

# Food Allergen Sensitisation Patterns in Omani Patients with Allergic Manifestations

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## أنماط التحسس للمواد الغذائية لدى مرضى عمانيين لديهم مظاهر الحساسية

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**ABSTRACT: Objectives:** This study aimed to evaluate the relationship between food allergen sensitisation patterns and allergic manifestations in Omani patients and highlight the importance of specific immunoglobulin E (IgE) testing. **Methods:** This retrospective study included all patients referred due to allergic manifestations to the Sultan Qaboos University Hospital (SQUH), Muscat, Oman, from November 2012 to November 2016. Specific IgE blood testing was performed to determine sensitisation to common foods known to cause allergic reactions. **Results:** A total of 164 patients were referred to SQUH over the study period, with 35.4% presenting with one allergic manifestation, 48.8% with 2–3 and 15.9% presenting with more than three manifestations. There was a family history of allergies in 70.7% of patients. Eosinophil counts and total and specific IgE levels were elevated in 18.9%, 54.9% and 73.2% of patients, respectively. Patients demonstrated sensitisation to cow milk (47.6%), wheat (41.5%), chicken eggs (34.8%), mixed tree nuts (34.1%), lentils (33.5%), peanuts (32.9%), soy (32.3%), shrimp (23.2%) and fish (15.2%). Overall, 19.5% were sensitised to a single allergen, 14% were sensitised to 2–3 and 39.6% were sensitised to more than three allergens. Almost one-third (29.3%) of patients suffered from food-induced anaphylaxis, of which 85.4% were prescribed self-injectable adrenaline. **Conclusion:** To the best of the authors' knowledge, this study is the first to describe food allergen sensitisation patterns among Omani patients with allergic manifestations. In conjunction with clinical symptoms, the correct interpretation of specific IgE levels is important to diagnose food allergies and make safe decisions about reintroducing foods.

**Keywords:** Hypersensitivity; Food Allergies; Anaphylaxis; Urticaria; Atopic Dermatitis; Asthma; Immunoglobulin E; Oman.

**المخلص:** الهدف: تهدف هذه الدراسة إلى تقييم العلاقة بين أنماط التحسس للمواد الغذائية وظهور أعراض الحساسية لدى مرضى عمانيين وإبراز أهمية اختبار الغلوبولين المناعي E. الطريقة: شملت هذه الدراسة الاستيعابية جميع المرضى المحولين بسبب مظاهر الحساسية لمستشفى جامعة السلطان قابوس، مسقط، عُمان، من نوفمبر 2012 إلى نوفمبر 2016. تم إجراء اختبارات الدم المحددة للغلوبولين المناعي E لتحديد حساسية الأطعمة الشائعة والمعروفة بالتسبب في الحساسية. النتائج: تم إحالة ما مجموعه 164 مريضاً إلى مستشفى جامعة السلطان قابوس خلال فترة الدراسة، مع 35.4% لديهم ظهور واحد من مظاهر الحساسية، 48.8% مع 2–3 و 15.9% مع أكثر من ثلاثة مظاهر. كان هناك تاريخ عائلي من الحساسية في 70.7% من المرضى. كان معدل التعداد اليوزيني ومجموع الغلوبولين المناعي الكلي مرتفع عند 18.9%، 54.9% و 73.2% من المرضى على التوالي. أظهر المرضى التحسس لحليب البقر (47.6%)، والقمح (41.5%)، وبيض الدجاج (34.8%)، وخليط جوز الشجر (34.1%)، والعدس (33.5%)، والفول السوداني (32.9%)، وفول الصويا (32.3%)، والروبيان (23.2%) و الأسماك (15.2%). بشكل عام، كان هناك 19.5% مصابين بحساسية لمسبب واحد للحساسية، 14% متحسسين إلى 2–3 و 39.6% متحسسين لثلاثة مسببات للحساسية. ما يقرب من ثلث (29.3%) من المرضى يعانون من التأق بسبب الغذاء، بحيث تم وصف الأدرينالين القابل للحقن الذاتي لمجموعة 85.4% من المرضى. الخلاصة: حسب أفضل معرفة للباحثين، فإن هذه الدراسة هي الأولى التي تصف أنماط التحسس للمواد الغذائية بين المرضى العمانيين الذين لديهم مظاهر الحساسية. بالاقتران مع الأعراض السريرية، فإن التفسير الصحيح للمستويات المحددة للغلوبولين المناعي E مهم لتشخيص الحساسية الغذائية واتخاذ قرارات آمنة بشأن إعادة تقديم الأطعمة.

الكلمات المفتاحية: فرط الحساسية؛ حساسية الطعام؛ تأق؛ الشرى؛ التهاب الجلد التأتبي؛ الربو؛ الغلوبولين المناعي E؛ عمان.

### ADVANCES IN KNOWLEDGE

- The current study provides baseline information on food allergen sensitisation patterns and their relationship with different allergic manifestations among Omani patients.

### APPLICATION TO PATIENT CARE

- The current study highlights the importance of specific immunoglobulin E testing as an integral part of food allergy evaluations, in conjunction with clinical symptoms.

- These findings may help treating physicians in the management of Omani patients with allergies in order to reduce the risk of anaphylaxis.

**A**LLERGIC DISEASES CONSTITUTE A GROUP OF hypersensitivity disorders resulting in clinical symptoms involving different organs, such as the skin (i.e. *urticaria* and angioedema), respiratory system (i.e. coughing, wheezing and breathing difficulties), gastrointestinal system (i.e. vomiting, diarrhoea and abdominal pain) and cardiovascular system (i.e. flushing, tachycardia and syncope).<sup>1</sup> The most severe form of allergic reaction is anaphylaxis, which can be life-threatening.<sup>2</sup> The underlying mechanism of immediate or type I hypersensitivity is primarily due to the formation of specific immunoglobulin E (IgE) molecules against a particular allergen, usually a peptide or protein. Upon subsequent exposure, the crosslinking of IgE receptors on mast cells triggers the activation and release of mediators responsible for the symptoms, primarily histamine, leukotrienes, prostaglandins and tryptase.<sup>3,4</sup>

Food is a common cause of allergic symptoms, although the exact prevalence of food allergies varies in different countries due to differences in dietary habits. Generally, studies in developed countries report food allergy rates of 8% and 4% among children and adults, respectively.<sup>5,6</sup> Common trigger foods include cow milk, eggs, soy, wheat, fish, seafood, peanuts and tree nuts among children and fish, seafood, peanuts and tree nuts among adults.<sup>7,8</sup> For most patients, the diagnosis is made based on clinical symptoms; however, an *in vivo* skin prick test may be necessary. More recently, diagnoses have been achieved by measuring *in vitro* levels of IgE-specific antibodies in the blood *sera*.<sup>4,9</sup>

Both *in vivo*- and *in vitro*-specific IgE testing are very sensitive, with high false-positive rates; however, both forms of testing have an excellent negative predictive value, which helps in excluding allergies, especially in doubtful cases.<sup>9</sup> Parents or physicians often suspect food after an allergic manifestation and patients are advised to avoid foods that are considered allergenic prior to a proper evaluation by a specialist. Double-blind placebo-controlled food challenges are the gold-standard diagnostic tool for food allergies and are usually used in research centres; however, such testing is time-consuming and often requires special precautions.<sup>10,11</sup>

To the best of the authors' knowledge, local food allergen sensitisation patterns have not been previously studied in Oman. As such, this study aimed to evaluate the relationship between food allergen sensitisation patterns and allergic manifestations in Omani patients. In addition, the importance of specific IgE testing is highlighted.

## Methods

This retrospective study included all patients referred to the allergy clinic of the Sultan Qaboos University

Hospital (SQUH), Muscat, Oman, between November 2012 and November 2016. For each patient, a routine history was taken and a physical examination was conducted. A diagnosis of an allergic manifestation was made based on clinical symptoms of anaphylaxis, acute or chronic *urticaria*/angioedema, eczema/dermatitis, angioedema without *urticaria*, asthma, rhinitis or vomiting/diarrhoea.

As part of their diagnostic work-up, patients underwent blood investigations to determine their eosinophil count and total and specific IgE levels for common food triggers (i.e. cow milk, chicken eggs, fish, soy, wheat, shrimp, peanuts, lentils and mixed tree nuts). Total and specific IgE levels were measured using the ImmunoCAP® Phadia® 100 immunoassay analyser (Thermo Fisher Scientific, Waltham, Massachusetts, USA), as per the manufacturer's instructions. Assays were calibrated to the 75/502 IgE standard of the World Health Organization.<sup>12</sup> Reference cut-off values were established at <165 and <0.35 kIU/L for normal total and specific IgE levels, respectively. Eosinophil counts of  $>0.8 \times 10^9/L$  were considered raised. The coefficient of variation between runs was <10%.

Allergic symptoms were correlated with any obvious food triggers based on information received from the patients or their parents/caregivers. In addition, the patients were questioned regarding the consumption of other common allergenic food triggers. Other information, such as demographic characteristics, a family history of allergies and age at the onset of symptoms, was retrieved from the patients' electronic medical records. Patients with allergic manifestations who had ingested common food triggers and reported no symptoms or signs of sensitisation on exposure to those foods were not tested and were excluded from the study.

All patients were given medical advice based on available clinical information at post-investigation follow-up visits. Symptomatic treatment was provided in cases of dermatitis, asthma, rhinitis or chronic *urticaria*. In cases of anaphylaxis, patients were prescribed self-injectable adrenaline and trained on its use.<sup>13,14</sup>

Analysis of the data was performed using the Statistical Package for the Social Sciences (SPSS), Version 20.0 (IBM Corp., Armonk, New York, USA). Frequencies and percentages were calculated using simple functions. Statistical differences were measured using Pearson's Chi-squared test. Differences were considered significant at  $P < 0.05$ .

This study was approved by the Medical Research & Ethics Committee of the College of Medicine & Health Sciences, Sultan Qaboos University (MREC #1648).

**Table 1:** Frequency of raised eosinophil counts and total immunoglobulin E levels and sensitisation to common food triggers among Omani patients according to allergic manifestation (N = 164)

Sensitivity	Allergic manifestation, n (%)							
	Eczema/ dermatitis (n = 108)	Acute <i>urticaria</i> / angioedema (n = 96)	Anaphylaxis (n = 48)	Asthma (n = 41)	Vomiting/ diarrhoea (n = 31)	Rhinitis (n = 20)	Chronic <i>urticaria</i> / angioedema (n = 6)	Angioedema without <i>urticaria</i> (n = 3)
Raised EC	25 (23.1)	18 (18.8)*	12 (25)	10 (24.4)	6 (19.4)	3 (15)	1 (16.7)	0 (0)*
Raised total IgE level	62 (57.4)	60 (62.5)*	38 (79.2)*	30 (73.2)*	13 (41.9)	18 (90)*	4 (66.7)	0 (0)*
Cow milk	53 (49.1)	50 (52.1)	23 (47.9)	15 (36.6)	19 (61.3)	5 (25)	2 (33.3)	2 (66.7)
Chicken eggs	46 (42.6)*	39 (40.6)	21 (43.8)	16 (39)	9 (29)	5 (25)	1 (16.7)	1 (33.3)
Fish	20 (18.5)	17 (17.7)	15 (31.3)*	9 (22)	4 (12.9)	3 (15)	2 (33.3)	0 (0)
Lentils	44 (40.7)*	36 (37.5)	23 (47.9)*	20 (48.8)*	8 (25.8)	10 (50)*	2 (33.3)	1 (33.3)
Peanuts	41 (38)*	38 (39.6)	26 (54.2)*	17 (41.5)	9 (29)	7 (35)	2 (33.3)	1 (33.3)
Shrimp	27 (25)	25 (26)	19 (39.6)*	16 (39)*	5 (16.1)	10 (50)*	2 (33.3)	0 (0)
Soy	40 (37)*	36 (37.5)	25 (52.1)*	21 (51.2)*	9 (29)	9 (45)*	2 (33.3)	1 (33.3)
Wheat	53 (49.1)*	44 (45.8)	32 (66.7)*	25 (61)*	11 (35.5)	9 (45)	2 (33.3)	1 (33.3)
Mixed tree nuts	44 (40.7)*	41 (42.7)*	26 (54.2)*	19 (46.3)	12 (38.7)	8 (40)	0 (0)	0 (0)*

EC = eosinophil count; IgE = immunoglobulin E. \*Significant at  $P < 0.05$  according to a Pearson's Chi-squared test.

## Results

A total of 164 new patients were referred to SQUH during the study period because of suspected food allergies. Of these, 53 (32.3%) were female and 111 (67.7%) were male. At referral, 92.5% of patients were <18 years old, with a mean age at presentation of 5.8 years old (range: one month–53 years). The mean age at onset of symptoms was 3.3 years old (range: one week–48 years). The mean interval between onset of symptoms and diagnosis was 30.5 months. Allergies presented as a single manifestation in 58 patients (35.4%), while 2–3 manifestations were present in 80 patients (48.8%) and more than three manifestations occurred in 26 patients (15.9%). There was a family history of allergies in 116 patients (70.7%).

Allergies most commonly manifested as eczema/dermatitis (65.9%) and acute *urticaria*/angioedema (58.5%), followed by anaphylaxis (29.3%), asthma (25%), vomiting/diarrhoea (18.9%), rhinitis (12.2%), chronic *urticaria*/angioedema (3.7%) and angioedema without *urticaria* (1.8%). In total, 48 (29.3%) patients received a diagnosis of food-induced anaphylaxis. Of these, seven (14.6%) had normal levels of total IgE but positive specific IgE levels and one (2.1%) had normal levels of both total and specific IgE. Most patients with anaphylaxis (85.4%) were prescribed self-injectable adrenaline.

Eosinophil counts ranged from 0– $8.3 \times 10^9/L$  with a mean of  $0.6 \times 10^9/L$ . In total, 18.9% of patients had raised eosinophil counts. Total IgE levels were elevated in 90 patients (54.9%). The mean total IgE level was

1,567.9 kIU/L, with a maximum level of 34,522.4 kIU/L. Specific IgE levels were positive in 120 patients (73.2%), occurring in response to cow milk in 78 patients (47.6%; mean = 4.8 kIU/L), wheat in 68 patients (41.5%; mean = 5.1 kIU/L), chicken eggs in 57 patients (34.8%; mean = 4.4 kIU/L), mixed tree nuts in 56 patients (34.1%), lentils in 55 patients (33.5%; mean = 6.4 kIU/L), peanuts in 54 patients (32.9%; mean = 3.7 kIU/L), soy in 53 patients (32.3%; mean = 2.5 kIU/L), shrimp in 38 patients (23.2%; mean = 4.1 kIU/L) and fish in 25 patients (15.2%; mean = 0.6 kIU/L).

Table 1 illustrates the frequency of sensitisation to common food triggers according to allergic manifestation. Normal total IgE levels were observed in 67 patients (40.9%), of which 35 (52.2%) had positive specific IgE levels. Overall, 21.3% of patients had positive specific IgE levels and normal total IgE levels. Sensitisation to a single allergen was present in 19.5% of patients, sensitisation to 2–3 allergens in 14% and sensitisation to more than three allergens in 39.6%. The remaining 26.8% were not sensitive to any allergens. Figure 1 presents monosensitisation and polysensitisation rates according to allergic manifestation.

## Discussion

Food allergies represent a management challenge for the affected patient, their parents and/or caregivers and the healthcare provider. However, a thorough patient history, physical examination and diagnostic testing can

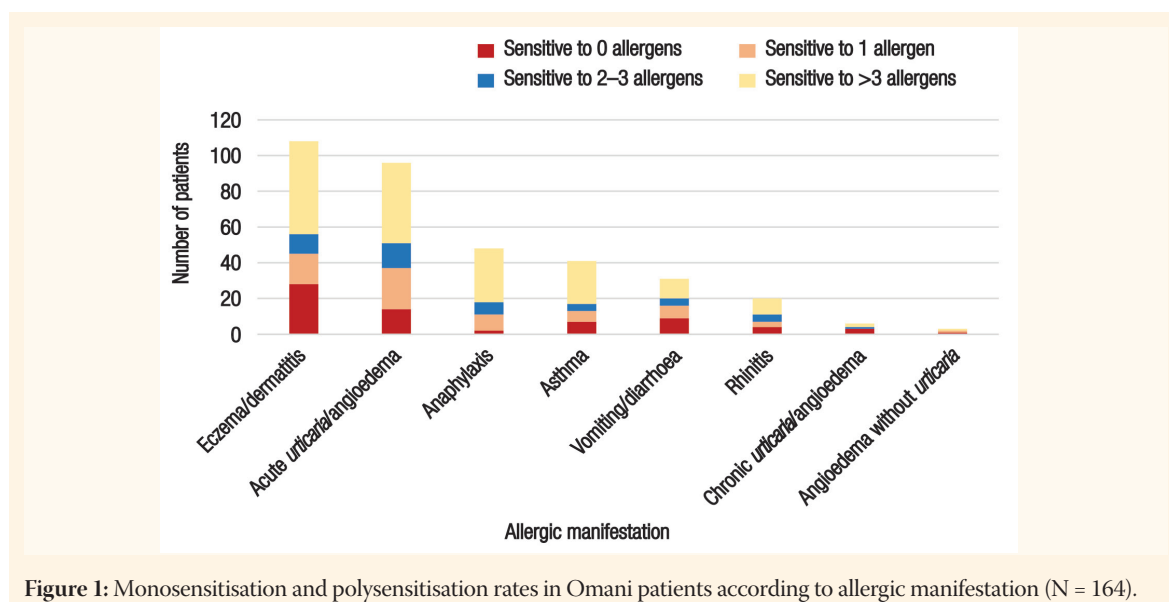


Figure 1: Monosensitisation and polysensitisation rates in Omani patients according to allergic manifestation (N = 164).

help in managing the condition and minimising the risk of complications. After diagnosis, food allergies should be treated with strict avoidance of the identified allergenic foods. Patients and/or their parents or caregivers should be educated about possible allergen sources, taught to check the labels of processed foods and cautioned to be careful about eating in restaurants to minimise the risk of cross-contamination and accidental exposure. In cases of anaphylaxis, patients should be prescribed self-injectable adrenaline and trained on its use in case of accidental exposure.<sup>13,14</sup> However, while adrenaline can be a life-saving measure, delays in administration or the presence of other comorbidities such as uncontrolled asthma may be fatal.<sup>15–18</sup>

To the best of the authors' knowledge, this study is the first to describe food allergen sensitisation patterns in Omani patients with allergic manifestations. The true prevalence of food allergies in Oman is unknown; however, recent data indicate that the prevalence of allergic manifestations such as asthma, rhinitis and eczema in schoolchildren is increasing.<sup>19,20</sup> Moreover, given changing sociodemographic patterns and dietary habits in the Gulf region, it is expected that allergies will continue to have a significant impact on the national healthcare system.<sup>21</sup> In the current study, the majority of patients had atopic manifestations and most had a family history of allergies and elevated total IgE levels; these factors may explain the high rate of positive specific IgE reactions to common food triggers. Moreover, the majority of patients presented with 2–3 allergic manifestations; this finding is to be expected in light of the natural progression of allergic diseases—known as atopic march—which starts in early infancy with a single allergy and progresses over time to other allergies.<sup>22–24</sup> However, the mean period of time between onset of symptoms and diagnosis was approximately two years, indicating that there is a need

to enhance awareness of food allergies and promote early referral services in Oman.

Varying rates of monosensitisation and polysensitisation have been reported in the international literature depending on the baseline characteristics of the studied population.<sup>25</sup> In the present study, the rate of monosensitisation (positive specific IgE levels to one allergen) was 19.5%, with 14% of patients positive for 2–3 allergens. Polysensitisation (i.e. a reaction to more than three allergens) was seen in 39.6% of patients, manifesting mostly as atopic dermatitis. However, not all positive sensitising allergens are responsible for clinical symptoms. In such cases, the predictive value of specific IgE levels is useful in conjunction with clinical symptoms to confirm an allergy diagnosis. In addition, specific IgE testing can help allergists to determine the correct time to reintroduce certain allergenic foods.

Both skin prick and specific IgE tests are very sensitive with excellent negative predictive values.<sup>26–28</sup> Published specific IgE cut-off values reflect a high probability of patients reacting to certain foods, such as cow milk, chicken eggs and peanuts.<sup>29–31</sup> The role of specific IgE to food allergens has been well established in acute *urticaria*/angioedema, anaphylaxis, atopic dermatitis and, to some extent, gastrointestinal allergies such as eosinophilic oesophagitis; however, its role in respiratory allergic manifestations such as asthma and rhinitis is probably marginal.<sup>32,33</sup> While patients with clinical allergic manifestations do have positive specific IgE results to food allergens, they may also have other manifestations or allergies which might account for the results. In the presence of normal total IgE levels, certain patients may also display positive specific IgE reactions to certain foods, as was the case for 21.3% of patients in the current study. This finding may be accompanied by clinical allergic manifestations; for example, 14.6% of anaphylactic

patients had normal total IgE levels, yet high specific IgE levels. This finding emphasises the importance of searching for specific allergens in the presence of normal total IgE levels and consistent allergic manifestations.

Prior to commencing school, most children outgrow food allergies such as those to cow milk, chicken eggs and wheat.<sup>34,35</sup> In fact, parents may sometimes continue feeding common food triggers to allergic children if the resulting reaction is mild or not anaphylactic. A double-blind oral food challenge is considered the gold standard for diagnosing food allergies; however, such an approach may not necessarily be applied to all patients as it is time-consuming and logistically difficult to safely perform.<sup>10,11,32</sup> Based on earlier studies, professional recommendations for primary allergy prevention involve introducing a weaning diet at 4–6 months of age and delaying the introduction of certain allergenic foods such as eggs, fish and peanuts until children reach 12, 24 and 36 months of age, respectively.<sup>36–38</sup> Recent evidence, however, does not support restriction of these foods beyond four months of age.<sup>39</sup>

## Conclusion

This study determined sensitisation rates to common food triggers by measuring specific IgE levels in Omani patients with different clinical allergic manifestations. The results were in line with previous research in other populations. Further studies would be helpful for healthcare policy makers, especially with regards to reducing allergy-related mortality rates due to food-induced anaphylaxis and other causes. Preventative measures would help to minimise comorbidities and reduce the economic burden of allergies on the Omani healthcare system.

## CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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