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Original Article

# Evaluation of the natural course and effective factors in egg allergy

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## ABSTRACT

**Objective:** Egg allergy (EA) is one of the most common food allergies in early childhood, often resolving spontaneously over time. However, the course of the disease varies among individuals, and several factors have been proposed to influence its persistence. This study aimed to evaluate the clinical and laboratory features of children diagnosed with EA, assess the frequency and timing of tolerance development, and identify risk factors associated with persistent allergy.

**Material and Methods:** A retrospective review was conducted on children diagnosed with EA and followed for at least six months between June 2010 and June 2016. Demographic characteristics, clinical manifestations, laboratory parameters, skin prick test (SPT) results, and coexisting atopic conditions were recorded. Patients were classified as either tolerant or persistent based on follow-up oral food challenge results and clinical history.

**Results:** Among the 173 patients diagnosed with egg allergy, 83.2% (n=144) developed tolerance, while 16.8% (n=29) had persistent allergy. Tolerance was observed in 61% (n=105) by age 3, 73% (n=126) by age 4, and 79% (n=136) by age 5. Patients with persistent EA had significantly higher egg-specific IgE levels at both admission (5.34 kU/L [0.42–3.74] vs. 1.27 kU/L [0.42–3.74], p=0.002) and final control (8.56 kU/L [1.18–40.4] vs. 0.96 kU/L [0.29–3.30], p<0.001), as well as larger wheal diameters in SPTs with raw egg at admission (9 mm [6–14] vs. 6 mm [5–9], p=0.008) compared to those who developed tolerance. The presence of nut allergy (persistent: 6/27, 22.2% vs. tolerant: 8/141, 5.7%; p=0.004) and legume allergy (persistent: 5/27, 18.5% vs. tolerant: 9/141, 6.4%; p=0.037) was also significantly associated with persistence.

**Conclusion:** Higher initial and sustained egg-specific IgE levels, larger SPT responses, and concomitant nut and legume allergies are potential risk factors for the persistence of EA. Additionally, the younger age of tolerance development observed in this cohort compared to previous studies may reflect population-specific differences in allergy phenotype.

**Keywords:** Egg allergy, IgE, food allergy

## INTRODUCTION

Worldwide prevalence of food allergy (FA) ranges from 1-10% percent and is estimated at approximately 4% in children and 1% in adults, with an increasing trend over the past two decades. Approximately 6% of children experience an allergic food reaction in the first three years of their lives. When the frequencies of FAs are examined, it has been shown that cow's milk (2.5%), egg (1.5%) and peanut (1%) allergies are the most frequently seen allergies (1–3). FA is a growing health concern in childhood, with varying prevalence rates reported worldwide. Among the most common food allergens, egg allergy (EA) is particularly prominent during early childhood. The prevalence of egg allergy in children has been reported to range from 1.6% to 10.1% in different studies (4–6). While egg allergy is more frequently observed in early childhood, its prevalence decreases in later years (7). Approximately half of children are expected to develop tolerance within the first 2 to 3 years of life, with up to 80% achieving tolerance by the time they reach school age (8). Natural resolution has been reported in up to



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80% of cases by the age of 3, and in 38–90% of children by the age of 5 to 6 years (4,6,9). Additionally, approximately 70% of children with EA can tolerate egg in baked forms (10–12). In a study conducted in the United States, it was reported that 64.2% of children with EA were able to tolerate baked egg (7). Baked egg allergy tends to resolve more rapidly, with 94% of affected children developing tolerance by 12 years of age (6). On the other hand, FA has been shown to negatively impact the quality of life of affected individuals, placing significant limitations on the social activities of both patients and their families (13–15). Previous studies have identified several factors associated with the resolution of EA, including age at first egg introduction, egg-specific IgE levels, skin prick test (SPT) results, and the presence of coexisting atopic diseases and other food allergies (7,8,16).

This study aimed to evaluate the clinical and laboratory characteristics of children diagnosed with EA and to assess the frequency and timing of tolerance development. Additionally, it sought to identify potential factors associated with the persistence of EA.

## MATERIALS and METHODS

The study was carried out in pediatric allergy and immunology clinic of Ankara Child Health and Disease Hematology Oncology Training and Research Hospital. Patients diagnosed with EA between June 2010 and June 2016 who had been followed for at least six months were included in the study. Data from patients' initial visits and final follow-up evaluations regarding sociodemographic characteristics, personal and family history, clinical complaints and symptoms, laboratory findings, SPT results, egg-specific IgE levels, peripheral eosinophil counts, and coexisting atopic diseases and FAs were recorded.

### Diagnosis of egg allergy

Diagnosis of IgE-mediated EA was made when patients met the following criteria; history of recurrent urticaria/angioedema, respiratory distress, abdominal pain/vomiting, or anaphylaxis emerging within the first 2 hours after egg consumption and positive SPT results and/or egg-specific IgE levels. In the diagnosis of mixed type (IgE and cell-mediated) EA, the SPT and/or egg-specific IgE results were evaluated in children with atopic findings such as skin itching and dryness, especially on the face and extensor areas in the history and/or detected during physical examination. In patients with egg atopy, the diagnosis was made according to the improvement in clinical findings after appropriate skin care and elimination of egg from patients' diet and maternal diet of the breastfed infants and recurrence of complaints after re-addition of egg to the diet. The elimination period in our study was applied for 4–8 weeks, after which reintroduction was performed. Reintroduction was carried out in a stepwise manner, beginning with extensively heated/baked egg and progressing to less cooked forms, as recommended in the guidelines (17).

The diagnosis of non-IgE-mediated EA was made by the history, physical examination findings, and the recurrence of the complaints when the symptoms were regressed with the elimination of egg from diet and recurred when the egg was added to the diet.

According to the results of OFC performed at the last controls of the patients, or the statements of the families about the development of a reaction after accidental or deliberately ingestion of egg at home, "development of tolerance" and "persistence of allergy" were decided. SPT and egg-specific IgE tests were repeated in children whose parents' consent could be obtained, and Oral Food Challenges (OFCs) were performed with egg and baked egg according to their results. Baked-egg OFC was performed in patients with IgE-mediated egg allergy who were sensitized to unheated egg, as an initial and safer step for tolerance assessment. Subsequently, raw or less-cooked egg OFC was conducted in those who tolerated baked egg, to further evaluate their level of tolerance, following a stepwise approach as recommended in the guidelines (18). Patients who could consume egg without any problem were considered to have developed tolerance. Those who could not consume egg in any way, or who could only consume egg in baked form, were recorded separately and both groups were classified as "persistent allergy" groups.

### Laboratory methods

Egg-specific IgE levels were measured by UniCAP (up to April 2015) and IMMULITE (after April 2015) techniques. Quantitative values were given in units of "kU/L". An egg-specific IgE level of ≥0.35 kU/L was considered indicative of sensitization to egg (8).

In the SPT, the commercial egg white antigen and/or raw egg was applied on the skin of the inner surfaces of both forearms or in younger patients applied on the back. SPT testing for house dust mites, animal epithelium, cockroach, mold fungi, and pollen was performed in patients who generally reported rhinitis symptoms or had a history of bronchiolitis. However, not all of these patients were classified as having allergic rhinitis.

Histamine (10mg/ml) was used as positive control. The test was read by waiting 15-20 minutes after the application. Diameters of induration of 3 millimeters and above were accepted positive (19).

### Oral food challenge

Oral food challenge tests were performed on the patients in order to diagnose EA and to evaluate tolerance status during follow-up. Test was not performed in patients with signs of active infection or a history of using antihistamines in the last week. Egg elimination test was performed by the mother for 2-4 weeks before OFC for sick or breastfed babies. Reactions that developed during the OFC or within 2 hours after termination of the test were accepted as early reactions (including urticaria, erythema, angioedema, cough, wheezing, and vomiting), and reactions observed within 72 hours after termination of the test as late reactions (such as eczematous skin lesions, abdominal pain, diarrhea, or exacerbations of atopic dermatitis [AD]).

Boiled egg or baked egg (in muffins) were fed in increasing doses at 15-minute intervals, depending on the type of OFC. For the egg, the patient was fed with a whole of one boiled egg (6 g of egg protein), and, a whole muffin (each muffin was prepared to contain 2 g of egg protein) for a baked egg (11).

### Statistical analysis

IBM Statistical Package for the Social Sciences, version 23.0 (SPSS Inc., Armonk, NY, IBM Corp., USA) was used for statistical analysis. Categorical variables were evaluated as numbers and percentages, while numerical measurements were evaluated as mean, standard deviation, median, interquartile range (IQR). The chi-square test was used to compare categorical variables between patient groups, and the Mann–Whitney U test was applied to compare numerical variables that did not show a normal distribution. $p<0.050$ indicated statistical significance.

## RESULTS

A total of 173 patients with EA were included in the study. The median age at the initial visit was 7 months (IQR= 5–12 months), with a median symptom onset at 4 months (IQR= 2–6 months) and a median age at diagnosis of 7 months (IQR= 5–11 months). The median duration of follow-up was 19 months (range: 6–80 months).

Of the patients, 123 (69.4%) were male. Comorbid atopic conditions were observed in 54 (31.2%) of patients for asthma, 7 (4%) for allergic rhinitis, and 16 (11% in 146 aeroallergen-tested patients) showed aeroallergen sensitivity. In addition to EA, 95 (54.9%) of patients had other food allergies, most commonly to cow's milk 82 (47.4%), followed by legumes 15 (8.7%), nuts 14 (8.1%), wheat 11 (6.4%), and fish 6 (3.5%). Demographic and clinical characteristics of the study population are detailed in Table I.

A family history of allergic disease was reported in 38% of the patients (49/129). Maternal smoking during pregnancy was noted in 10.3% (12/117) of the cohort.

The most frequent clinical manifestation of EA was skin involvement 168 (97.1%), particularly AD 140 (81%). Anaphylaxis was documented in 6 (3.5%) of patients, and gastrointestinal symptoms were present in 5 (2.9%).

At the time of admission, the median egg protein-specific IgE level was 1.53 kU/L (IQR= 0.43–4.85). SPT results showed a median wheal diameter of 5 mm (IQR= 4–7) with commercial egg antigen and 7 mm (IQR= 5–9) with raw egg. The median eosinophil percentage was 5.35 (IQR= 3.33–8.08), with a median absolute eosinophil count of 500/mm³ (IQR= 300–800). The median total IgE level was 66 U/L (IQR= 11.5–141.5).

After excluding five patients diagnosed with eosinophilic esophagitis and proctocolitis based on gastrointestinal symptoms, the remaining 168 patients were classified into two groups as IgE-mediated and mixed-type EA, and a comparison between these groups was performed (Table II). There were 35 patients with IgE-mediated and 133 patients with mixed-type EA. The median age at initial visit was significantly higher in the IgE-mediated group compared to the mixed-type group (12 months [IQR= 7–20] vs. 7 months [IQR= 5–11], $p<0.001$). Similarly, the median age at symptom onset (6 months [IQR= 4–9] vs. 4 months [IQR= 2–6], $p<0.001$) and the median age at diagnosis (10 months [IQR= 6–18] vs. 7 months [IQR= 5–10], $p=0.001$) were significantly higher in the IgE-mediated group.

In contrast, no statistically significant differences were found between the two groups regarding egg protein-specific IgE levels, SPT results (both with commercial egg antigen and raw egg), eosinophil percentages, absolute eosinophil counts, or total IgE levels at admission (all $p>0.050$).

Table III presents the number of patients followed in each age range and the frequencies of tolerance development within these age ranges. According to the Table III, 63 patients developed tolerance before the age of two years and were subsequently discharged from follow-up. Among the 110 patients followed up to two years of age, 42 (38.2%) developed tolerance between two and three years. Of the 61 patients followed up

**Table I: Patient characteristics**

| Variable | n | Values |
|---|---|---|
| Age at initial visit (month)* | 173 | 7 (5-12) |
| Age at symptom onset (month)* | 173 | 4 (2-6) |
| Age at diagnosis (month)* | 173 | 7 (5-11) |
| Duration of follow-up * | 173 | 19 (6-80) |
| Gender† | | |
| Male | 173 | 123 (69.4) |
| Other atopic conditions† | | |
| Asthma | 173 | 54 (31.2) |
| Allergic rhinitis | 173 | 7 (4) |
| Aeroallergen sensitivity | 146 | 16 (11) |
| Any food allergy besides egg† | 173 | 95 (54.9) |
| Cow's milk | 173 | 82 (47.4) |
| Legumes | 173 | 15 (8.7) |
| Nuts | 173 | 14 (8.1) |
| Wheat | 173 | 11 (6.4) |
| Fish | 173 | 6 (3.5) |
| Family history of an allergic disease† | 129 | 49 (38) |
| Pregnant smokers† | 117 | 12(10.3) |
| Symptoms of egg allergy† | | |
| Skin | 173 | 168 (97.1) |
| AD | 173 | 140 (81) |
| Anaphylaxis | 173 | 6 (3.5) |
| Gastrointestinal | 173 | 5 (2.9) |
| Laboratory at admission | | |
| Egg protein-specific IgE (kU/L)* | 173 | 1.53 (0.43-4.85) |
| SPT (commercial egg antigen) (mm)* | 173 | 5 (4-7) |
| SPT (egg) (mm)* | 173 | 7 (5-9) |
| Eosinophilia (%)* | 173 | 5.35 (3.33-8.08) |
| ANE (/mm³)* | 173 | 500 (300-800) |
| Total IgE (U/L)* | 173 | 66 (11.5-141.5) |

***:** *median (IQR),* **†:** *n(%),* ***ANE:*** Absolute number of eosinophils ***AD:*** *Atopic dermatitis,* ***IQR=*** *Interquartile range,* ***SPT:*** *Skin prick test*

**Table II: Comparison of patients with IgE-mediated and Mixed-Type (AD) Egg allergies**

| | IgE-mediated | | Mixed (AD) | | p† |
|---|---|---|---|---|---|
| | n | Values | n | Values | |
| Age at initial visit (month)* | 35 | 12 (7-20) | 35 | 7 (5-11) | <0.001 |
| Age at symptom onset (month) | 35 | 6 (4-9) | 35 | 4 (2-6) | <0.001 |
| Age at diagnosis (month) | 35 | 10 (6-18) | 35 | 7 (5-10) | 0.001 |
| Laboratory at admission | | | | | |
| Egg protein-specific IgE (kU/L)* | 31 | 2.5 (0.66-6.97) | 120 | 1.47 (0.42-4.71) | 0.266 |
| SPT (commercial egg antigen) (mm)* | 24 | 5 (5-7) | 106 | 5 (4-7) | 0.457 |
| SPT (egg) (mm)* | 24 | 7.5 (5-9) | 105 | 7 (5-9) | 0.451 |
| Eosinophilia (%)* | 30 | 4.75 (3.3-7.7) | 101 | 5.4 (3.3-8.2) | 0.543 |
| ANE (/mm$^3$)* | 30 | 550 (300-725 | 100 | 500 (300-800) | 0.733 |
| Total IgE (U/L)* | 24 | 70.1 (29.9-140) | 93 | 63.1 (10.4-141) | 0.463 |

***:** *median (IQR),* **†:** *Mann-Whitney U test,* ***AD:*** *Atopic dermatitis,* ***ANE:*** Absolute number of eosinophils ***IQR=*** *Interquartile range,* ***mo:*** *Months,* ***SPT:*** *Skin prick test*

**Table III: Frequency of tolerance development of patients according to reaction type and age range**

| Age range | Age of tolerance* | | IgE-mediated age of tolerance | | Mixed (AD) age of tolerance | |
|---|---|---|---|---|---|---|
| | n | Values | n | Values | n | Values |
| <2 years | 63 | 63(100%); 17(13-20) | 8 | 8 (100%); 19 (14-21) | 52 | 48 (92.3%); 17 (13-21) |
| 2 to 3 years | 110 | 42 (38.2%); 28 (25-33) | 27 | 10 (37%); 27 (25-29) | 81 | 32(39.5%); 29 (25-33) |
| 3 to 4 years | 61 | 21(34.4%); 40 (38-45) | 17 | 2 (11.8%); 47 | 42 | 19 (45.2%); 39 (38-45) |
| 4 to 5 years | 34 | 10 (29.4%); 51 (50-53) | 12 | 3 (25%); 50 | 20 | 7 (35%); 51 (48-52) |
| Total | 173 | 144 (83.2%); 25 (18-38) | 35 | 28 (80%); 27 (21-50) | 133 | 113 (85%); 24 (17-36) |

***:** *Months,* **†:** *n(%); median (IQR),* ***AD:*** *Atopic dermatitis*

to three years of age, 21 (34.4%) developed tolerance between three and four years. Among the 34 patients followed up to four years of age, 10 (29.4%) developed tolerance between four and five years. Finally, of the 15 patients followed up to five years of age, 8 developed tolerance after the age of five. The frequencies of tolerance development according to allergy type are also presented in the Table III. Figure 1 illustrates that while both groups showed an increase in tolerance rates with age, the mixed-type group consistently exhibited slightly higher tolerance rates compared to the IgE-mediated group across all age ranges.

Finally, when comparing the groups of patients who developed tolerance and those whose EA persisted, the findings presented in Table 4 were obtained. A total of 168 patients were compared based on the persistence or resolution of EA. No significant differences were found between the groups regarding sex distribution, breastfeeding duration, maternal smoking during pregnancy, family history of allergy, eczema, anaphylaxis, coexistence of asthma or allergic rhinitis, aeroallergen sensitivity, or coexisting food allergies (all p>0.050).

However, several factors were significantly associated with persistent EA. Patients with persistent allergy had a significantly higher prevalence of nut allergy (6 [22.2%] vs. 8 [5.7%], p= 0.004) and legume allergy (5 [18.5%] vs. 9 [6.4%], p=0.037) compared to those who developed tolerance.

In terms of laboratory findings at the time of admission, patients with persistent allergy exhibited significantly higher median egg protein-specific IgE levels (5.34 kU/L [IQR=0.42-3.74] vs. 1.27 kU/L [IQR=0.42-3.74], p=0.002) and larger wheal diameters in SPT performed with raw egg (9 mm [IQR=6-14] vs. 6 mm [IQR=5-9], p=0.008).

Similarly, at the final follow-up, egg-specific IgE levels remained significantly elevated in the persistent group compared to the tolerance group (8.56 kU/L [IQR=1.18-40.4] vs. 0.96 kU/L [IQR= 0.29 - 3.30], p<0.001), and the wheal sizes in SPT with raw egg continued to be larger (9 mm [IQR=5-12] vs. 5 mm [IQR=0-10], p=0.034).

These findings suggest that higher initial and persistent egg-specific IgE levels, larger SPT reactions, and the coexistence of nut and legume allergies are associated with a greater likelihood of persistent EA.

## DISCUSSION

The present study investigated the clinical course and determinants of tolerance development in children with egg allergy. Our findings demonstrated that the majority of patients developed tolerance during follow-up, while higher egg-specific IgE levels and larger skin prick test responses were associated with persistence. In addition, having concomitant nut and legume allergies was also found to be associated with the persistence of egg allergy. These results support previous reports while also providing new insights into the predictive factors of disease outcome.

**Table IV: Comparison of characteristics of patients with persistent allergies and those who developed tolerance**

| | Persistent allergy | | Tolerance | | p |
|---|---|---|---|---|---|
| | n | Values | n | Values | |
| Demographic factors | | | | | |
| Sex (male)* | 27 | 19 (70.4) | 141 | 99 (70.2) | 0.990† |
| Breastfeeding duration‡(month) | 27 | 20 (9-24) | 141 | 19 (10-24) | 0.960† |
| Pregnant smokers* | 13 | 1(7.7) | 100 | 11 (11) | 0.720† |
| Family history of food allergy* | 17 | 1 (5.9) | 106 | 2 (1.9) | 0.363† |
| Family history of any allergy* | 17 | 9 (52.9) | 107 | 39 (36.4) | 0.195† |
| Clinical factors* | | | | | |
| Eczema (AD) | 27 | 21 (77.8) | 141 | 118 (83.7) | 0.419† |
| Skin | 27 | 11 (40.7) | 141 | 34 (24.1) | 0.740† |
| Anaphylaxis | 27 | 3 (11.1) | 141 | 3 (2.1) | 0.053† |
| Coexistence of asthma | 27 | 5 (18.5) | 141 | 46 (32.6) | 0.144† |
| Coexistence of allergic rhinitis | 27 | 2 (7.4) | 141 | 5 (3.5) | 0.313† |
| Coexistence of aeroallergen sensitivity | 23 | 1 (4.3) | 119 | 15 (12.6) | 0.473† |
| Any food allergy besides egg | 27 | 19 (70.4) | 141 | 71 (50.4) | 0.056† |
| Allergies to | | | 141 | | |
| Cow's milk | 27 | 16 (59.3) | 141 | 61 (43.3) | 0.126† |
| Nuts | 27 | 6 (22.2) | 141 | 8 (5.7) | 0.004† |
| Wheat | 27 | 3 (11.1) | 141 | 8 (5.7) | 0.384† |
| Legumes | 27 | 5 (18.5) | 141 | 9 (6.4) | 0.037 |
| Fish | 27 | 1 (3.7) | 141 | 5 (3.5) | 1.000† |
| Laboratory parameters‡,(n) | | | | | |
| At admission | | | | | |
| Egg protein-specific IgE (kU/L) | 25 | 5.34 (0.42-3.74) | 126 | 1.27 (0.42-3.74) | 0.002‖ |
| SPT (commercial egg antigen) (mm) | 19 | 6 (5-9) | 111 | 5 (4-7) | 0.211‖ |
| SPT (raw egg) (mm) | 19 | 9 (6-14) | 110 | 6 (5-9) | 0.008‖ |
| Eosinophilia (%) | 19 | 7.2 (4.4-10.9) | 112 | 5.1 (3.3-7.6) | 0.076‖ |
| ANE (/mm$^3$) | 19 | 600 (400-1200) | 111 | 500 (300-800) | 0.189‖ |
| Total IgE (U/L) | 17 | 89 (53-368) | 97 | 57 (11-124) | 0.069‖ |
| Final control | | | | | |
| Egg-specific IgE (kU/L) | 22 | 8.56 (1.18-40.4) | 79 | 0.96 (0.29-3.30) | <0.001‖ |
| SPT test (commercial egg antigen)(mm) | 15 | 6 (4-7) | 81 | 4 (0-7) | 0.087‖ |
| SPT test (egg) (mm) | 15 | 9 (5-12) | 80 | 5 (0-10) | 0.034‖ |
| Eosinophilia (%) | 18 | 4.2 (2.7-6) | 54 | 3.7 (2.2-6.4) | 0.474‖ |
| ANE (/mm$^3$) | 18 | 400 (200-500) | 54 | 300 (200-500) | 0.793‖ |
| Total IgE (U/L) | 12 | 249 (107-828) | 33 | 169 (25-243) | 0.151‖ |

***:** *n(%),* **†:** *Chi-square,* **‡:** *median (IQR),* **‖:** *Mann-Whitney U test,* ***AD:*** *Atopic dermatitis,* ***ANE:*** Absolute number of eosinophils, ***IQR=*** *Interquartile range,* ***mo:*** *Months,* ***SPT:*** *Skin prick test*

A review of the literature on the prognosis of EA. reveals that similar estimates have been reported regarding the age of tolerance development. Several studies in the literature have reported comparable ages for the development of tolerance in patients with EA, supporting the general understanding of its natural resolution. Sicherer et al. (8) reported that 50% of patients developed tolerance by age 6, while Ohtani et al. (9) demonstrated age-specific tolerance rates of 30% of children by 3 years of age, 59% by 5 years of age, and 73% by 6 years of age. In our study, tolerance developed at a younger age compared with that reported in previous studies. One possible explanation for this difference may be the variation in median egg-specific IgE levels. In the study by Sicherer et al.(8), higher egg-specific IgE levels (37% had levels of 2 kU/L, 34% had levels between 2–10 kU/L, and 28% had levels ≥10 kU/L) were reported, whereas lower levels were observed in our study. This discrepancy may be attributed to the higher proportion of patients with mixed-type allergic reactions in our cohort.

It is known that elevated egg-specific IgE levels and SPT results at the time of diagnosis are associated with the persistence of EA (20–22). In the study by Peters et al. (23), higher egg-specific IgE levels at both diagnosis and follow-up, as well as elevated SPT wheal sizes, were associated with persistent allergy. A similar relationship was reported by Sicherer et al. (8). In the study conducted by Yilmaz et al. (16) demonstrated a significant association between egg-specific IgE levels and persistent allergy, but no such association was found with SPT results. In our study, higher egg-specific IgE levels at admission were observed in patients with persistent allergy compared to those who developed tolerance, indicating a potential role in predicting disease course. In addition, patients with higher SPT results with raw egg at the initial visit were found to have a higher frequency of persistent allergy. These findings are consistent with previous reports in the literature.

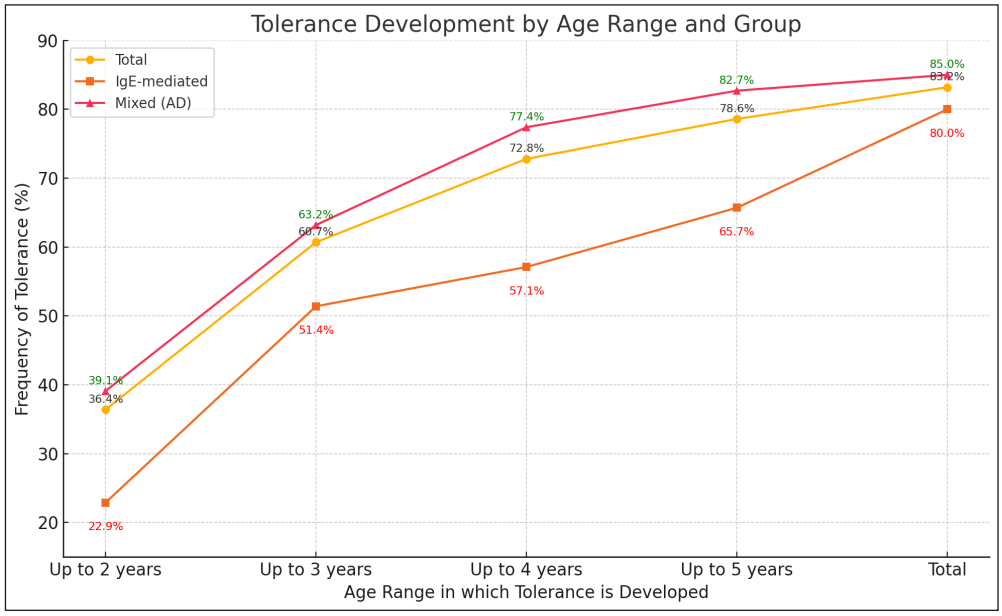


**Figure 1:** Tolerance development by age range and allergy type

In a population-based study, infants with eczema were found to be 5.8 times more likely to have hen's EA compared to healthy infants (24). There are few studies investigating the relationship between EA and AD. In a study by Kim et al. (25), moderate-to-severe AD was identified as a prognostic factor for persistent egg allergy and similar associations have been demonstrated in other studies (20,26). In another study which included 106 children with both AD and EA, 41% of patients developed tolerance by the age of 3, and 60% by the age of 5 and in infants with atopic dermatitis, and it was demonstrated that egg sensitization in infants with atopic dermatitis is frequently associated with a more prolonged or persistent course of egg allergy (27). In contrast to some studies suggesting that atopic dermatitis may be associated with a more persistent course of egg allergy, other reports have not confirmed this relationship. Peters et al. (4) reported that eczema was not a risk factor for persistent egg allergy. Similarly, Yilmaz et al.(16) found no association between the presence of skin symptoms and the development of tolerance. In our study, the presence of atopic dermatitis also had no significant impact on the development of tolerance.

Previous studies have demonstrated that a history of anaphylaxis is associated with a more persistent course of egg allergy (5,16). In our study, the number of patients with a history of anaphylaxis was limited; therefore, a definitive evaluation regarding its association with the persistence of egg allergy could not be made.

EA may occur in isolation or in combination with other FAs. Savage et al. (28) reported that 93% of 881 patients diagnosed with EA also had other concomitant FAs, and that these patients developed tolerance at a later age. In a study by Sicherer et al. (8) involving 213 patients with EA, 46.4% of patients who developed tolerance and 53.6% of those with persistent EA had additional FAs. Similarly, Peters et al. (23) found that 13% of patients who developed tolerance and 35% of those with persistent EA had multiple FAs, indicating a significantly higher rate of coexisting FAs in the persistent group. In our study, the presence of additional FAs was not significantly associated with tolerance development.

The major strengths of our study include the identification of key factors influencing the natural course of egg allergy through a comprehensive review of longitudinal patient data, and the ability to highlight critical considerations for clinical follow-up and management. However, the retrospective design, variability in follow-up durations, and inconsistency in the timing and frequency of control visits represent notable limitations that may affect the uniformity and generalizability of the results. In addition, the fact that the majority of the patients had atopic dermatitis and that the number of patients with IgE-mediated food allergy was very limited constitutes one of the major limitations of the study. Furthermore, the use of two different methods (UniCAP until April 2015 and IMMULITE after April 2015) for measuring egg-specific IgE levels during the study period can also be considered a limitation.

In conclusion, our study demonstrated that a higher egg-specific IgE level at the time of admission is a significant risk factor for the persistence of EA. These findings suggest that egg-specific IgE levels measured at diagnosis and during follow-up may serve as useful predictors of clinical prognosis. Additionally, when evaluating the age distribution of tolerance development, our results indicated an earlier resolution of EA compared to previous studies in the literature. This discrepancy may reflect differences in the natural course of EA across populations, potentially influenced by the type of allergic reaction.

## Ethics committee approval

This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Ankara Children's Hematology Oncology Education and Research Hospital (05.06.2017, reference number: 2017-051).

## Contribution of the authors

Study conception and design: HY, EDM; data collection: HY, HG, İKÇ, TG; analysis and interpretation of results: HY, EDM, BB, EC; draft manuscript preparation: HY, EDB, MT, CNK, İKÇ; Reviewing the article before submission scientifically besides spelling and grammar: İKÇ, MT, EDM. All authors reviewed the results and approved the final version of the article.

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## Conflict of interest

The authors declare that there is no conflict of interest.

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