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developing severe allergic reactions to spices and to highlight the importance of checking for hidden allergens in patients presenting with allergic reactions without a known cause. Because of its widespread use in spices, processed foods, and cosmetic products, allspice can be a potential hidden allergen when it is an ingredient.

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References
1. Jessica Elizabeth DLT, Sassara F, Kouassi AP, Brar SK, Belkacemi K. Spice use in food: properties and benefits. Crit Rev Food Sci Nutr. 2017;57(6):1078–1088.
2. Chen JL, Bahna SL. Spice allergy. Ann Allergy Asthma Immunol. 2011;107(3):191–199.
3. Baker MC, Saf S, Tsuang A, Nowak-Wegrzyn A. Hidden allergens in food allergy. Ann Allergy Asthma Immunol. 2018;121(3):285–292.
4. Britannica. Allspice. Available at: https://www.britannica.com/plant/allspice. Accessed April 9, 2022.
5. Zhang L, Lokeshwar BL. Medicinal properties of the Jamaican pepper plant Pimenta dioica and allspice. Curr Drug Targets. 2012;13(14):1900–1906.
6. Allergen encyclopedia-thermosher. Allergy and autoimmune disease. Available at: https://www.thermosher.com/diagnostic-education/hcp/us/en/resource-center/allergen-encyclopedia/whole-allergens.html?key=f339. Accessed April 9, 2022.
7. Faber MA, van Gasse AL, Decuyper II, Sabato V, Hagendorens MM, Mertens C, et al. Cross-reactive aeroallergens: which need to cross our mind in food allergy diagnosis? J Allergy Clin Immunol Pract. 2018;6(6):1813–1823.
8. US Food and Drug Administration. How are ingredients listed on a product label? Available at: https://www.fda.gov/food/food-ingredients-packaging/overview-food-ingredients-additives-colors. Accessed April 23, 2022.

Decreased food allergy-specific anxiety and increased general anxiety in parents of children with food allergies during the coronavirus disease 2019 pandemic

The coronavirus disease 2019 (COVID-19) pandemic continues to affect the mental health of children and youth worldwide, particularly for those with chronic physical conditions and socioeconomic adversity. For children and youth with food allergies (FA), the early COVID-19 pandemic led to immediate changes to allergy-related services; emergency department visits for anaphylaxis also decreased. Youth whose parents report negative impacts of COVID-19 have also reported poorer well-being, affected by difficulties accessing “safe” foods and health services.

Moderate anxiety in parents of children with FA is generally adaptive given risks of allergen exposure. However, excess anxiety can lead to increased parental burden and impaired health-related quality of life. FA-specific anxiety (FAA) includes emotional, cognitive, behavioral, and physical domains; although associated with generalized anxiety—in which worries about a number of events or activities are difficult to control—it is a distinct construct. To our knowledge, there have been no analyses of impacts of the pandemic on parental FAA and implications for family support. In this study, we sought to describe parental experiences of FAA during the COVID-19 pandemic and to evaluate the relationship between general anxiety symptoms and FAA.
This was a cross-sectional online survey of Canadian parents of children and youth with FA completed in May to June 2020, at which time in-person medical visits for non-urgent care were limited and most schools had transitioned to a virtual model. A survey link was distributed electronically through national and local patient advocacy groups and by public lectures. Survey components included demographic information, allergy history, and the General Anxiety Disorder—7, a measure of generalized anxiety symptoms. Furthermore, current and pre–COVID-19 aspects of FAA were queried using a 28-item questionnaire undergoing validation, the Impairment Measure for Parental food Allergy-related Anxiety and Coping Tool or IMPAACT. This study was approved by The University of British Columbia Children’s and Women’s Research Ethics Board.

A convergent parallel mixed-methods design was used to allow for triangulation of results and elaboration of quantitative results with qualitative findings. Associations were evaluated with bivariate Spearman correlations. Significance was determined by 2-tailed t-test or χ² test, accounting for multiple comparisons using the Benjamini-Hochberg correction with a false discovery rate of 0.05. Predictors of self-reported change in FAA with COVID-19 on a 5-point scale from 1 (decreased greatly) to 5 (increased greatly) were determined by ordinal regression modeling. Mean ± SD of continuous variables, median (interquartile range, IQR) of ordinal variables, and 95% confidence intervals for odds ratios (ORs) are reported. Qualitative content analysis using an inductive approach was used to describe open-ended responses. There were 2 researchers who independently coded responses, with differences resolved through discussion. Codes were grouped into categories with corresponding frequencies and then further grouped into themes. Qualitative and quantitative analyses were conducted independently with results synthesized at the point of integration in the interpretation.

Of the 383 parents who consented to participate, 293 completed the FAA questionnaire (77% completion rate). Most of the respondents lived in Ontario (46%), British Columbia (28%), Alberta (8%), or Manitoba (5%). Mean age was 43.3 ± 7.0 (range 27-64). In addition, 92% of the respondents were mothers, reporting a greater share of FA management responsibility than fathers (79% ± 18% vs 58% ± 23%, P < .001). Post-secondary training had been completed by 65%, and 30% had a postgraduate or professional degree. Most (56%) reported household income of $100,000 per year or more. Half (49%) reported that only essential services and businesses were operating in their region and 79% that schools were either completely closed or virtual only (with the remaining in-person or hybrid). Other measures included social distancing and limitations on gatherings. Most respondents had 1 (85%) or 2 (14%) children with FA, with mean age of 10.4 ± 5.6 years, on average age 8.3 ± 5.3 years from diagnosis. Parent-reported biological sex was fairly evenly distributed between males (56%) and females (44%). Most respondents perceived their child’s FA as severe (75%) rather than mild or moderate, and 70% reported a history of anaphylaxis. The most frequently reported allergen was peanuts (80%) followed by tree nuts (56%), eggs (34%), milk (34%), sesame (20%), soy (10%), shellfish (9%), fish (8%), wheat (7%), mustard (2%), and others (21%). With respect to multiple FAs, 32% of the respondents reported that their child had to avoid 1 to 2 foods; 31%, 3 to 6 foods; 10%, 7 to 9 foods; and 28%, 10 or more. Approximately one-third (36%) reported a history of asthma.

With respect to overall stress and anxiety, 67% of the respondents reported an increase that they attributed to COVID-19, whereas only 28% reported increased FAA owing to COVID-19 (P < .001). Most respondents reported unchanged (30%) or decreased (42%) FAA attributable to COVID-19, even among those with increased overall anxiety (in whom FAA was decreased or unchanged in 35% and 24%, respectively). Significant predictors of parent-reported increased FAA owing to COVID-19 were increased overall anxiety (OR, 3.29 [2.46-4.41], P < .001), non-nut allergies (OR, 2.86 [1.4-5.5]), prior emergency department visits (OR, 2.50 [1.23-5.09], P = .01), and greater than 2 foods avoided owing to FA (OR, 1.44 [1.14-1.81], P = .002) but not parent or child demographics or other medical factors.

With respect to aspects of FAA measured by IMPAACT, participants reported that the pandemic was associated with a decrease in all FAA dimensions, with the greatest reductions related to worries about unfamiliar places and management of allergic reactions by other caregivers. Compared with before COVID-19, parents reported improvement in all items and reduced interference with functioning in all domains, except for worry about finding specific “safe” foods at the grocery store. Current vs retrospective (pre–COVID-19) report of anxiety-related symptoms increased slightly based on General Anxiety Disorder—7 total score (6.2 ± 5.7 vs 5.4 ± 4.9, d = 0.15, P = .01), less than the reported minimal clinically important difference of 4. However, current vs retrospective IMPAACT score was significantly lower (89 ± 37 vs 105 ± 35, d = −0.44, P < .001). The minimal clinically important difference for IMPAACT has not yet been determined. Qualitative responses included both positive and negative impacts as described and integrated with quantitative findings in Table 1.

This study has several limitations, including sampling bias associated with online surveys and lack of demographic representativeness given high education and income levels. Data on racialized identity were not collected and must be addressed by future work, together with parents’ personal medical histories including that of FA. Given concerns about safe food availability and limited access to medical care identified herein, it is likely that families of children and youth who experience food insecurity and systemic discrimination remain disproportionately affected. More work is required to address the effects of sociodemographic and systemic factors on FA management during COVID-19.

Taken together, these data suggest that in a population of parents attributing increased overall anxiety to the COVID-19 pandemic, FAA was largely unchanged or decreased. Existing measures for general anxiety and self-report of pandemic-related anxiety failed to capture the dimensions of FAA. Parents attributed decreased worry to increased control over exposures and reduced risk of allergic reactions. Thus, the pandemic may have unique impacts on emotional distress in families of children with chronic conditions, particularly when anxiety is alleviated by public health restrictions. Further studies should evaluate methods for identifying families requiring additional support, particularly with iterative implementation and relaxation of restrictions as new variants emerge. These families will require close follow-up with primary and potentially specialist care providers with resources offered for mental health support as restrictions are relaxed, particularly given the likelihood for increasing FAA in association with typical daily exposures.
Most respondents reported unchanged or decreased FAA with COVID-19. Worry about severe reactions was lower during COVID-19 than prepandemic (d = 1.6, \( P < .001 \)).

“...eat, not going to parties, not going to grandparents, not going to school, or anywhere that used to cause the anxiety about potential accidental allergen exposure.”

Integration: Increased time at home and in the care of parents concomitant with fewer social activities allowed for increased parental control over potential allergen exposures (QUAL, QUAN), which was the most frequently reported mechanism to explain reduced worry about allergic reactions (QUAL, QUAN) and fewer allergy-related avoidance behaviors (QUAN).

Shared experience of “being cautious”

Relief regarding increased hygiene “...no birthday parties for which I need to be ‘that mom’ who sends her kid with their own cupcake and has to have a conversation with the hosting family.”

Integration: Decreased impact of FAA on relationships and daily activities/stress (QUAN) was consistent with participants’ reports of less frequently needing to explain themselves and their child’s restrictions to others (QUAL). This was largely owing to normalized/required avoidance of physical interaction associated with public health restrictions and perceived increased understanding of their situation owing to a now shared experience of environmental risk (QUAL). Decreased worry about allergic reactions during COVID-19 (QUAN) may also be partially explained by the perception that increased attention to hygiene/cleaning would protect from allergen cross-contamination (QUAL).

Difficulty finding scarce resources

Usual safe foods out of stock in grocery stores; unknown ingredients in alternate foods; limited epinephrine autoinjector availability.

“The most difficult part is when all my sons ‘safe foods’ are out of stock. ...It isn’t easy to just grab whatever is left on the shelves, as they usually have a ‘may contain’ label.”

Integration: Not being able to find specific “safe” (allergen-free) foods at the grocery store was the only aspect of FAA that increased overall with COVID-19 (QUAN); this was associated with potential and actual shortages of regular food products and stress associated with needing to carefully read labels of unknown products, particularly for children with non-nut allergies (QUAL). Concerns about food availability may partially explain why parents of children with non-nut allergies were more likely to report increased FAA attributable to the COVID-19 pandemic (QUAL).

Interactions between FA and ED

Increased risk of infection in the ED if care is needed for patient if not treated adequately for anaphylaxis.

“Initially when things shut down there was great fear about a possible 24 (19) reaction and having to go to ER.”

Prior ED visits were significant predictor of parent-reported increased FAA attributed to COVID-19.
I worry about her having a severe reaction and needing to go to the hospital, possibly increasing her risk of getting COVID-19. “I know COVID is more survivable than anaphylaxis, so I am really working on separating those in my mind to calm down.” “Since food allergies are often linked to asthma, I do worry about my daughter who has had to use a puffer on many occasions…” “I also don’t know how COVID impacts allergy kids, so that increases my stress.”

Integration: Fear of the consequences of having to attend hospital—in particular, the risk of acquiring COVID-19 in the ED (QUAL)—may explain why previous ED visits were associated with parent report of increased FAA attributable to COVID-19 (QUAN). Concerns about potential allergic reactions (and therefore ED visits) in response to new foods or when introducing foods for other children did not decline as much as other aspects of FAA with COVID-19 (QUAN), perhaps because of fear of the risks involved in seeking medical care (QUAL) or concerns it would not be available (see “Unavailable medical care”).

Table 1 (Continued)

| Theme | Category | Impact on FAA | Description | Examples | Frequency, n (%) | Related quantitative findings |
|-------|----------|---------------|-------------|----------|-----------------|-----------------------------|
| COVID-19 health risks | | anaphylaxis; concern about unknown direct effects of COVID-19 infection and interactions with asthma or allergies in children with FA. | “I worry about her having a severe reaction and needing to go to the hospital, possibly increasing her risk of getting COVID-19.” “I know COVID is more survivable than anaphylaxis, so I am really working on separating those in my mind to calm down…” “Since food allergies are often linked to asthma, I do worry about my daughter who has had to use a puffer on many occasions…” “I also don’t know how COVID impacts allergy kids, so that increases my stress.” | | COVID-19. The magnitude of reduction in hesitation about food introduction for younger children and avoidance of foods beyond identified allergens were 2 aspects of FAA queried that did not decrease to the same extent as other FAA-related items during the COVID-19 pandemic. |

Integration: Not applicable; major QUAL finding only. This category represents recognition by parents of the potential perpetuating role of avoidance in FAA and possible impacts on both FA-related distress and family functioning with loosening of public health restrictions and increased potential exposures.

| Decreased support | Unavailable medical care | Increased availability of pediatric allergist assessment, food challenges, and OIT; possibly limited availability of emergency services in the event of a severe reaction. | “We are on the waitlist for OIT to begin… & fear that this pandemic has delayed the chances of accessing it indefinitely.” “My baby was just diagnosed by our doctor but we are doing a video call with the allergist instead of going to his office. I am also worried that testing won’t happen or that more tests than normal will happen in one appointment to reduce the amount of appointments.” “Worry if he was to have an anaphylactic reaction, we would not be able to get him the help we need in a timely manner.” | 5 (4) | No direct quantitative data; this category reflects parental recognition of reduced risk of allergen exposure and associated stressors during COVID-19, with the potential to increase as public health restrictions and associated psychosocial circumstances change. |

Integration: In addition to the risk of COVID-19 infection (see “Interactions between FA and COVID-19 health risks”), worry about lack of available emergency care (QUAL) may further explain why previous ED visits were associated with increased FAA during COVID-19 (QUAL). Concerns regarding lack of FA assessment and treatment related to reduced in-person medical care were restricted to QUAL findings.

| Lack of FA awareness and accommodation | | Sense of social isolation and minimal understanding by others of challenges associated with managing FA, including shopping during the pandemic; concern regarding preoccupation of others (including restaurant staff) with COVID-19 to neglect of FA considerations. | “Grocery shopping is more difficult. I need time to read the labels and always feel rushed because people are impatiently waiting to come down the grocery aisles behind me.” “It begs the question if, just like seniors had special hours for grocery shopping at some point - people with food allergies should be prioritized, as their choices of food are limited.” “Are gloves changed?? Is cross contamination an issue now?? The workers are stressed in the restaurants - are they also having trouble keeping it all straight - are they rushing not to touch things - are their glasses fogging up - so many issues.” | 6 (5) | See “Difficulty finding scarce resources” |

Integration: Despite an overall decrease in FAA and perception of associated risk (QUAL), some respondents were more concerned that the predominant focus on COVID-19 risk would lead to more carelessness in handling of allergens (QUAL). Some respondents also suggested that specific accommodations were needed for grocery shopping owing to store rules about not touching products (thus, making label-reading difficult) and described stress related to other shoppers’ impatience in this context (QUAL), consistent with increased worry about finding “safe” foods at the grocery store (QUAL).

Abbreviations: COVID-19, coronavirus disease 2019; ED, emergency department; ER, emergency room; FA, food allergy; FAA, food allergy-specific anxiety; OIT, oral immunotherapy; QUAL, qualitative; QUAN, quantitative.

*n = 126 total free-text responses (43% of 293 participants); categories comprising 5 or more responses are illustrated.

*Cohen’s d calculated using the sample SD of the mean difference/reduction for each item during COVID-19 compared with retrospective report before the pandemic (negative values indicate higher/worsening score during COVID-19 whereas positive values suggest improvement). Note that frequency/agreement was rated on a 7-point Likert scale for each item as described in the text and previously.°

°Integration provides a summary of convergent quantitative (QUAL) and qualitative (QUAL) findings and use of qualitative data for elaboration/illustration.
A case of coronavirus disease 2019 messenger RNA vaccine tolerance and immune response despite presence of anti-polyethylene glycol antibodies

The role of anti-polyethylene glycol (PEG) immunoglobulin (Ig)M, IgG, or IgE antibodies in coronavirus disease 2019 (COVID-19) messenger RNA (mRNA) vaccine anaphylaxis is unknown. We highlight a case with preexisting anti-PEG antibodies that tolerated vaccination.

A 60-year-old woman with debilitating gout experienced HLA-B*58:01-restricted allopurinol drug reaction with eosinophilia and systemic syndrome. After 2 years, following therapeutic failure with febuxostat, pegloticase was trialed. After 12 days from initial infusion, she developed angioedema and a diffuse erythematous pruritic rash. She self-treated with diphenhydramine, but symptoms persisted for 2 days. She then developed shortness of breath and throat constriction, requiring antihistamines and systemic steroids from an outside emergency department. She was later discharged with steroids, and symptoms resolved after 7 days. After 7 months, she had negative results from skin prick test (SPT) and intradermal test (IDT) to PEG3350. She was not sure to pegloticase and then presence of anti-PEG IgE after her reaction to pegloticase in our patient remains unclear. However, the positive signal criterion is defined as "target beads MFI equal to 1.2 times control beads MFI (median fluorescence intensity) more than or equal to 1.2 times control beads MFI" and "free PEG inhibition reduces more than or equal to 50% of target beads MFI."1

Given the potential risk from anti-PEG IgE antibodies with future infusions, pegloticase desensitization was completed and followed by tolerance to 3 infusions, each 2 weeks apart.2 However, pegloticase was discontinued when hyperuricemia and gout symptoms persisted. After 6 weeks from desensitization, anti-PEG IgM was present. Anti-PEG IgG titer increased over 6 months after desensitization; however, results from PEG3350 SPT/IDT and PEG8000 SPT were negative (Table 1). After negative SPT/IDT results, she tolerated oral challenges with 0.17 g/1.7 g of PEG8000. She was not sure to pegloticase and then presence of anti-PEG IgE after her reaction to pegloticase in our patient remains unclear. However, the patient had confirmed absence of serum anti-PEG IgE before exposure to pegloticase and then presence of anti-PEG IgE after her reaction. Therefore, the decision to desensitize before the next infusion of anti-PEG monoclonal antibody-conjugated cytometric bead array beads conjugated with pegloticase as the target antigen.1 The control beads were conjugated with the same anti-PEG antibodies without pegloticase.1 The positive signal criterion is defined as "target beads MFI (median fluorescence intensity) more than or equal to 1.2 times control beads MFI" and "free PEG inhibition reduces more than or equal to 50% of target beads MFI."1

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References

1. Samji H, Wu J, Ladak A, Vossen C, Stewart E, Dove N, et al. Review: mental health impacts of the COVID-19 pandemic on children and youth - a systematic review. Child Adolesc Ment Health. 2022;27(2):173–189.
2. Abrams EM, Greenhawt M, Shaker M, Pinto AD, Sinha I, Singer A. The COVID-19 pandemic: adverse effects on the social determinants of health in children and families. Ann Allergy Asthma Immunol. 2022;128(1):19–25.
3. D’Auria E, Anania C, Cuomo B, Decimo F, Indirli GC, Mastrollirri V, et al. COVID-19 and food allergy in children. Acta Biomed. 2020;91(2):204–206.
4. Pu Ozvyigit I, Khalil C, Choudhry T, Williams M, Khan N. Anaphylaxis in the emergency department unit: before and during COVID-19. Allergy. 2021;76(8):2624–2626.
5. Chen G, DunnGalvin A, Campbell DE. Impact of COVID-19 pandemic on quality of life for children and adolescents with food allergy. Clin Exp Allergy. 2022;52(1):162–166.
6. Westwell-Roper C, To S, Andjelic G, Lu C, Lin B, Soller L, et al. Food-allergy-specific anxiety and distress in parents of children with food allergy: a systematic review. Pediatr Allergy Immunol. 2022;33(1):e13965.
7. To S, Westwell-Roper C, Soller L, Evelyn Stewart S, Chan ES. Development of IMPAACT (Impairment Measure for Parental Food Allergy-Associated Anxiety and Coping Tool), a validated tool to screen for food allergy-associated parental anxiety [e-pub ahead of print]. Ann Allergy Asthma Immunol. 2022. https://doi.org/10.1016/j.anl.2022.03.011, accessed March 4, 2022.
8. Toussaint A, Hüsing P, Gumpa Z, Winginfeld K, Harter M, Schramm E, et al. Sensitivity to change and minimal clinically important difference of the 7-item Generalized Anxiety Disorder Questionnaire (GAD-7). J Affect Disord. 2020;265:395–401.
9. Greenwell TJ, Plano Clark VL. Designing and Conducting Mixed Methods Research. 3rd ed. SAGE Publications; 2017.
10. Greeneheim UH, Lindgren BM, Lundman B. Methodological challenges in qualitative content analysis: a discussion paper. Nurse Educ Today. 2017;56:29–34.