ORIGINAL ARTICLE

An Anatomy of a Fear: Clinical Outcomes of Measles-Mumps-Rubella Vaccination in Children with Egg Allergy

Bir Korkunun Anatomisi: Yumurta Alerjisi Olan Çocuklarda Kızamık-Kabakulak-Kızamıkçık Aşılamasının Klinik Sonuçları

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DOI:10.38175/phnx.1646261

Cite as:
Alkaya H, Altaş U, Çevik S, Altaş ZM, Özkars MY. Experience with Measles-Mumps-Rubella Vaccination in Children with Egg Allergy. Phnx Med J. 2025;7(2):74-77.

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Received: February 24, 2025
Accepted: April 11, 2025
Online Published: July 17, 2025

ABSTRACT

Objective: *This study aimed to evaluate the frequency and clinical characteristics of allergic reactions following Measles-Mumps-Rubella (MMR) vaccination in children with egg allergy. Our aim in selecting the MMR vaccine was to better understand vaccine-related allergic reactions in children with egg allergy and to assess its reliability.*

Material and Method: *A retrospective analysis was conducted on 202 patients diagnosed with egg allergy who received the MMR vaccine in our clinic between 2023 and 2024. Demographic, clinical, and laboratory data were reviewed. Patients' age, sex, concomitant allergic diseases, total IgE, specific IgE for milk, egg, and nuts, skin prick tests, and post-vaccination reactions were recorded.*

Results: *The median age of the patients was 12 months (range: 7-84 months), and 57.4% were male. Sensitization to cow's milk was detected in 29.2% of the patients, while 6.9% had nut allergen sensitivity. The most common clinical conditions were urticaria (43.1%) and atopic dermatitis (36.6%). Following vaccination, only four patients (2%) developed localized rash, and none had a history of anaphylaxis.*

Conclusion: *No severe systemic reactions were observed following MMR vaccination in children with egg allergy. Our findings support current guidelines, suggesting that MMR vaccination can be safely administered under standard conditions in children with egg allergy. In our study, 29.2% of patients with egg allergy had cow's milk allergy, and 6.9% had nut allergy, suggesting that food allergies are often seen together in childhood. Additionally, it is emphasized that the India-made MMR vaccines used in Turkey contain milk proteins, which may increase the risk of anaphylaxis in individuals with milk and egg allergies, highlighting the need for careful evaluation of the vaccine prospectus before vaccination in these children.*

Keywords: *Egg allergy, Measles-Mumps-Rubella vaccine, Allergic reaction, Anaphylaxis, Cow's milk allergy*

ÖZET

Amaç: *Bu çalışma, kızamık-kabakulak-kızamıkçık (KKK) aşısı sonrası yumurta alerjisi olan çocuklarda alerjik reaksiyonların sıklığını ve klinik özelliklerini değerlendirmeyi amaçlamaktadır. KKK aşısını seçme amacımız, özellikle yumurta alerjisi olan çocuklarda aşıya bağlı alerjik reaksiyonların daha iyi anlaşılması ve güvenilirliğinin değerlendirilmesidir.*

Gereç ve Yöntem: *2023-2024 yılları arasında kliniğimizde KKK aşısı yapılan ve yumurta alerjisi tanısı almış 202 hasta üzerinde retrospektif bir analiz gerçekleştirildi. Hastaların demografik, klinik ve laboratuvar verileri incelendi. Yaş, cinsiyet, eşlik eden alerjik hastalıklar, total IgE, süt, yumurta ve kuruyemişlere özgü IgE düzeyleri, deri prick testleri ve aşılama sonrası reaksiyonlar kaydedildi.*

Bulgular: *Hastaların medyan yaşı 12 ay (dağılım: 7-84 ay) olup, %57,4'ü erkekti. Hastaların %29,2'sinde inek sütü duyarlılığı, %6,9'unda ise kuruyemiş alerjeni duyarlılığı saptandı. En sık görülen klinik durumlar ürtiker (%43,1) ve atopik dermatit (%36,6) idi. Aşılama sonrasında yalnızca dört hastada (%2) lokal döküntü gelişti ve hiçbir hastada anafilaksi öyküsü bulunmadı.*

Sonuç: *Yumurta alerjisi olan çocuklarda KKK aşısı sonrası ciddi sistemik reaksiyon gözlenmedi. Bulgularımız, mevcut kılavuzları desteklemekte olup, yumurta alerjisi olan çocuklarda KKK aşısının standart koşullar altında güvenle uygulanabileceğini göstermektedir. Çalışmamızda, yumurta alerjisi olan hastaların %29,2'sinde inek sütü alerjisi, %6,9'unda kuruyemiş alerjisi görülmesi çocukluk çağında gıda alerjilerinin sıklıkla bir arada görüldüğünü düşündürmektedir. Ayrıca Türkiye'de kullanılan Hindistan menşeili KKK aşılarının süt proteinleri içerdiği ve bu durumun süt ve yumurta alerjisi olan bireylerde anafilaksi riskini artırabileceği, bu çocuklar aşılanmadan önce aşı prospektüslerinin titizlikle değerlendirilmesi gerektiği vurgulanmaktadır.*

Anahtar Kelimeler: *Yumurta alerjisi, Kızamık-Kabakulak-Kızamıkçık aşısı, Alerjik reaksiyon, Anafilaksi, İnek sütü alerjisi*

INTRODUCTION

Food allergies can be classified as IgE-mediated (urticaria, angioedema, anaphylaxis), non-IgE-mediated (food protein-induced enterocolitis, food protein-induced proctocolitis), and mixed-type (eosinophilic esophagitis, atopic dermatitis). IgE-mediated reactions typically have an acute onset and primarily affect the skin, gastrointestinal system, and respiratory system. In contrast, non-IgE-mediated food allergies manifest

as vomiting, abdominal pain, bloody stools, failure to thrive, and diarrhea (1,2). Over the years, the prevalence of food allergies has increased worldwide, with rates ranging from 1% to 10% in children globally, and approximately 8% in Western societies (3,4).

Egg allergy is one of the most common food allergies in childhood and can significantly impact the quality of life from an early age. Its prevalence ranges between 0.5% and 2.5% (5). In adults, it tends to decrease, with an estimated prevalence of around 0.1% (6). Egg allergy can cause symptoms such as urticaria, atopic dermatitis, cough, wheezing, vomiting, diarrhea, and even anaphylaxis (7). While most reactions are IgE-mediated, non-IgE and mixed-type reactions can also occur. The diagnosis of egg allergy is based on clinical history, skin prick tests, specific IgE tests, and oral food challenge tests (8). The allergic reaction is mediated by specific IgE antibodies against ovalbumin (Gal d 2) and/or ovomucoid (Gal d 1) found in egg white (9).

Vaccines such as measles-mumps-rubella (MMR), influenza, and yellow fever, which are produced using egg embryos, may contain trace amounts of egg protein. The MMR vaccine is produced in fibroblast cultures derived from chicken embryos and contains minimal amounts of egg protein (0.5–1 nanogram of ovalbumin per 0.5 mL dose) (10,11). However, several studies suggest that allergic reactions associated with these vaccines are primarily due to gelatin and neomycin rather than egg protein (12,13). Additionally, some vaccine brands may include milk protein in their manufacturing process, which necessitates careful evaluation of vaccine content in children with milk allergies.

The most recent guidelines from the European Academy of Allergy and Clinical Immunology (EAACI) state that MMR vaccines can be safely administered under standard conditions to children with egg allergy (14). Nevertheless, there are case reports of anaphylaxis occurring after MMR vaccination in egg-allergic patients (15). A study by Altaş et al. suggested that children with severe egg allergy may be evaluated in pediatric allergy clinics, but this should not lead to delays in the MMR vaccination schedule (16).

Given the conflicting findings in the literature regarding MMR vaccination in egg-allergic children, we aimed to present our clinical experience in this area. Our study seeks to provide a detailed analysis of allergic reactions and clinical features following MMR vaccination in children with egg allergy, thereby contributing to the existing body of knowledge.

MATERIALS AND METHODS

The study included a total of 202 patients aged 0-7 years who were diagnosed with egg allergy and received the MMR vaccine at our clinic between January 1, 2023, and December 31, 2024. Patients with primary or secondary immunodeficiency, those vaccinated during an acute infection, those receiving systemic steroids or immunosuppressive treatment, and those whose families did not provide consent for participation were excluded.

The demographic, clinical, and laboratory data of the retrospectively analyzed patients were evaluated. The parameters examined included age, sex, age at diagnosis, comorbid allergic diseases, and reactions following the MMR vaccine (Priorix, GlaxoSmithKline, Belgium). Laboratory assessments included eosinophil count and percentage, total IgE levels, and sensitization to milk, egg, and nut allergens (specific IgE levels and skin prick test results). Eosinophil counts were obtained from complete blood count parameters, while total IgE levels were measured using a nephelometric method with a Siemens Healthcare Diagnostics Products device (Marburg, Germany). Specific IgE levels were analyzed using the ImmunoCAP system (UniCAP; Uppsala, Sweden), with values ≥0.35 kIU/L considered positive. In the skin prick test, results were deemed positive if there was no wheal formation or dermographism in the negative control, and an induration of ≥3 mm was present (17,18). Patients with positive skin prick test and/or specific IgE results underwent oral egg provocation testing, and those with a positive result were considered to have egg allergy.

Ethics

This study was approved by the Ethics Committee of the University of Health Sciences Ümraniye Training and Research Hospital (Date: 12.12.2024, decision no: 419). The study was conducted in accordance with the principles of the Helsinki Declaration.

Statistical Analysis

Statistical analyses were performed using SPSS for Windows 25.0. Normal distribution was assessed using visual (graphs) and analytical methods (Kolmogorov–Smirnov/Shapiro–Wilk tests). Descriptive results were presented as medians, minimum and maximum values, numbers (n), and percentages (%). In all analyses, a statistical significance level of $p < 0.05$ was considered.

Table 1: Patients' Age, Gender, and Additional Food Allergy Data

Age (months), median (min-max)		12.0 (7.0-84.0)
		n (%)
Gender	Female	86 (42.6)
	Male	116 (57.4)
Milk allergen sensitivity		59 (29.2)
Nut allergen sensitivity		14 (6.9)

RESULTS

A total of 202 patients with egg allergen sensitivity were evaluated. The median age was 12.0 months (7.0–84.0). Of the patients, 57.4% (n=116) were male. Sensitization to milk allergens was observed in 29.2% (n=59) of the patients, while

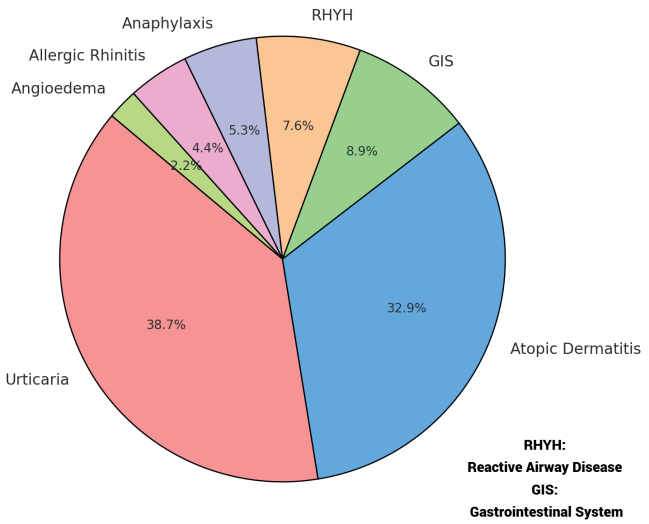

Figure 1: Distribution of Patients' Clinical Characteristics

Table 2: Patients' Laboratory Values

	Median	Minimum	Maximum
Absolute Eosinophil Count (cells/mm³)	380..0	0.0	3320.0
Eosinophil Percentage (%)	3.70	0.30	23.50
Total IgE (IU/mL)	58	0	5657
Specific IgE – Egg (kIU/L)	4.23	0.35	100.00
Specific IgE – Milk (kIU/L)	1.14	0.41	100.00
Skin Prick Test - Egg	5	3	11
Skin Prick Test - Milk	6	3	7

Table 3: Characteristics of Patients with Post-Vaccination Reactions

	Gender	Age (Month)	Reaction	History of Anaphylaxis	Eosinophil (cells/mm³)	Eosinophil (%)	Total IgE (IU/mL)	Egg spesific IgE (kIU/L)
1st Patient	Male	13.0	Local-Rash	No	260.0	2.80	2	0.85
2nd Patient	Female	12.0	Local-Rash	No	-	-	-	-
3rd Patient	Male	12.0	Local-Rash	No	390.0	4.20	87	0.81
4th Patient	Female	9.0	Local-Rash	No	650.0	7.70	151	0.40

6.9% (n=14) had nut allergen sensitivity (Table 1).

When assessing clinical conditions associated with egg allergy, 43.1% of patients had urticaria, and 36.6% had a history of atopic dermatitis. Angioedema was observed in five patients, and anaphylaxis occurred in twelve patients. Additionally, ten patients had concomitant allergic rhinitis (Figure 1).

The median absolute eosinophil count was 380.0 cells/mm³ (0–3320.0), and total IgE levels had a median of 58.0 IU/mL (0–5657.0). The median specific IgE level for egg was 4.23 kIU/L (0.35–100.0) (Table 2).

Following vaccination, reactions were observed in four patients, all of whom experienced localized rash. In two patients, the rash appeared 30 minutes after injection, in one patient after 15 minutes, and in another after 1 hour. None of the patients who developed post-vaccination reactions had a prior history of anaphylaxis (Table 3).

DISCUSSION

In Turkey, the national vaccination schedule recommends the administration of the Measles, Mumps, and Rubella (MMR) vaccine at 12 months of age. However, due to the presence of migrant children, this vaccine may also be administered at 9 months in certain cases. Some physicians exhibit hesitation in vaccinating children with egg allergy, leading to referrals to pediatric allergy centers for vaccine administration (19).

In our study, 202 patients with egg allergen sensitivity were evaluated. The median age was 12.0 months, and 57.4% (n=116) of the patients were male. Similarly, another study examined 130 patients and reported that 55.3% (n=72) were male, with a mean age of 13.7 months (20). The relatively high number of patients in our study enhances the reliability of statistical analyses. In both studies, the proportion of male patients was higher, aligning with literature findings that allergic diseases are more prevalent in male children. The fact that patients were vaccinated around 12 months of age indicates a high level of vaccine awareness in our clinic and appropriate guidance for families. This finding suggests adherence to the vaccination schedule in allergic children, without significant delays. In our clinic, families receive regular information to ensure timely vaccination at 12 months.

In our study, 29.2% (n=59) of the patients had concomitant cow's milk allergen sensitivity, while 6.9% (n=14) had nut allergen sensitivity. In the study by Keleş et al., 41.3% (n=33) of the patients had cow's milk allergy in addition to egg allergy, and 18.8% (n=15) had food allergies other than cow's milk. The most common concomitant allergies with egg allergy were milk, wheat, and nuts (19). Food allergies frequently coexist in childhood, and the immunological mechanisms in polyallergic individuals are believed to be more complex. Egg and milk proteins commonly cause allergies together due to their structural and immunological characteristics. The prevalence of cow's milk allergy was higher in the study by Keleş et al. (41.3%) compared to our study. This discrepancy may be attributed to variations in sample size, diagnostic methods, and regional differences in patient populations. The prevalence of allergens such as wheat and nuts is influenced by regional dietary habits and genetic predisposition. The frequency of food allergies varies across populations, which may account for differences in study results. Additionally, some series of measles and MMR vaccines used in Turkey may contain milk proteins, posing a risk of anaphylaxis in individuals allergic to cow's milk and egg. There is evidence suggesting that certain vaccines, such as the India-originated Tresivac, may cause severe reactions in patients with such allergies. Therefore, the composition and production conditions of each vaccine should be thoroughly examined, and package inserts should be carefully reviewed when vaccinating children with food allergies.

When evaluating comorbidities, 38.7% of our patients had urticaria, 32.9% had atopic dermatitis (AD), 7.6% had reversible airway disease, 8.9% had GIS, 4.4% had allergic rhinitis, and 5.3% had a history of anaphylaxis. The higher number of Reversible airway disease and GIS cases compared to anaphylaxis or rhinitis suggests a possible link to the patients' clinical profiles and the diversity of pathophysiological mechanisms in allergic reactions. In another study, it was reported that 79% (n=49) of egg-allergic patients had a history of atopic dermatitis, 12% (n=8) had urticaria, and 3.2% (n=2) had a history of anaphylaxis. These differences may be attributed to variability in patient populations, diagnostic criteria, and environmental factors.

However, to enhance the accuracy and generalizability of these results, further advanced studies with larger sample sizes and different populations are needed.

In our study, the median absolute eosinophil count was 380.0 cells/mm³ (0-3320.0), total IgE was 58.0 IU/mL (0-5657.0), and egg white-specific IgE median was 4.23 kIU/L (0.35-100.0). In Sayar's study, the mean egg white-specific IgE was 3.18 ± 6.3 kIU/L, while the mean total IgE and eosinophil count were 54.3 ± 78.1 IU/mL and 370.6 ± 218 cells/mm³, respectively (22). The eosinophil count, total IgE, and egg white-specific IgE levels observed in our study are comparable to those reported by Sayar et al. However, our study reported a higher median egg white-specific IgE level (4.23 kU/L). This difference may be due to variations in the severity of allergy, age distribution of patient groups, and methodological differences between studies. Larger sample-sized studies are essential for a detailed evaluation of the clinical correlations of these parameters.

Among the 202 patients we followed, four experienced post-vaccination reactions, all of which were localized rashes. In two patients, the rash appeared 30 minutes after injection, in one patient after 15 minutes, and in another after 1 hour. None of the patients who developed post-vaccination reactions had a prior history of anaphylaxis. In the study by Özdemir et al., macular rash was observed in only 1 (2.9%) of 36 vaccine doses administered to 18 patients (23). Similarly, in the study by Altaş et al., urticaria developed in only 1 out of 179 vaccinated patients, with no other adverse reactions observed (16). The fact that only four patients (1.98%) in our study developed localized rashes post-MMR vaccination, consistent with other studies, supports the overall safety of the vaccine in children with egg allergy. Additionally, the mild nature of the reactions and the absence of anaphylaxis in any patient indicate that the vaccine does not cause severe allergic side effects.

Our findings align with existing literature and confirm that the MMR vaccine is largely safe for patients with egg allergy. However, some MMR vaccines have been reported to contain trace amounts of milk protein. Although larger sample-sized and long-term follow-up studies are needed, the current data suggest that vaccination in allergic children is generally safe. Nonetheless, the composition of vaccines should be carefully reviewed, particularly in patients with milk allergy, and clinical observation should be recommended for potential reactions.

Limitations and Strengths: As a retrospective study, data deficiencies may be present. Since the evaluation of allergic reactions is based on patient records, mild reactions may have been underreported. The generalizability of the results is limited as the study was conducted at a single center. Additionally, due to the lack of long-term follow-up after vaccination, delayed reactions could not be assessed. Among the strengths of the study is the relatively large patient population.

Conflict of Interest: No conflict of interest was declared by the authors

Ethics: The Ethics Committee of the University of Health Sciences, Ümraniye Training and Research Hospital, approved the study (date: 12.12.2024, decision no: 419).

Funding: There is no financial support of any person or institution in this research.

Approval of final manuscript: All authors.

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