

Original Article

Hand eczema as a risk factor for food allergy among occupational kitchen workers

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OKW occupational kitchen workers

NOKW non-occupational kitchen workers

ABSTRACT

Background: An increasing number of studies in children is highlighting the importance of transdermal routes of exposure to food allergens through damaged skin in the pathogenesis of food allergies. However, data on this in adults are limited. A few case-series studies has documented development of food allergy among kitchen workers with hand eczema after direct contact exposure to foods.

Methods: To explore the significance of hand eczema as a risk factor for food allergies in adults at the epidemiological level, we performed a cross-sectional web-based questionnaire survey on kitchen workers whose exposures were classed as occupational (cooks and food handlers, n = 1592) or non-occupational (housewives, n = 1915). Logistic regression was used to explore the association between the presence/severity of hand eczema and the risk of food allergy after adjustment for potential confounders.

Results: Current hand eczema and current diagnosed food allergy were more common among occupational kitchen workers (OKW) than among non-occupational kitchen workers (NOKW) (32.3%-vs-29.9% and 9.9%-vs-3.8%, respectively). Current hand eczema was significantly associated with increased risk of current diagnosed food allergy in OKW (adjusted odds ratio 2.4, 95% CI 1.6–3.7). Those with more severe hand eczema were more likely to suffer from allergic symptoms for foods, and diagnosed food allergy.

Conclusions: This study illustrates a significant public health problem in the adult population, documenting a major impact of hand eczema on the ongoing adult food allergy epidemic.

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Introduction

A growing number of studies suggest that a transdermal route of exposure to food allergens via damaged skin is important for the pathogenesis of food allergy in children.^{1–4} This has been well-documented for the relationship between infant atopic dermatitis and allergy to egg, milk, and peanuts.⁵ However, studies on this topic in adults are limited, and the situation is a little different than in children^{6,7} in that the most common causes of adult food allergy worldwide are more likely to be fruits and other plant foods, such as apples, peaches, and hazelnuts rather than egg, milk or peanuts.^{8–11} In most cases, the primary sensitizers for fruit allergies

are inhaled pollen allergens, which are cross-reactive with the relevant food allergens.¹² Hence, the respiratory route of sensitization has the strongest impact on adult food allergy epidemics.^{9,13–15} In general, sensitization to food-related proteins via the mucosa of the nose or conjunctiva as a cause of the development of food allergy is common in adults. An example of this which is more or less unique to adults is food allergy associated with sensitization to food-related proteins contained in cosmetics or personal care products.^{16,17} In Japan, we have recently experienced more than 2000 cases of wheat allergy in women using facial soap containing hydrolyzed wheat protein.^{18–21} In this case, the major route of sensitization to wheat-related protein is considered to be the mucosa of the eyelids, conjunctiva, or nose, not the skin of the face (in view of the accompanying eyelid swelling and nasal symptoms, not wheals on the face, as the most common symptom after wheat ingestion).^{18,20} As far as we know, the significance of transdermal exposure to food allergens via damaged skin as the major risk factor for food allergy has in general not been as well-documented in the literature in adults than children, except for

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the latex-fruit allergy syndrome. In this case, the presence of hand eczema has been documented as a significant risk factor for sensitization to latex proteins.^{22,23}

Occupational hand eczema is a common health problem in cooks, food handlers and kitchen staff^{24–27}; a similar problem is also sometimes seen in non-occupational kitchen workers (i.e. housewives).^{28,29} A few case-series studies suggests that direct contact exposure to food through inflamed/damaged skin of the hand could be causing the development of food allergies among such kitchen workers with occupational hand eczema.^{30–32} Considering that such kitchen work is a relatively common occupation among adults, it is possible that the contribution of direct contact exposure to food through damaged hands on the current epidemic of adult food allergy is not negligible. However, epidemiological studies regarding this topic have been limited so far.

To establish the epidemiological relationship between the presence and severity of hand eczema, and the risk of food allergy among kitchen workers, we performed a cross-sectional questionnaire-based survey of occupational versus non-occupational kitchen workers, recruited from a large-scale web-based research panel. The primary subjects of this study were occupational kitchen workers (OKW) because they are very frequently exposed to foods as part of their job, and represent a group at high risk for the development of allergies after transdermal exposures. As comparators, we also included non-occupational kitchen workers (NOKW, i.e. housewives), in this study as a population with a lower but not absent risk of transdermal exposure.

Methods

Study design

A cross-sectional questionnaire-based survey of occupational or non-occupational kitchen workers aged 20–54 yr was performed.

Both occupational and non-occupational kitchen workers were selected from people living in Japan using a large-scale web-based research panel (Macromill, Tokyo, Japan). The number of subjects aged 20–54 yrs in the research panel is approximately 1.3 million, one of the largest in Japan. Members of research panels are voluntary registrants who have agreed to answer various web-based survey questions for a small fee (Membership point). Detailed characteristics of this population have been published previously.²⁰ The Ethics Committee of Sagami National Hospital approved the study protocol (No. 160104).

Web-based survey

Figure 1 shows the protocol for the web-based survey. First, the research company sent e-mails inviting participation in the screening survey in order to identify OKW and NOKW. The screening survey consisted of 3 questions regarding occupation (QS1 to QS3, shown in [Supplementary Methods](#)). Subjects were considered as OKW if they had indicated “work that involves frequently processing food or cooking food, including cutting, boiling, broiling, serving, etc.” in their responses to QS1 “Are you currently engaged in any of the following in your profession or part-time job?” or QS2 “Have you done any of the following as part of your full-time job or part-time job for at least one consecutive year in the last 5 years?” Subjects were considered as NOKW if they met the following two criteria: i) not indicating “work that involves frequently processing food or cooking food, including cutting, boiling, broiling, serving, etc.” in their responses to QS1 or QS2, and ii) indicating “More than five times a week” in their responses to QS3 “On average, how often do you cook at home (e.g., cutting vegetables or meat using a knife, cleaning and gutting fish, etc.) for yourself or your family during a one-week period?”

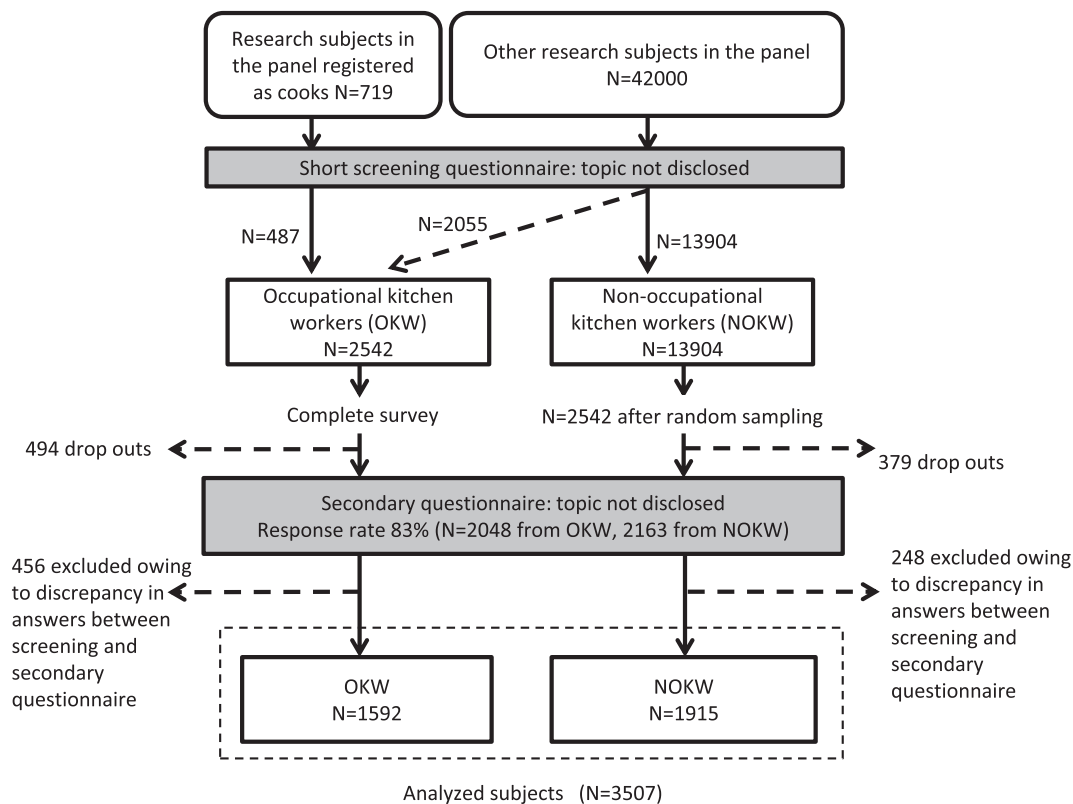


Fig. 1. Protocol of web-based survey.

Pre-registered subject information regarding occupation was available on approximately 12% of the panel and was used for identification of OKW. Invitation e-mails to participate in the screening survey were preferentially sent between 16th and 22nd March, 2016, to subjects reporting themselves as cooks ($n = 1162$). Of the panel members ($n = 719$) responding to the screening questionnaire, 487 were considered as OKW. To further increase the number of study subjects, invitation e-mails were also sent to an age-gender-stratified (20–24, 25–29, 30–34, 35–39, 40–44, 45–49, and 50–54 yr for men and women) random sample of the research panel without pre-registered information on occupation (approximately 88% of the overall subjects) in the same period. No further invitations were sent once 3000 responses had been received for each age-gender-cell (42,000 total). From this population, 2055 and 13,904 subjects were additionally identified as OKW and NOKW, respectively. After random sampling of the subjects in the NOKW group, 2534 OKW and 2534 NOKW were identified as candidates for the secondary questionnaire.

The first E-mail inviting participation in the secondary survey was sent on 22nd March, 2016, and reminders were sent up to 3 times. The secondary survey ended on 29th March, 2016. The secondary questionnaire contained detailed questions regarding hand eczema, allergic symptoms in response to foods, allergic diseases other than food allergy, and other potential risk factors (Supplementary Methods). To ensure the validity of the answers in the screening questionnaire, the secondary questionnaire included the same questions as QS1, QS2, and QS3 of the screening questionnaire (Q1, Q2, and Q4). After excluding 704 subjects (456 and 248 subjects from OKW and NOKW, respectively) with discrepancies between the answers to these 3 questions in the screening and secondary questionnaires, data from 1592 OKW and 1915 NOKW could be finally analyzed here.

Questions on hand eczema in the secondary questionnaire

The participants were asked to answer questions Q9: “Are you currently experiencing hand eczema or severe cracking of your hands?” (Current hand eczema); Q10: “Have you experienced hand eczema or severe cracking of your hands in the last 12 months?” (Hand eczema in the last 12 months); and Q11: “Have you ever experienced hand eczema or severe cracking of your hands before?” (Hand eczema ever). They were also asked to state how troublesome they found their current hand eczema (Q14) using a numerical rating scale, ranging from 0 (not troublesome at all) to 10 (extremely troublesome).

The severity of current hand eczema was evaluated using self-reported responses to the web-based questions regarding detailed symptoms (Q15). Each hand was subdivided into 5 areas, and photos showing each area were presented on the web page. Subjects were asked to state whether (present/absent) they suffered from 1) pain, 2) itchiness, 3) redness, 4) blisters, 5) pustules, 6) dry skin, 7) skin sore, 8) crusts, and 9) chapped hands for each of the 5 areas of both hands; and 10) deformed nails for both hands. The severity scores for current hand eczema were calculated by counting the total number of reported symptoms (0–92).

Questions on symptoms in response to foods in the secondary questionnaire

Because allergic symptoms to foods among food handlers can be induced by different exposure routes, several questions included whether there were contact symptoms on the hands when food was touched (selecting any foods in Q17), oral symptoms when eaten (selecting any foods in Q18), symptoms after respiratory exposure (Q19 and Q20), or systemic symptoms after eating

(selecting any food in Q21). These were asked separately, and the specific foods causing each symptom were also identified. Avoidance of eating specific foods due to food allergy (selecting any specific food in Q22) and self-reported lifetime-diagnosis of food allergy (selecting any specific food in Q23) was also queried. For subjects with lifetime-diagnosed food allergy, age of onset (Q24) and the presence or absence of current symptoms (Q25) was also determined. Subjects who reported lifetime-diagnosis of allergy to any specific food with current symptoms to the same food were considered to have “current diagnosed food allergy”. The kind of food that the subjects most frequently handled while cooking at work (OKW) or at home (NOKW) was also recorded (Q3 and Q5).

Statistical analysis

The collected data were analyzed using SPSS ver. 23.0 (IBM, Tokyo, Japan). Descriptive statistics were used to characterize OKW and NOKW. Significance testing was performed using Chi-squared analysis for categorical variables and the Mann–Whitney U test for continuous variables. Both scores for hand eczema troublesome status and for severity were divided into tertiles, with 1–5 (1st tertile), 6–7 (2nd tertile), and 8–10 (3rd tertile) for the former, and 1–8 (1st tertile, mild), 9–16 (2nd tertile, moderate), and 17–92 (3rd tertile, severe) for the latter, respectively. Logistic regression was used to explore the association between the presence/troublesome feeling/severity of hand eczema and allergic symptoms to foods, and adjusted odds ratios (OR) and 95% confidence intervals (CIs) were calculated after adjusting for potential confounders including atopic dermatitis among OKW and NOKW separately.

Tests for trends were evaluated by assigning consecutive integers to each tertile of the troublesome feeling scale and the severity scale. Possible interactions of the presence or severity of hand eczema with OKW/NOKW classification were accessed by including interaction terms of presence/severity of hand eczema \times OKW/NOKW classification into the logistic regression model. A p value of ≤ 0.05 was considered statistically significant.

Results

Study subject characteristics

Table 1 shows demographic characteristics, allergic comorbidities, presence and severity of hand eczema, and food allergy symptoms among OKW ($n = 1592$) and NOKW ($n = 1915$). OKW were more likely to be younger, male, and current smokers compared to NOKW. The prevalence of asthma and atopic dermatitis was significantly higher in OKW than NOKW. Additionally, the prevalence of hand eczema was significantly higher and the symptoms more severe in OKW than NOKW. Of note, the prevalence of current diagnosed food allergy was 9.9% among OKW, which was markedly higher than in NOKW (3.8%). Prevalence of the other allergic outcomes were also significantly higher in OKW.

Hand eczema status as risk factor for diagnosed food allergy and allergic symptoms

Associations between presence/severity of hand eczema and current diagnosed food allergy among OKW and NOKW are shown in Table 2 and Figure 2A. In OKW, the association between the presence of current hand eczema and a current diagnosed food allergy was significant even after adjusting for age, sex and allergic comorbidities including atopic dermatitis, yielding an odds ratio of 2.4 (95% CI, 1.6–3.7). In contrast, associations of “hand eczema in the last 12 months” and “hand eczema ever” with outcome were not significant, indicating that the current status of hand eczema

Table 1
Study subject characteristics.

	OKW (n = 1592)	NOKW (n = 1915)	p-Value
Age (yr, mean ± SD)	35.0 ± 10.2	39.6 ± 9.0	<0.001
Gender (=female), n (%)	987 (62.0)	1715 (89.6)	<0.001
Occupational kitchen working, n (%)			
Currently engaged in (4 on Q1)	1124 (70.6)	0 (0)	
Have engaged in the last 5 yrs (4 on Q2)	1592 (100)	0 (0)	
Frequency of cooking at home ≥5 times/week (6 on Q4)	779 (48.9)	1915 (100)	<0.001
BMI (mean ± SD)	23.6 ± 65.2	22.2 ± 40.4	
Current smoker, n (%)	401 (25.2)	226 (11.8)	<0.001
Allergic comorbidities, n (%)			
Allergic rhinitis (Q36)	880 (55.3)	1022 (53.4)	0.137
Allergic conjunctivitis (Q35)	735 (46.2)	822 (42.9)	0.029
Atopic dermatitis (1 in Q41)	205 (12.9)	182 (9.5)	0.005
Current bronchial asthma (Q39 + Q40)	142 (8.9)	109 (5.7)	<0.001
Prevalence of hand eczema, n (%)			
Current hand eczema (Q9)	514 (32.3)	496 (25.9)	<0.001
Hand eczema in the last 12 months (Q10)	719 (45.2)	714 (37.3)	<0.001
Hand eczema ever (Q11)	1012 (63.6)	1059 (55.3)	<0.001
Feeling troubled by current hand eczema (Q14), n (%)			
No hand eczema	1078 (67.7)	1419 (74.1)	<0.001
1st tertile	200 (12.6)	184 (9.6)	
2nd tertile	176 (11.1)	171 (8.9)	
3rd tertile	138 (8.7)	141 (7.4)	
Severity of current hand eczema (Q15), n (%)			
No hand eczema	1078 (67.7)	1419 (74.1)	
Mild (1st tertile)	156 (9.8)	222 (11.6)	
Moderate (2nd tertile)	173 (10.9)	149 (7.8)	
Severe (3rd tertile)	185 (11.6)	125 (6.5)	
Prevalence of allergic symptoms to foods, n (%)			
Contact symptoms to any specific foods (Q17)	719 (45.2)	812 (42.4)	0.054
Oral symptoms to any specific foods (Q18)	532 (33.4)	508 (26.5)	<0.001
Respiratory symptoms to any specific foods (Q19 + Q20)	119 (7.5)	34 (1.8)	<0.001
Systemic symptoms to any specific foods (Q21)	341 (21.4)	236 (12.3)	<0.001
Avoidance of eating any specific foods (Q22)	281 (17.7)	224 (11.7)	<0.001
Lifetime diagnosis of food allergy (Q23)	223 (14.0)	128 (6.7)	<0.001
Current diagnosed food allergy (Q23 + Q25)	157 (9.9)	72 (3.8)	<0.001

OKW, occupational kitchen worker; NOKW, non-occupational kitchen worker; QOL, quality of life.

3rd tertile indicates stronger troublesome feeling than 1st tertile.

For the number of Q, please see [Supplementary Methods](#).

was a more important risk factor than past status. Feeling more troubled by current hand eczema and severity of current hand eczema were also associated with current diagnosed food allergy among OKW also after adjusting for potential confounders (test for trends, $p < 0.001$, and $p < 0.001$, respectively) indicating that the

OKW subjects with more severe hand eczema were more likely to suffer from food allergy.

Unlike in the OKW, the association between presence/severity of current hand eczema and current diagnosed food allergy did not reach statistical significance after adjusting for confounders in the

Table 2
Association of the presence and severity of hand eczema with current diagnosed food allergy.

	OKW		NOKW		P-interaction [†]
	Crude OR (95% CIs)	Adjusted OR [†] (95% CIs)	Crude OR (95% CIs)	Adjusted OR [†] (95% CIs)	
Current hand eczema	6.2 (4.3–8.9)	2.4 (1.6–3.7)	1.5 (0.9–2.4)	0.8 (0.5–1.4)	<0.001
Hand eczema in the last 12 months	4.1 (2.8–5.9)	1.5 (1.0–2.4)	1.5 (1.0–2.5)	1.0 (0.6–1.7)	0.021
Hand eczema ever	2.8 (1.8–4.2)	1.1 (0.7–1.8)	2.5 (1.5–4.3)	1.9 (1.1–3.3)	0.590
Feeling troubled by current hand eczema					
No hand eczema	1.0	1.0	1.0	1.0	
1st tertile	5.3 (3.3–8.3)	2.2 (1.3–3.8)	1.5 (0.7–3.1)	0.9 (0.4–2.0)	0.016
2nd tertile	6.2 (3.9–9.8)	2.0 (1.2–3.6)	0.7 (0.2–1.9)	0.4 (0.2–1.3)	0.003
3rd tertile	7.6 (4.7–12.4)	3.3 (1.8–6.1)	2.4 (1.2–4.8)	1.1 (0.5–2.5)	0.003
Test for trend	<0.001	<0.001	0.068	0.713	
Severity of current hand eczema					
No hand eczema	1.0	1.0	1.0	1.0	
Mild (1st tertile)	2.4 (1.3–4.4)	1.8 (0.9–3.6)	0.8 (0.3–1.9)	0.5 (0.2–1.3)	0.020
Moderate (2nd tertile)	6.1 (3.8–9.8)	2.0 (1.2–3.6)	1.8 (0.9–3.8)	1.3 (0.6–2.8)	0.220
Severe (3rd tertile)	10.5 (6.9–16.1)	3.2 (1.9–5.5)	2.2 (1.1–4.6)	0.7 (0.3–1.7)	<0.001
Test for trend	<0.001	<0.001	0.021	0.716	

OKW, occupational kitchen worker; NOKW, non-occupational kitchen worker; OR, odds ratio; 95% CI, 95% confidence interval.

[†] Adjusted for age, sex, allergic conjunctivitis, allergic rhinitis, atopic dermatitis, and current bronchial asthma.

NOKW group. Additionally, statistically significant interactions were observed between the presence/severity of current hand eczema and the OKW/NOKW classification, indicating that OKW were more likely to suffer from food allergy when they had current hand eczema than NOKW even when they also had current hand eczema (Table 2). Figure 2B and Table 3, Supplementary Tables 1–4 show associations between current hand eczema and oral, contact, respiratory, and systemic allergic symptoms for any specific foods, and avoidance of eating any specific food due to food allergy. Similar statistically significant associations between severity of current hand eczema and risk of allergic outcomes were also observed in OKW.

The types of food that the subjects frequently handled at work in the OKW group and at home in the NOKW are shown in Supplementary Figure 1, and Supplementary Figure 2 shows the frequency with which handling that food caused hand irritation. The most common causal agent for both OKW and NOKW was yam, but this is also known to contain non-allergic irritants. Shrimp/crab and squids/octopuses were the second and the third most common cause of hand irritation in OKW at frequencies of 9.0% and 5.2%, respectively. Figure 3 shows the prevalence of current diagnosed allergy to individual foods. Hen's egg and shrimp/crab were the most and the second most common causes for both OKW (3.1% and 2.7%, respectively) and NOKW (1.7%, and 1.0%, respectively).

Hand eczema status as a risk factor for allergies to individual foods in OKW

Considering the heterogeneous nature of adult food allergy, we further analyzed associations between hand eczema in the OKW group and allergic symptoms caused by individual foods (Table 4). We focused particularly on four individual foods, namely shrimp/crab, fish, hen egg and apple. We selected shrimp/crab and fish for this analysis because they are commonly associated with hand irritation (Supplementary Fig. 2) and diagnosed allergies (Fig. 3). Hen egg was selected because it is the most common cause of childhood-onset food allergy. Finally, apple was selected because it is a well-described birch pollen-related allergen and commonly causes food allergies in adults. Contact allergic symptoms caused by shrimp/crab (9.0%), fish (2.4%) and hen egg (2.3%) were more common than oral allergic symptoms to the same foods (4.9%, 1.4% and 1.9%, respectively). In contrast, symptoms on contact with apple (1.1%) were less common than when it was ingested (2.4%), implying that contact exposure and sensitization to apple is less common. Consistent with this, for shrimp/crab, fish and hen egg, there were statistically significant associations between severity of current hand eczema and oral allergic symptoms to each food, whereas there was no significant association for apples. This indicates that shrimp/crab, fish and hen eggs, but not apple, are important contact sensitizers for OKW. However, we found no

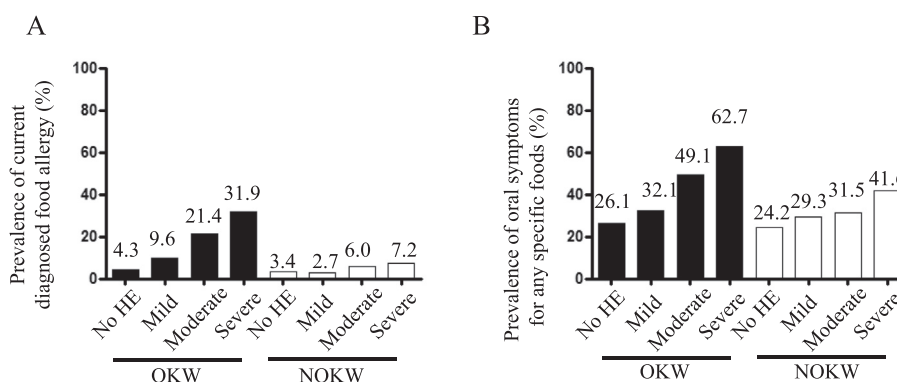


Fig. 2. Proportion of subjects with current diagnosed food allergy (A), oral allergic symptoms to any specific foods (B) according to hand eczema severity, among OKW and NOKW. HE, hand eczema; OKW, occupational kitchen worker; NOKW, non-occupational kitchen worker.

Table 3

Association between hand eczema and oral allergic symptoms to any specific foods.

	OKW		NOKW		P-interaction [†]
	Crude OR	Adjusted OR [†]	Crude OR	Adjusted OR [†]	
Current hand eczema	2.7 (2.2–3.4)	1.7 (1.3–2.2)	1.5 (1.2–1.9)	1.2 (0.9–1.5)	0.003
Hand eczema in the last 12 months	2.1 (1.7–2.5)	1.3 (1.0–1.6)	1.6 (1.3–2.0)	1.3 (1.0–1.6)	0.364
Hand eczema ever	2.1 (1.7–2.6)	1.4 (1.1–1.8)	1.7 (1.4–2.1)	1.4 (1.2–1.8)	0.552
Feeling troubled by current hand eczema					
No hand eczema	1.0	1.0	1.0	1.0	
1st tertile	2.4 (1.8–3.3)	1.6 (1.2–2.3)	1.3 (0.9–1.8)	1.1 (0.7–1.5)	0.020
2nd tertile	2.7 (2.0–3.8)	1.5 (1.1–2.2)	1.7 (1.2–2.4)	1.4 (1.0–2.0)	0.370
3rd tertile	3.2 (2.2–4.6)	2.0 (1.4–3.0)	1.7 (1.2–2.4)	1.1 (0.8–1.7)	0.008
Test for trend	<0.001	<0.001	<0.001	0.133	
Severity of current hand eczema					
No hand eczema	1.0	1.0	1.0	1.0	
Mild (1st tertile)	1.3 (0.9–1.9)	1.2 (0.8–1.7)	1.3 (1.0–1.8)	1.1 (0.8–1.6)	0.725
Moderate (2nd tertile)	2.7 (2.0–3.8)	1.6 (1.1–2.3)	1.4 (1.0–2.1)	1.2 (0.8–1.7)	0.074
Severe (3rd tertile)	4.8 (3.4–6.6)	2.6 (1.8–3.7)	2.2 (1.5–3.2)	1.4 (0.9–2.2)	0.002
Test for trend	<0.001	<0.001	<0.001	0.081	

OKW, occupational kitchen worker; NOKW, non-occupational kitchen worker; OR, odds ratio; 95% CI, 95% confidence interval.

[†] Adjusted for age, sex, allergic conjunctivitis, allergic rhinitis, atopic dermatitis, and current bronchial asthma.

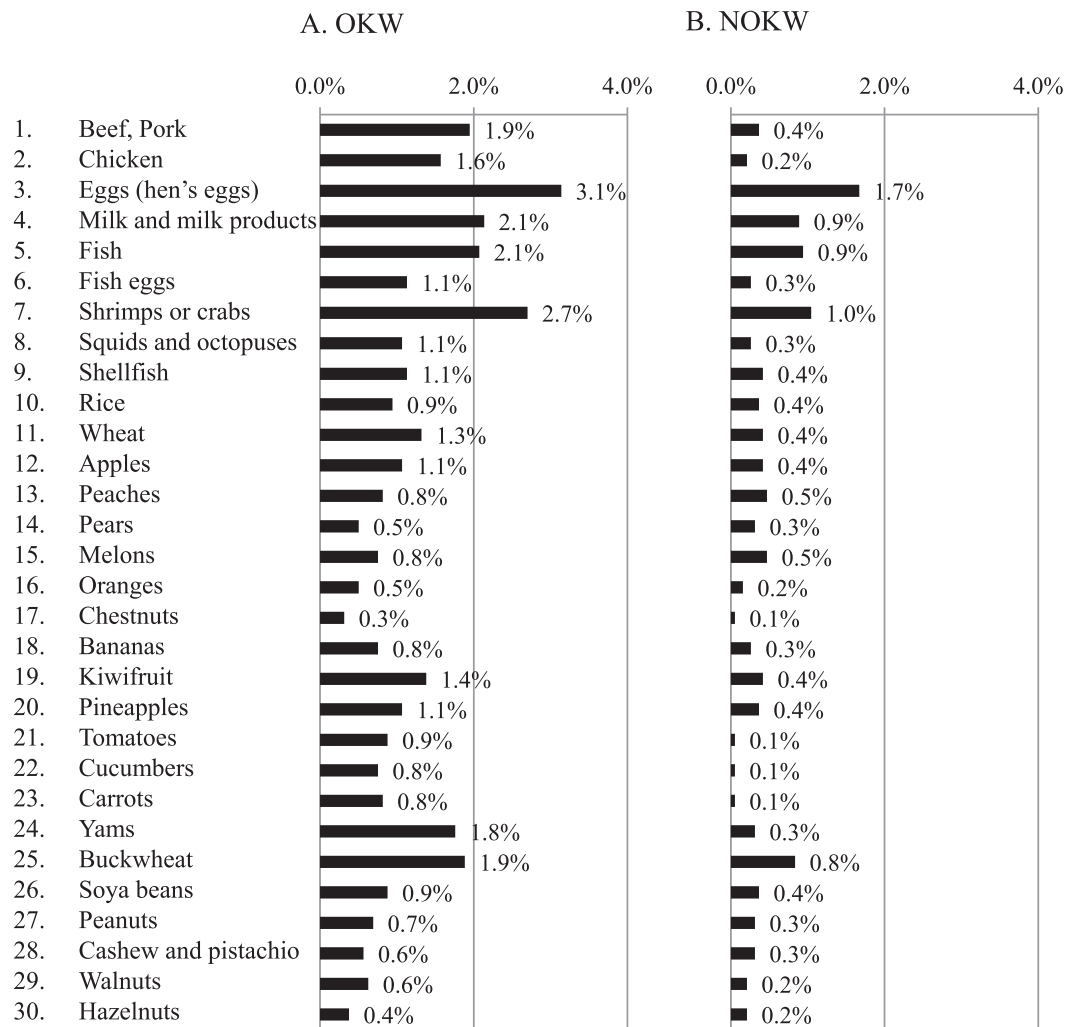


Fig. 3. Prevalence of current diagnosed allergy to individual foods among OKW (A) and NOKW (B).

significant associations between severity of hand eczema and risk of systemic symptoms (data not shown), avoidance of eating (data not shown), or current diagnosed allergy to any of these individual foods, probably due to the limited sample size.

Discussion

This web-based survey examined epidemiological relationships between hand eczema and the risk of food allergy in adults. Among occupational kitchen workers like chefs, the presence of current hand eczema was significantly associated with an increased risk for current diagnosed food allergy. The more severe the hand eczema was, the more likely the person was to be suffering from food allergy. To the best of our knowledge, this is the first study clearly documenting an impact of hand eczema on the food allergy epidemic in adults.

Cooks, kitchen staff and food handlers are familiar and common occupations for people worldwide. This is reflected in the large number of OKW in the web-based research panel population studied here – around 5% (data not shown). Therefore, we consider that the findings of this study do imply a significant worldwide public health problem in the fields of allergy and occupational medicine. Moreover, in the present study, subjects who had engaged in but were not currently engaged in kitchen working

were also included in the OKW population, because some of the occupationally sensitized food-allergic patients had to change the nature of their work due to their allergic symptoms.

Allergic comorbidities such as atopic dermatitis can be significant confounding factors for the relationship between hand eczema and food allergy because they are known to be risk factors for both hand eczema^{33–36} and food allergy.³⁷ In the present study, we included allergic comorbidities in the multivariate logistic regression models for assessing associations between hand eczema and food allergy and found that in OKW associations remained significant even after this adjustment. However, in NOKW, although there were statistically significant associations between severe current hand eczema and current diagnosed food allergy or other allergic outcomes in the univariate analyses, these associations did not remain significant after adjustment for allergic comorbidities, with the exception of respiratory symptoms. Therefore, we conclude that there was no clear independent effect of hand eczema on the risk of food allergy in NOKW in this study. However, we believe that physicians also need to consider the possible risk that NOKW with hand eczema may still develop food allergies. Indeed, a few cases of food allergy developing in housewives with hand eczema has been reported.^{28,30}

Interactions between the presence/severity of current hand eczema and OKW/NOKW classification were significant, indicating

Table 4

Prevalence of allergic symptoms to specific foods according to hand eczema severity and the adjusted odds ratio for the association between hand eczema severity and symptoms to foods among OKW.

	Contact symptoms		Oral symptoms		Diagnosed food allergy	
	%	aOR	%	aOR	%	aOR
Symptoms to shrimp/crab						
Overall prevalence	9.0		4.9		2.7	
Prevalence by severity of current hand eczema						
No hand eczema	5.4	1	3.2	1	1.5	1
Mild	9.0	1.6 (0.8–2.9)	5.1	1.5 (0.7–3.4)	1.9	1.0 (0.3–3.5)
Moderate	19.7	3.3 (2.0–5.4)**	8.1	1.8 (0.9–3.6)	8.1	2.6 (1.1–6.0)*
Severe	20.5	3.2 (2.0–5.3)**	11.9	2.7 (1.4–5.1)**	5.4	1.3 (0.5–3.4)
Test for trend		<0.001		0.002		0.280
Symptoms to fish						
Overall prevalence	2.4		1.4		2.1	
Prevalence by severity of current hand eczema						
No hand eczema	0.7	1	0.3	1	0.8	1
Mild	0.6	0.6 (0.1–5.3)	1.3	3.6 (0.6–22.5)	1.9	1.8 (0.5–6.9)
Moderate	6.4	4.4 (1.6–12.0)**	4.0	5.4 (1.2–24.2)*	5.2	2.8 (1.0–8.2)
Severe	10.3	6.0 (2.3–15.7)**	5.9	7.6 (1.8–32.6)**	6.5	3.2 (1.1–9.0)*
Test for trend		<0.001		0.006		0.064
Symptoms to hen's egg						
Overall prevalence	2.3		1.9		3.1	
Prevalence by severity of current hand eczema						
No hand eczema	0.3	1	0.2	1	1.7	1
Mild	1.3	2.5 (0.4–16.7)	0.6	2.1 (0.2–26.2)	3.8	1.7 (0.6–4.6)
Moderate	4.6	4.1 (0.9–17.9)	5.2	4.3 (0.8–23.0)	5.8	1.2 (0.5–2.9)
Severe	13.0	12.1 (3.1–46.6)**	10.3	9.6 (1.9–48.9)**	8.6	1.4 (0.6–3.3)
Test for trend		<0.001		0.003		0.460
Symptoms to apple						
Overall prevalence	1.1		2.4		1.1	
Prevalence by severity of current hand eczema						
No hand eczema	0.2	1	1.6	1	0.6	1
Mild	0.6	2.4 (0.2–28.3)	1.9	1.1 (0.3–3.8)	0.6	0.7 (0.1–6.4)
Moderate	5.8	9.9 (1.9–52.6)**	5.8	2.2 (0.9–5.4)	2.3	1.2 (0.3–5.0)
Severe	2.7	3.2 (0.5–19.5)	4.3	1.3 (0.5–3.5)	2.7	1.0 (0.2–4.1)
Test for trend		0.180		0.330		0.967

OKW, occupational kitchen worker; NOKW, non-occupational kitchen worker; aOR, adjusted odds ratio with 95% confidence interval after the adjustment with age, sex, allergic conjunctivitis, allergic rhinitis, atopic dermatitis, and current bronchial asthma.

* $p < 0.05$; ** $p < 0.01$ compared to no hand eczema group.

that individuals in the OKW group were more likely to suffer from food allergy than NOKW even when the latter were also suffering from current hand eczema. We hypothesize that this is because the degree of exposure to food is much higher among OKW than among NOKW, and the former cannot easily avoid handling the foods they know will cause irritation because of the nature of their job.

An analysis of associations between hand eczema and risk of allergic symptoms caused by individual foods revealed significant associations for shrimp/crab, fish and eggs, but not for apples. Thus, these 3 foods are considered to be important contact sensitizers in the occupational setting. Although shrimp/crab and fish have previously been reported as foods causing occupationally-developed food allergies in kitchen workers,^{28,30,31} occupational transdermal sensitization to egg via damaged skin has not been reported in the literature, as far as we are aware. However, in our daily clinical practice, we sometimes do encounter young adult patients with infant-onset hen's egg allergy who report contact symptoms when handling eggs during occupational or non-occupational activities. Thus, the findings of the present study are consistent with our own clinical experience. Some such patients also report that their allergic symptoms induced by eating eggs became more severe or were more easily provoked by lower amounts after several months' occupational exposure to hen's egg, despite the fact that their allergic symptoms after eating eggs had been becoming gradually milder over the years. Therefore, it cannot be excluded that occupational contact exposure to food can be associated with worsening

allergy to foods to which the individual was already sensitized, as well as de novo sensitization to food.

The main limitation of the present study relates to the definition of food allergy, which was self-reported. It is generally recognized that diagnosis by an allergist after provocation testing is more reliable than the definition of diseases by self-reporting. Additionally, actual sensitization to the food was not evaluated in this study. Thus, there remains the possibility that the mechanism of some of the reported food allergic symptoms was not actually an IgE-mediated reaction. However, we believe that frequency of non-IgE mediated reactions to foods is unlikely to be so high as we saw, except possibly for yam, melon, pineapples and kiwifruits, which are known to contain non-allergic irritants. Another limitation may relate to the definition of the presence and severity of hand eczema; this was also self-reported. However, many studies have validated self-reported answers to paper-based structured questionnaires defining the presence and severity of hand eczema.^{38–42}

In conclusion, this study documents an epidemiological relationship between hand eczema and the risk of food allergy among kitchen workers in occupational settings. Considering that cooks and food handlers are common occupations among the global adult population, more attention should be paid to the risk of transdermal sensitization to food via hands affected by eczema. The findings of this study also suggest that controlling occupational hand eczema will be important for the prevention of adult food allergy.

Appendix A. Supplementary data

Supplementary data related to this article can be found at <http://dx.doi.org/10.1016/j.alit.2017.08.005>.

Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

YF designed the study. TM and YF performed the analysis and wrote the manuscript. KS, AA, and MT contributed to the critical revision of the manuscript. All authors read and approved the final manuscript.

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