

# CLINICAL CHARACTERISTICS OF – AND PREDICTIVE DIAGNOSTIC FACTORS FOR – SESAME SEED ALLERGY IN FOOD-ALLERGIC CHILDREN

**Ru-Xin Melanie Foong**, MD, MA, MB BS, BSc Hons  
*King's College London, UK*

**Kirsty Logan**, PhD

*MRC and Asthma UK Centre in Allergic Mechanisms of Asthma, Division Asthma, Allergy and Lung Biology, King's College London, UK*

**Adam T Fox**, MD, MA, MB BS, London, MSc, DCH, FHEA, FRCPCH, Dip. Allergy

**George du Toit**, MB BCh, DCH, Dip Allergy, FCP, MMed, FRCPCH

*MRC and Asthma UK Centre in Allergic Mechanisms of Asthma, Division Asthma, Allergy and Lung Biology, King's College London; Guy's and St Thomas's NHS Foundation Trust, London, UK*

## ABSTRACT

**Background:** Sesame-seed allergy (SSA) is common in children. Our aim was to identify clinical correlations between SSA and other food allergies and predictive factors associated with SSA with regard to skin-prick testing (SPT) and specific IgE (Sp-IgE) testing in children.

**Method:** Data were collected from food allergy questionnaires returned by 79 patients in a tertiary paediatric allergy service; additional clinical information was obtained from the patient database.

**Results:** Of 79 patients, 42 (53.2%) met the study definition for SSA. As compared with children without SSA, those with SSA had a significant association with allergy to other seeds (unadjusted odds ratio (OR) 5.42, 95% confidence interval (CI) 1.53-19.17,  $p=0.009$ ), especially poppy seed (7/42 (16.7%)). SSA was also significantly associated with tree-nut allergies (unadjusted OR 7.50, 95% CI 1.51-37.28,  $p=0.014$ ) but not peanut allergy. A high sensitivity and specificity for determining SSA could be obtained using a SPT cut-off of 2 mm (sensitivity 70.1% and specificity 73.1%) and a Sp-IgE level cut-off of 1.7 IU/ml (sensitivity 76.5% and specificity 84.6%). SSA had been outgrown in 8/79 (10.1%) of the children who at the time of the questionnaire did not have SSA. Low amounts of sesame ingestion (median 0.43 g (range 0-19.71 g)) were tolerated by 7/42 (16.7%) SSA children; the majority of allergic reactions occurred to foods containing high amounts of sesame protein.

**Conclusion:** Sesame-seed-allergic children are at risk of allergies to other seeds and tree nuts. In this cohort, sesame Sp-IgE testing performed well, and better than SPT, at low levels, for the diagnosis of SSA. Similar studies are required in a general population to provide diagnostic cut-off levels that are applicable to unselected children.

## BACKGROUND

Sesame seed allergy (SSA) is a common food allergy in children with clinical presentations ranging from cutaneous allergic manifestations to anaphylactic shock.<sup>1</sup> Evidence suggests that SSA is rarely outgrown.<sup>1,2</sup> With increased consumption and the strong allergenic potential of sesame, the identification of sesame-seed allergic patients is becoming increasingly important.<sup>3,4</sup>

Oleosins and seed storage proteins 2S albumin, 7S and 11S have been identified as major allergens in peanut, tree nuts and seeds, including sesame<sup>1,5</sup> and there is evidence of a high degree of co-reactivity and cross-reactivity between them.<sup>6,7</sup> Few studies focus on sesame-allergic patients. We aimed to identify predictive and characteristic factors associated with SSA in a paediatric population and determine the effectiveness of skin-prick test (SPT) and specific IgE (Sp-IgE) levels in diagnosing SSA in at-risk children. We also wanted to identify any correlation between SSA and allergy to peanut, tree nuts and other seeds.

## METHODS

Children up to the age of 18 years seen in a tertiary paediatric allergy clinic were recruited retrospectively from the department database if they had a possible, probable or confirmed SSA based on clinical history or testing performed in the department (SPT, Sp-IgE and/or oral food challenge (OFC)). Patients who had a clear history of reaction to sesame in the community and/or had a positive OFC result for sesame were recruited into the SSA group. They were defined as being sesame-seed-allergic if they met at least one of the following criteria:

- A clinical reaction to sesame within 60 minutes of exposure either based on clinical history (e.g. reaction at home) or following a supervised incremental OFC (4 doses were used in total – 0.5 g, 2 g, 4 g and 10 g which equates to a total of 8-10 g dried weight of protein)
- Not tolerant to sesame concentrates (e.g. hummus and tahini) while participating in the study
- Evidence of sensitisation to sesame following SPT and/or IgE testing.

Children tolerant to sesame but with a past history of probable reaction and/or a history of positive tests (SPT and/or IgE test) who had been seen in the department were recruited into the non-sesame allergic group.

Patients meeting the inclusion criteria were sent a food allergy questionnaire, based on validated questionnaires<sup>8</sup> previously used for peanut and sesame consumption, to obtain a detailed history about tolerance or allergy to seeds (poppy seed, pumpkin seed, linseed, rapeseed, mustard seed), nuts, egg and milk. Questions about the type of reaction (with symptom prompts), age of

first reaction, sibling food allergies, and the ingestion (in days, weeks and past 4 weeks) of common sesame-containing foods were included. Information about other seed and other nut allergies was also collected from the questionnaires based on patient reporting of a clinical reaction or testing performed in the department. Clinical information on SPT and IgE tests were obtained from the departmental database.

SPT to sesame was performed using fresh tahini (sesame paste); testing to other ingested allergens – when clinically indicated – was to raw hen's egg white (Red Lion salmonella-free egg), pasteurised hen's egg white, peanut, cow's milk, and select tree nuts (ALK-Abelló, Horsholm, Denmark). A small amount of the testing substance was placed on the patient's skin and the skin was pricked with a standardised lancet (ALK-Abelló). The wheal and flare were recorded at 15 minutes at the widest wheal diameter. When clinically indicated, Sp-IgE assays (Pharmacia Cap, Uppsala Sweden) were taken.

Factors associated with SSA were identified using unadjusted univariable logistic regression for categorical variables and linear regression for continuous variables in comparison to the baseline identified by the odds ratios of 1.00 in Table I. Receiver operating characteristic (ROC) curves were used to identify sensitivity and specificity using SPT and Sp-IgE cut-offs at 0, 2 and 5 mm, and 1.7, 5 and 10 IU/ml, respectively. Sensitivity calculated the proportion of children with SSA, correctly identified as such, while specificity calculated the proportion of children without SSA, correctly identified as such by a specified test and cut-off level. Statistical analyses were performed using STATA software version 10 (STATA Corporation, College Station, Texas, USA).

**Ethics:** The study was approved by the South West London Research Ethics Committee (REC Ref: 10/H0801/26) and informed consent was obtained from the participants' parents.

## RESULTS

A total of 79/214 patients recruited for the study returned the questionnaire (response rate of 37%) with a median age of 7.4 years (range 1.5–18.4 years) among respondents. Forty-five (57%) patients were male and the majority (70/79 (89%)) had a history of atopic disease (defined as having asthma, hay fever or eczema). Forty-two (53%) patients met our criteria for SSA. The median age of the first reaction to sesame was 2 years (range 18.2 months–7.0 years) with most experiencing skin (78%), oral upper respiratory (33%) or gastrointestinal symptoms (40%). Eight (19%) children reported having lower respiratory symptoms (i.e. wheeze, difficulty in breathing). Two (4.8%) children reported having had an anaphylactic reaction to sesame (i.e. loss of consciousness or hypovolaemic shock). We found no significant increased risk of SSA if the patient had a sibling who was sesame-allergic. The majority of this high-risk cohort was peanut allergic (SSA group 64%, non-SSA group 68%) (Table I).

Comparisons were made between the sesame-allergic ( $n=42$ ) and the non-sesame allergic participants ( $n=37$ ). SSA was significantly associated with allergy to other seeds (unadjusted odds ratio (UOR) 5.42, 95% confidence interval (CI) 1.53–19.17,  $p=0.009$ ), most commonly poppy seed (7 (17%)). SSA was also significantly associated with tree-nut allergies (UOR 7.50, 95% CI 1.51–37.28,  $p=0.014$ ) with cashew nut and hazelnut being the most common (60% and 55%, respectively). There was a significant association between SSA and egg allergy (UOR 3.0, 95% CI 1.18–7.67,  $p=0.022$ ).

Increasing sesame SPT and Sp-IgE test results were

significantly associated with being sesame-allergic. For 63 children with SPT results available (37 sesame-allergic and 26 non-sesame allergic), we found that the highest sensitivity and specificity could be obtained using an SPT wheal diameter cut-off of only 2 mm (sensitivity 70% and specificity 73%, using fresh tahini). For 30 children with Sp-IgE results available (17 sesame-allergic and 13 non-sesame-allergic), an Sp-IgE cut-off of 1.7 IU/ml represented the highest sensitivity (77%) and specificity (85%). According to the questionnaire response, 7 (17%) sesame-allergic children tolerated low amounts of sesame ingestion (median 0.43 g (range 0–19.71 g)); the majority of reactions occurred to foods containing high amounts of sesame protein, e.g. hummus, tahini.

Twenty-five OFCs for sesame were conducted on patients in both groups. Nine (36%) had positive challenges confirming their diagnosis of SSA. For the same subgroup of patients who had an OFC, an Sp-IgE level of less than 1.7 IU/ml correctly identified 91% (10/11) of non-sesame allergic patients and an Sp-IgE level of 1.7 IU/ml or greater identified 57% (4/7) of sesame-allergic patients.

Of the total participants 8 (10.1%) children had outgrown their SSA, 7 (87.5%) of whom were actively eating sesame at the time of this study according to the questionnaire response. The median number of grams of sesame eaten was 19.95 g (range 0.48–75.16). Of the children who had an OFC, 16 had negative challenges, of whom 14 (88%) went on to successfully include sesame in their diet.

## DISCUSSION

While clinical cross-reactivity between peanut and tree nuts is well described, little is known about cross-reactivity between sesame and other seeds. In this cohort we demonstrate a significantly higher risk of food allergies to tree nuts and other seeds, especially poppy seed. The nature of data collection by questionnaire limited further analysis of the correlation between sesame seed and other seeds.

The lack of association between SSA and peanut allergy probably arises as an artefact of the all the patients being recruited from a tertiary allergy centre; hence we find similar high rates in both groups. However, we did find SSA to be significantly associated with egg allergy which has been identified as a common food allergy in peanut-allergic children.<sup>9</sup> Further studies into this association between egg, sesame and nuts would be beneficial to investigate its clinical relevance. We also found that boys were more commonly allergic to sesame compared to girls ( $p=0.022$ ) (Table I); this is similar to the questionnaire-based rates of SSA in children in the UK (boys 18/2278 (0.9%) and girls 13/279 (0.68%)).<sup>10</sup>

We find that SSA typically presents early in life; that 2 children reported having had an anaphylactic reaction to sesame justifies the consideration of inclusion of adrenaline in the emergency plan of sesame-seed-allergic children. The majority of allergic reactions occurred to foods containing high amounts of sesame protein; a significant proportion of sesame-seed-allergic children were able to tolerate low amounts of sesame ingestion. This seems to be a common clinical finding in sesame allergy, perhaps reflecting peculiarities of sesame allergens and digestive processing thereof. A high degree of clinical suspicion and allergy screening is therefore required in nut-allergic children who tolerate low amounts of sesame but who have not yet consumed concentrated sesame foods. Indeed, we find that sesame Sp-IgE testing performs well, and better than SPT, at low levels. The relatively high levels

**Table I. Characteristics of 79 study participants and associations with sesame allergy**

|                                                    | <b>Sesame-allergic (n=42)</b>   | <b>Not sesame-allergic (n=37)</b> | <b>Comparison</b>                           |
|----------------------------------------------------|---------------------------------|-----------------------------------|---------------------------------------------|
| <b>Median age at survey completion (range)</b>     | 5.98 years<br>(1.75-18.44)      | 8.02 years<br>(0.04-17.78)        | $z=0.747$ , $p=0.455$                       |
| <b>Median age at first sesame reaction (range)</b> | 1.8 years (0.58-7.00)<br>(n=36) | 2.0 years (1.50-5.00)<br>(n=5)    | $z=0.179$ , $p=0.238$                       |
| <b>Sex (%)</b>                                     |                                 |                                   |                                             |
| Male                                               | 29 (69)                         | 16 (43)                           | 1.00                                        |
| Female                                             | 13 (31)                         | 21 (57)                           | OR 0.34<br>95% CI (0.14-0.86)<br>$p=0.022$  |
| <b>Sibling with sesame allergy (%)</b>             |                                 |                                   |                                             |
| No                                                 | 35 (90)                         | 24 (89)                           | 1.00                                        |
| Yes                                                | 4 (10)                          | 3 (11)                            | OR 0.91<br>95% CI (0.19-4.46)<br>$p=0.912$  |
| Missing                                            | 3                               | 10                                |                                             |
| <b>Atopy (%)</b>                                   |                                 |                                   |                                             |
| No                                                 | 3 (7)                           | 6 (16)                            | 1.00                                        |
| Yes                                                | 39 (93)                         | 31 (84)                           | OR 2.52<br>95% CI (0.58-10.88)<br>$p=0.217$ |
| <b>Other seed allergies (%)</b>                    |                                 |                                   |                                             |
| No                                                 | 18 (58)                         | 30 (88)                           | 1.00                                        |
| Yes                                                | 13 (42)                         | 4 (12)                            | OR 5.42<br>95% CI (1.53-19.17)<br>$p=0.009$ |
| Missing                                            | 11                              | 3                                 |                                             |
| <b>Peanut allergy (%)</b>                          |                                 |                                   |                                             |
| No                                                 | 11 (29)                         | 10 (29)                           | 1.00                                        |
| Yes                                                | 27 (71)                         | 25 (71)                           | OR 0.98<br>95% CI (0.36-2.71)<br>$p=0.972$  |
| Missing                                            | 4                               | 2                                 |                                             |
| <b>Other nut allergies (%)</b>                     |                                 |                                   |                                             |
| No                                                 | 2 (5)                           | 10 (29)                           | 1.00                                        |
| Yes                                                | 36 (95)                         | 24 (71)                           | OR 7.50<br>95% CI (1.51-37.28)<br>$p=0.014$ |
| Missing                                            | 4                               | 3                                 |                                             |
| <b>Egg allergy (%)</b>                             |                                 |                                   |                                             |
| No                                                 | 16 (40)                         | 24 (67)                           | 1.00                                        |
| Yes                                                | 24 (60)                         | 12 (33)                           | OR 3.0<br>95% CI (1.18-7.67)<br>$p=0.022$   |
| Missing                                            | 2                               | 1                                 |                                             |

of sensitivity and specificity achieved using an IgE cut-off of 1.7 IU/ml is encouraging, especially in the context of a cohort where other allergies are likely to be present and access to OFCs may be limited or unacceptable to multiple-food-allergic children and families. Our data also highlight the need for performing OFCs to sesame in cases which are equivocal for sesame allergy; such challenges were safe and not infrequently negative.

Study limitations include a relatively small sample size and that allergy investigations (SPT, Sp-IgE and OFCs) were not available for all in our database. The questionnaire response rate is not dissimilar to other studies that make use of questionnaires to determine rates of food allergy; nonetheless selection bias may be active.

## CONCLUSION

In this cohort of patients we find that sesame-seed-allergic children are at risk of anaphylaxis as well as allergies to nuts and other seeds. SSA develops early in life and is outgrown in some 10% of food-allergic children; tolerance of loose seeds does not always confirm tolerance of sesame concentrates. Whether these findings and clinical implications in this cohort also apply to a community setting needs to be determined in large population-based studies using similar methodologies.

## Declaration of conflict of interest

The authors declare no conflict of interest.

## REFERENCES

1. Cohen A, Goldberg M, Levy B, Leshno M, Katz Y. Sesame food allergy and sensitization in children: the natural history and long-term follow-up. *Pediatr Allergy Immunol* 2007;18(3):217-223.
2. Dalal I, Binson I, Levine A, Somekh E, Ballin A, Reifen R. The pattern of sesame sensitivity among infants and children. *Pediatr Allergy Immunol* 2003;14(4):312-316.
3. Gangur V, Kelly C, Navuluri L. Sesame allergy: a growing food allergy of global proportions? *Ann Allergy Asthma Immunol* 2005;95:4-11.
4. Morisset M, Moneret-Vautrin DA, Kanny G, et al. Thresholds of clinical reactivity to milk, egg, peanut and sesame in immunoglobulin E-dependent allergies: Evaluation by double-blind or single-blind placebo-controlled oral challenges. *Clin Exp Allergy* 2003;33(8):1046-1051.
5. Van Ree R. Clinical importance of cross-reactivity in food allergy. *Curr Opin Allergy Clin Immunol* 2004;4:235-240.
6. Derby CJ, Gowland MH, Hourihane JO. Sesame allergy in Britain: A questionnaire survey of members of the anaphylaxis campaign. *Pediatr Allergy Immunol* 2005; 16(2):171-175.
7. Stutius LM, Sheehan WJ, Rangsithienchai P, et al. Characterizing the relationship between sesame, coconut and nut allergy in children: *Pediatr Allergy Immunol* 2010;21:1114-1118.
8. Sofianou-Katsosulis A, Mesher D, Sasieni P, et al. Assessing peanut consumption in a population of mothers and their children in the UK: Validation study of a food frequency questionnaire. *World Allergy Organization Journal* 2011;4(2):38-44.
9. Fleischer DM, Conover-Walker MK, Matsui EC, et al. The natural history of tree nut allergy. *J Allergy Clin Immunol* 2005;116:1087-1093.
10. Du Toit G, Katz Y, Sasieni P, et al. Early consumption of peanuts in infancy is associated with a low prevalence of peanut allergy. *J Allergy Clin Immunol* 2008;122: 984-919.

## CHAIRMAN'S REPORT



Dear Colleagues

This mid-year issue of the journal coincides with our Combined Congress at Sun City. I really hope to see you all during this week. We have a fabulous programme and my sincere gratitude goes to the overall Congress Chair and ALLSA Excom Member Dr André van Niekerk and ALLSA Congress Chair Prof Sam Risenga. Both of you have worked really hard to get

this Congress to look so good and please accept my heartfelt thanks.

This issue of the journal is probably the last in this old format. Profs Matt Haus and Eugene Weinberg (CACI Editors) have a very exciting new look and feel up their sleeves. We should have that ready from late in 2013. That new look will certainly enhance the value of our flagship journal.

I trust you are enjoying the newsletters and case studies on the website. I am trying to keep you, our most valuable member, up to date with allergology and allergology news.

Let me also take this opportunity to invite you to the next ALLSA Focus Group Meeting in Gauteng.

At this Congress ALLSA is celebrating 25 years in existence and we would like to invite you to join us for a piece of cake and a drink in the exhibition hall to mark this historical milestone.

Join us for '25 minutes' of happy memories, bubbly and birthday cake during the lunchtime break on Saturday 8 June in the Trade Exhibition Area to celebrate ALLSA's 25th birthday!

ALLSA has become one of South Africa's leading medical societies and this has not happened by accident. We have been led by doctors who have brought a sense of organisational and scientific excellence to this organisation. I am listing our previous chairmen but I want to pay special homage to Prof Cas Motala. Cas was a legend in allergology and he brought so much to medicine in South Africa. Cas was an outstanding human being and paediatrician and it is at times like these that we miss him so much. Cas, be at peace, our special friend.

**Robin J Green**

Date: Tuesday 9 July 2013

Venue: Aspen Central Facilities, Healthcare Park, Woodlands Drive, Woodmead.

Time: 19h30 (dinner from 18h30)

### Speakers and topics:

'Allergic rhinitis': Is it different to 'chronic rhinitis'?

- **Prof Robin Green**

'Oddities in allergy'

- **Dr Carla Els**

Enquiries to Robbie Moss 082-453-9596

### List of past chairs of ALLSA

1989 – 1992 Prof Eugene Weinberg

1992 – 1995 Prof Paul Potter

1995 – 1998 Prof Cas Motala

1998 – 2001 Prof Matt Haus

2001 – 2004 Dr Ahmed Manjra

2004 – 2006 Prof Cas Motala

2006 – 2009 Prof Sharon Kling

2009 – 2012 Dr Ahmed Manjra