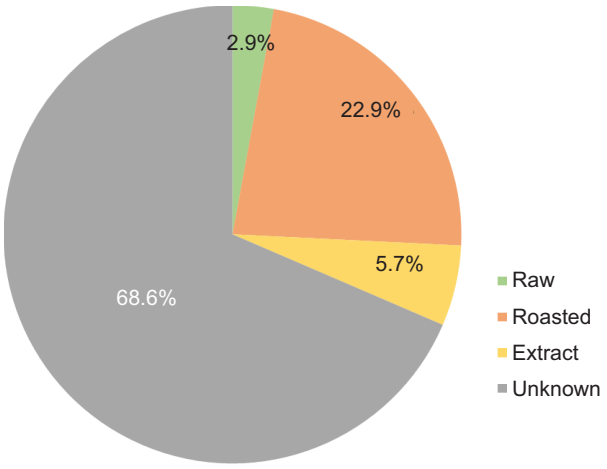
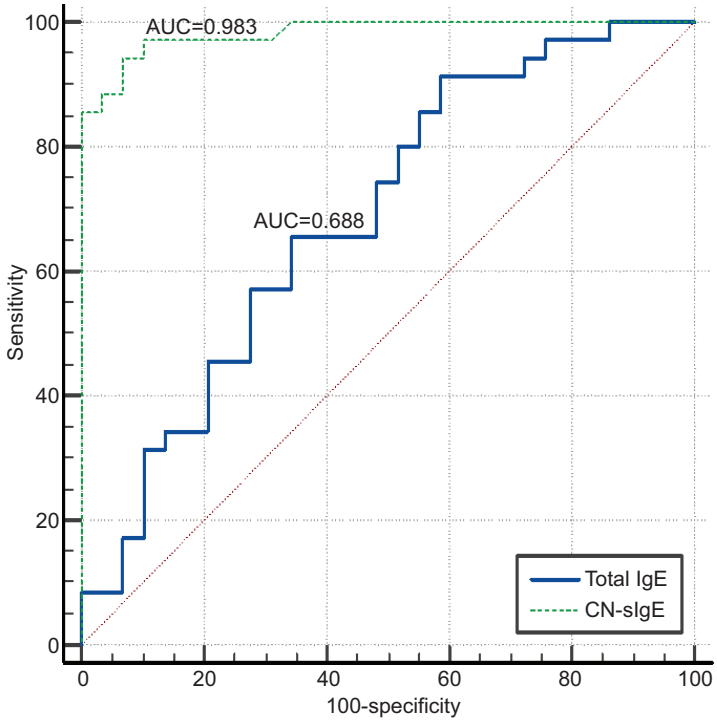


Figure 3 Types of CN ingested in CN-allergic group.

Table 2 Total IgE and CN-sIgE levels in the CN-allergic and tolerant groups.

	CN-allergic (n = 35)	CN-tolerant (n = 29)	P value
Total IgE, kU/L			
Median	310	178	0.010*
Minimum	51	1	
Maximum	2848	2024	
CN-sIgE, kU_A/L			
Median	5.5	0.06	< 0.001*
Minimum	0.13	< 0.05	
Maximum	> 100	0.88	

CN, cashew nut; CN-sIgE, cashew nut-specific immunoglobulin E.



Cut-off level of CN-sIgE(kU_A/L)	Sensitivity (%)	Specificity (%)
>0.1	100.00	65.52
>0.46	97.14	89.66
>0.55*	94.29	93.10
>0.78	88.57	96.55
>0.88	85.71	100.00

*Youden index (J) 0.8739

Figure 4 Receiver operating characteristic (ROC) curves representing the sensitivity and specificity of total IgE (blue) and CN-sIgE (green); the CN-allergic group versus the tolerant group.

onset was shorter in the anaphylactic group, although this difference was not statistically significant (P = 0.237).

Discussion

CNs belong to the Anacardiaceae family and are among the leading causes of tree nut allergies worldwide. CN allergy is a growing concern not only in Western countries but also in Korea as the consumption of CN increases. However, no studies have been reported in Korea. Hence, this study investigated the clinical characteristics and laboratory findings of Korean children with clinical CN allergy.

This study included 64 children with confirmed histories of CN exposure. Among them, 35 experienced immediate hypersensitivity reactions with a median age of 36 months (age range of the participants was 12-106 months), 65.7% of whom were male. The median age in this study was similar to that in a previous study, which showed that the first allergic reaction to CN occurred primarily in preschool children under 6 years of age.[24] The higher median age observed in the CN-tolerant group compared to the

CN-allergic group (63 vs. 36 months) may suggest that these patients followed a more conservative pattern when introducing new foods, possibly delaying CN exposure. However, this could not be clearly confirmed due to the retrospective nature of the study.

Recent research indicates that early introduction of common food allergens within the first 12 months can reduce the risk of developing food allergies. For instance, the early introduction of peanuts is recommended because it can lower the risk of developing peanut allergy by 81% at age 5 in the high-risk group[25]; however, the impact of the early introduction of tree nuts remains unclear. The HealthNut study, a large population-based longitudinal study conducted in Australia from 2007 to 2011 with 5,276 infants, revealed that none of the children who consumed CN by 12 months of age developed CN allergy at age 6; in contrast, 3.6% (95% CI, 2.9%–4.4%) of those who had not consumed CN within 12 months developed a CN allergy.[26] Additionally, the TreEAT study, a randomized controlled trial, is currently underway investigating the efficacy and safety of the early introduction of tree nuts in infants with IgE-mediated peanut allergy.[27] As our study was retrospective in design and all participants in both the CN-allergic and CN-tolerant groups were first exposed to CN after 12 months of age (range 12–152 months), it was not possible to assess the potential preventive effect of early CN introduction. Further prospective studies are warranted to explore this aspect.

Several studies have investigated the co-allergies between peanuts and CN. Maloney et al. found that 86% of patients with peanut allergies were sensitized to CN.[28] Additionally, Sicherer et al. reported that 20–60% of peanut-allergic patients exhibited clinical symptoms in response to CN.[6] A population-based study in Australia reported that 37% of children with peanut allergies also had a CN allergy.[10] In this study, 17.1% of the participants in the CN-allergic group reported having a clinical allergy to peanuts, which is notably higher than the 5.3% prevalence of peanut allergy found in a previously published study on immediate food allergies in Korean children.[4] Despite being a single-center study, the finding that a substantial number of Korean children with CN allergy also had concomitant peanut allergy is clinically significant.

Co-sensitization or cross-reactivity between CN and other tree nuts has been well documented in several studies.[10,29,30] This co-sensitization between tree nuts is associated with taxonomic relationships and structural similarities, although the exact mechanism remains unclear. A single-center retrospective study in the United States reported a co-allergy rate of 24% among tree nut allergies, while another study in Australia found that 47% of patients had a clinically defined co-allergy to tree nuts.[10,29] In our study, more than 60% of the CN-allergic group reported clinical co-allergies to other tree nuts, with the most common co-allergy being walnuts (48.6%), followed by almonds (14.3%), macadamias (11.4%), hazelnuts (8.6%), and pine nuts (5.7%); there was one case each of pecan and pistachio (2.9%). The higher rate of co-allergies to other tree nuts observed in this study compared to previous reports may be partly due to thorough history-taking by allergy specialists, although the data were based on medical records and may still reflect subjective reporting. While studies from the Western regions have reported high co-allergy rates of over 80% between CNs and pistachios—both belonging to the Anacardiaceae family—the clinical co-allergy rate to pistachios in this study was markedly lower at only 2.9%.[30] This discrepancy may be attributed to dietary patterns in Korea, where pistachio consumption is relatively uncommon, and most individuals with CN allergy reported never having consumed pistachios.

Clinical symptoms of CN allergy can range from mild cutaneous reactions and oral symptoms to severe anaphylaxis.[5,10,13] In our study, cutaneous symptoms were the most common, followed by respiratory and gastrointestinal symptoms, with 51.4% experiencing anaphylaxis. In a previous study examining OFCs, 80% of the participants who reacted to CN met the clinical criteria for anaphylaxis, highlighting its severity compared to other tree nuts, where the overall anaphylaxis rate was 19%.[31] The comparatively lower proportion of anaphylaxis observed in this study reflects differences in the study population and methodology, such as reliance on medical records, as well as variation in the amount and form of CNs ingested at the time of reaction—factors that can significantly influence the clinical presentation.

Table 3 Total IgE and CN-sIgE levels in the anaphylaxis and nonanaphylaxis groups.

	Anaphylaxis (n = 18)	Nonanaphylaxis (n = 17)	P value
Total IgE, kU/L			
Median	365	305	0.338
Minimum	60	51	
Maximum	2348	2848	
CN-sIgE, kU_A/L			
Median	17.35	4	0.029*
Minimum	0.67	0.13	
Maximum	>100	71.7	

CN-sIgE, cashew nut specific immunoglobulin E.

Table 4 Amounts of CN ingested and time interval between CN exposure and symptom onset in the anaphylaxis and nonanaphylaxis groups.

	Anaphylaxis	Nonanaphylaxis	P value
Amounts (number) (n = 21)	1.0 (0–3)	1.0 (0–10)	0.185
Time interval (minutes) (n = 25)	5.0 (0–60)	30.0 (0–120)	0.237

A recent study highlighted the organ-specific symptom pattern potentially associated with peanut and tree nut allergies, noting that peanut and CN allergies often present with more gastrointestinal symptoms compared to hazelnut and walnut allergies. In cases of CN allergy, gastrointestinal symptoms were the second most common, followed by cutaneous symptoms.[32] Notably, only one case of gastrointestinal symptom occurred without anaphylaxis in this study. Further large-scale studies are needed to better understand the organ-specific symptom patterns associated with CN allergies in Korea.

Our findings indicated that symptoms appeared within 0–120 minutes of exposure to CNs, with 63% of participants developing symptoms within the first 30 minutes. This is consistent with previous studies demonstrating that IgE-mediated food allergies typically manifest rapidly, often within minutes or up to 1–2 hours after ingestion, and provides one of the few detailed descriptions of symptom onset in CN allergy, a topic previously underreported in the literature.[33]

A recent German study identified the cumulative doses of allergens—such as peanut, hazelnut, walnut, and CN—that triggered positive OFC, with most symptoms occurring between 0.1 g and 4 g.[32] In this study, the amount of CN ingested at the onset of symptoms in the CN-allergic group varied from less than 1 to 10 nuts (approximately < 1.5-20 g), with no significant difference in the amount ingested between the anaphylactic and nonanaphylactic groups. To date, studies focusing on the relationship between the amount consumed and the occurrence of anaphylaxis in CN allergies remain limited; further studies are needed. Among the CN-allergic group in this study, excluding 24 individuals (68.6%) for whom the form of consumption was unknown, most experienced symptoms after ingesting processed forms of CNs such as roasted nuts or extract. Unlike egg or milk allergens, which tend to weaken in allergenicity with heating, CN allergens—including Ana o 3—are heat-stable, meaning that even extensively roasted CNs remain allergenic.[34]

The recently published European Academy of Allergy & Clinical Immunology (EAACI) guidelines recommend SPT or sIgE testing as the first-line diagnostic tools for suspected IgE-mediated food allergies.[35] In Korea, CNs have been infrequently consumed in the past; however, their intake has been rising in recent years, and reports of CN allergy appear to be increasing accordingly. This underscores the growing importance of accurate diagnosis and appropriate management strategies. Given the limitations of SPT—including the time required, poor cooperation in younger children, and the potential risk of systemic reactions—serum CN-sIgE testing is more commonly used in clinical practice in Korea. The optimal cutoff level for CN-sIgE identified in our study was 0.55 kU_A/L—lower than the 1.1 kU_A/L included in the EAACI guideline (sensitivity 94%, specificity 64%)—with a sensitivity of 94.29% and specificity of 93.10%, indicating a high diagnostic value for clinical CN allergy.[35] Ana o 3-sIgE is now widely recognized as a highly reliable diagnostic marker for CN allergy, with typical cutoff values ranging from 0.32 to 2.0 kU_A/L. However, as Ana o 3-sIgE testing is not commercially available in Korea, it was not included in this study. We found that the cutoff level of CN-sIgE predictive of anaphylaxis was 2.72 kUA/L, demonstrating a high sensitivity of 88.9% but relatively low specificity of 47.1% (data not shown). Given the likely variation in the quantity of CN ingested among individuals, further research is warranted to more precisely establish CN-sIgE thresholds associated with severe allergic reactions.

Tree nut allergy is generally considered unlikely to be naturally outgrown. A study by Fleischer et al. on the natural history of tree nut allergy reported that among 34 patients with a history of clinical CN allergy, 4 (11.8%) later successfully passed a double-blind, placebo-controlled food challenge.[36] In our study, most CN-allergic children maintained dietary avoidance, and prospective follow-up is needed to evaluate the development of tolerance over time.

The main limitation of this study is its retrospective design and the relatively small number of participants. It should also be noted that SPT and component-resolved diagnostics were not included, which may limit the depth of immunological characterization. However, clinical information was obtained through detailed history-taking by experienced pediatric allergy specialists, and efforts were made to minimize diagnostic errors by including only cases with an interval of no more than one year between documented symptoms and CN-sIgE measurement. Although the sample size was not large enough, this study provides a detailed clinical description of CN allergy in Asian children—an area where published data remain limited. Notably, it is the first study to propose an optimal CN-sIgE cutoff value for the diagnosis of clinical CN allergy in Korean children, demonstrating high sensitivity and specificity.

In conclusion, our findings reveal that over 50% of children with CN allergy experienced anaphylaxis, and co-allergy to other tree nuts is prevalent among CN-allergic children. The median CN-sIgE level was significantly higher in the allergic group than in the tolerant group, with an optimal cutoff level of 0.55 kU_A/L for the clinical diagnosis of CN allergy. Further studies involving larger cohorts would be beneficial, ideally including component-resolved diagnostics such as Ana o 3-sIgE, to improve diagnostic precision and advance our understanding of CN allergy in children.

Ethical Approval

This study was approved by the Institutional Review Board of Ajou University Hospital (AJOUIRB-DB-2023-441).

Protection of Human and Animal Subjects

The authors declare that no experiments were performed on humans or animals for this investigation.

Patient Data Protection

The authors declare that this study involved a retrospective review of anonymized medical records, for which the requirement for written informed consent was waived by the Institutional Review Board in accordance with applicable guidelines.

Right to Privacy and Informed Consent

The authors declare that no patient data appears in this article.

Authors Contributions

JK was responsible for conceptualization, data curation, formal analysis, writing of the original draft, and visualization. SY contributed to data curation, validation, and review & editing. SL was involved in conceptualization, methodology, and review & editing. KJ was in charge of conceptualization, methodology, formal analysis, validation, review & editing, and supervision.

Conflict of Interest

The authors have no potential conflicts of interest to declare.

Funding

None.

References

1. Warren CM, Jiang J, Gupta RS. Epidemiology and burden of food allergy. Curr Allergy Asthma Rep. 2020;20:6. https://doi.org/10.1007/s11882-020-0898-7
2. Jackson KD, Howie LD, Akinbami LJ. Trends in allergic conditions among children: United States, 1997-2011. NCHS Data Brief. 2013:1-8.
3. Ahn K, Kim J, Hahm MI, Lee SY, Kim WK, Chae Y, et al. Prevalence of immediate-type food allergy in Korean schoolchildren: A population-based study. Allergy Asthma Proc. 2012;33:481-7. https://doi.org/10.2500/aap.2012.33.3598
4. Kim M, Lee JY, Jeon HY, Yang HK, Lee KJ, Han Y, et al. Prevalence of immediate-type food allergy in Korean schoolchildren in 2015: A nationwide, population-based study. Allergy Asthma Immunol Res. 2017;9:410-6. https://doi.org/10.4168/aair.2017.9.5.410
5. McWilliam V, Koplin J, Lodge C, Tang M, Dharmage S, Allen K. The prevalence of tree nut allergy: A systematic Review. Curr Allergy Asthma Rep. 2015;15:54. https://doi.org/10.1007/s11882-015-0555-8
6. Sicherer SH, Munoz-Furlong A, Godbold JH, Sampson HA. US prevalence of self-reported peanut, tree nut, and sesame allergy: 11-year follow-up. J Allergy Clin Immunol. 2010;125:1322-6. https://doi.org/10.1016/j.jaci.2010.03.029
7. Motosue MS, Bellolio MF, Van Houten HK, Shah ND, Campbell RL. National trends in emergency department visits and hospitalizations for food-induced anaphylaxis in US children. Pediatr Allergy Immunol. 2018;29:538-44. https://doi.org/10.1111/pai.12908
8. Jeong K, Kim J, Ahn K, Lee SY, Min TK, Pyun BY, et al. Age-based causes and clinical characteristics of immediate-type food allergy in Korean children. Allergy Asthma Immunol Res. 2017;9:423-30. https://doi.org/10.4168/aair.2017.9.5.423
9. Jeong K, Ye YM, Kim SH, Kim KW, Kim JH, Kwon JW, et al. A multicenter anaphylaxis registry in Korea: Clinical characteristics and acute treatment details from infants to older adults. World Allergy Organ J. 2020;13:100449. https://doi.org/10.1016/j.waojou.2020.100449
10. McWilliam V, Peters R, Tang MLK, Dharmage S, Ponsonby AL, Gurrin L, et al. Patterns of tree nut sensitization and allergy in the first 6 years of life in a population-based cohort. J Allergy Clin Immunol. 2019;143:644-50 e5. https://doi.org/10.1016/j.jaci.2018.07.038
11. Sun X, Zhao J, Wang Q, Shi G, Yang J, Ming L. Prevalence of allergen sensitization among 15,534 patients with suspected allergic diseases in Henan province, China. Asian Pac J Allergy Immunol. 2019;37:57-64.
12. Sasaki M, Koplin JJ, Dharmage SC, Field MJ, Sawyer SM, McWilliam V, et al. Prevalence of clinic-defined food allergy in early adolescence: The schoolnuts study. J Allergy Clin Immunol. 2018;141:391-8 e4. https://doi.org/10.1016/j.jaci.2017.05.041
13. Ducharme L, Gabrielli S, Clarke AE, Morris J, Gravel J, Lim R, et al. Tree nut-induced anaphylaxis in Canadian emergency departments: Rate, clinical characteristics, and management. Ann Allergy Asthma Immunol. 2022;129:335-41. https://doi.org/10.1016/j.anai.2022.06.008
14. Lee SY, Ahn K, Kim J, Jang GC, Min TK, Yang HJ, et al. A multicenter retrospective case study of anaphylaxis triggers by age in Korean children. Allergy Asthma Immunol Res. 2016;8:535-40. https://doi.org/10.4168/aair.2016.8.6.535
15. Jeong K, Lee SY, Ahn K, Kim J, Lee HR, Suh DI, et al. A multicenter study on anaphylaxis caused by peanut, tree nuts, and seeds in children and adolescents. Allergy. 2017;72:507-10. https://doi.org/10.1111/all.13096
16. Dolle-Bierke S, Hofer V, Francuzik W, Naher AF, Bilo MB, Cichocka-Jarosz E, et al. Food-induced anaphylaxis: Data from the European Anaphylaxis Registry. J Allergy Clin Immunol Pract. 2023;11:2069-79 e7. https://doi.org/10.1016/j.jaip.2023.03.026
17. Robotham JM, Wang F, Seamon V, Teuber SS, Sathe SK, Sampson HA, et al. Ana o 3, an important cashew nut (Anacardium occidentale L.) allergen of the 2S albumin family. J Allergy Clin Immunol. 2005;115:1284-90. https://doi.org/10.1016/j.jaci.2005.02.028
18. Blazowski L, Majak P, Kurzawa R, Kuna P, Jerzynska J. Food allergy endotype with high risk of severe anaphylaxis in children—Monosensitization to cashew 2S albumin Ana o 3. Allergy. 2019;74:1945-55. https://doi.org/10.1111/all.13810
19. Brettig T, Dang T, McWilliam V, Peters RL, Koplin JJ, Perrett KP. The accuracy of diagnostic testing in determining tree nut allergy: A systematic review. J Allergy Clin Immunol Pract. 2021;9:2028-49 e2. https://doi.org/10.1016/j.jaip.2020.12.048
20. McWilliam V, Peters RL, Allen KJ, Dharmage SC, Ponsonby AL, Tang MLK, et al. Skin prick test predictive values for the outcome of cashew challenges in children. J Allergy Clin Immunol Pract. 2020;8:141-8 e2. https://doi.org/10.1016/j.jaip.2019.05.057
21. Elizur A, Appel MY, Nachshon L, Levy MB, Epstein-Rigbi N, Golobov K, et al. NUT co-reactivity - Acquiring knowledge for elimination recommendations (NUT CRACKER) study. Allergy. 2018;73:593-601. https://doi.org/10.1111/all.13353
22. Riggioni C, Ricci C, Moya B, Wong D, van Goor E, Bartha I, et al. Systematic review and meta-analyses on the accuracy of diagnostic tests for IgE-mediated food allergy. Allergy. 2024;79:324-52. https://doi.org/10.1111/all.15939
23. Sampson HA, Munoz-Furlong A, Campbell RL, Adkinson NF, Jr., Bock SA, Branum A, et al. Second symposium on the definition and management of anaphylaxis: Summary report—Second National Institute of Allergy and Infectious Disease/Food Allergy and Anaphylaxis Network symposium. Ann Emerg Med. 2006;47:373-80. https://doi.org/10.1016/j.annemergmed.2006.01.018

24. van der Valk JP, Dubois AE, Gerth van Wijk R, Wichers HJ, de Jong NW. Systematic review on cashew nut allergy. Allergy. 2014;69:692–8. https://doi.org/10.1111/all.12401
25. Du Toit G, Roberts G, Sayre PH, Bahnson HT, Radulovic S, Santos AF, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. N Engl J Med. 2015;372:803–13. https://doi.org/10.1056/NEJMoa1414850
26. Peters RL, Barret DY, Soriano VX, McWilliam V, Lowe AJ, Ponsonby AL, et al. No cashew allergy in infants introduced to cashew by age 1 year. J Allergy Clin Immunol. 2021;147:383–4. https://doi.org/10.1016/j.jaci.2020.07.003
27. McWilliam VL, Koplin JJ, Allen K, Robinson M, Smart J, Loke P, et al. TreEAT trial: Protocol for a randomized controlled trial investigating the efficacy and safety of early introduction of tree nuts for the prevention of tree nut allergy in infants with peanut allergy. Pediatr Allergy Immunol. 2023;34:e13930. https://doi.org/10.1111/pai.13930
28. Maloney JM, Rudengren M, Ahlstedt S, Bock SA, Sampson HA. The use of serum-specific IgE measurements for the diagnosis of peanut, tree nut, and seed allergy. J Allergy Clin Immunol. 2008;122:145–51. https://doi.org/10.1016/j.jaci.2008.04.014
29. Couch C, Franxman T, Greenhawt M. Characteristics of tree nut challenges in tree nut allergic and tree nut sensitized individuals. Ann Allergy Asthma Immunol. 2017;118:591–6 e3. https://doi.org/10.1016/j.anai.2017.02.010
30. Brough HA, Caubet JC, Mazon A, Haddad D, Bergmann MM, Wassenberg J, et al. Defining challenge-proven coexistent nut and sesame seed allergy: A prospective multicenter European study. J Allergy Clin Immunol. 2020;145:1231–9. https://doi.org/10.1016/j.jaci.2019.09.036
31. Abrams EM, Becker AB. Oral food challenge outcomes in a pediatric tertiary care center. Allergy Asthma Clin Immunol. 2017;13:43. https://doi.org/10.1186/s13223-017-0215-8
32. Dobbertin-Welsch J, Staudacher O, Yurek S, Trendelenburg V, Tschirner S, Ziegert M, et al. Organ-specific symptom patterns during oral food challenge in children with peanut and tree nut allergy. Pediatr Allergy Immunol. 2022;33:e13778. https://doi.org/10.1111/pai.13778
33. Boyce JA, Assa'ad A, Burks AW, Jones SM, Sampson HA, Wood RA, et al. Guidelines for the diagnosis and management of food allergy in the United States: Summary of the NIAID-sponsored expert panel report. J Allergy Clin Immunol. 2010;126:1105–18. https://doi.org/10.1016/j.jaci.2010.10.007
34. Venkatachalam M, Monaghan EK, Kshirsagar HH, Robotham JM, O'Donnell SE, Gerber MS, et al. Effects of processing on immunoreactivity of cashew nut (Anacardium occidentale L.) seed flour proteins. J Agric Food Chem. 2008;56:8998–9005. https://doi.org/10.1021/jf801199q
35. Santos AF, Riggioni C, Agache I, Akdis CA, Akdis M, Alvarez-Perea A, et al. EAACI guidelines on the diagnosis of IgE-mediated food allergy. Allergy. 2023;78:3057–76. https://doi.org/10.1111/all.15906
36. Fleischer DM, Conover-Walker MK, Matsui EC, Wood RA. The natural history of tree nut allergy. J Allergy Clin Immunol 2005 Nov;116(5):1087–93. https://doi.org/10.1016/j.jaci.2005.09.002