











MARIA BERNADETTE CILONA¹ , GIUSEPPE ALVISE RAMIREZ¹ , CHIARA ASPERTI¹ ,
ARIANNA FERLITO¹ , GIOVANNI BENANTI¹ , SERENA NANNIPIERI¹ ,
RAWAD MANSOUR ABDUL HADI², CARLO CAPELLINI² , LORENZO DAGNA^{1,2} ,
MARCELLO COTTINI³ , MONA-RITA YACCOUB¹ 

Impact of asthma on severe food-induced allergic reactions: a systematic review and meta-analysis

¹Unit of Immunology, Rheumatology, Allergy, and Rare Diseases, IRCCS San Raffaele Scientific Institute, Milan, Italy

²Vita-Salute San Raffaele University, Milan, Italy

³Allergy and Pneumology Outpatient Clinic, Bergamo, Italy.

KEY WORDS

Asthma; anaphylaxis; food allergy; risk factor; severe allergic reactions.

Corresponding author

Yacoub Mona-Rita
Unit of Immunology, Rheumatology, Allergy, and Rare Diseases
IRCCS San Raffaele Scientific Institute
via Olgettina 60
21132 Milan, Italy
ORCID: 0000-0003-2417-0410
E-mail: yacoub.monarita@hsr.it

Doi

10.23822/EurAnnACI.1764-1489.351

IMPACT STATEMENT

Patients with asthma and food allergy have an increased risk of severe, potentially fatal reactions. Optimizing management and prevention strategies is essential to reduce life-threatening events in this high-risk population.

Summary

Background. Food allergy can range from mild to severe, life-threatening reactions with various symptoms and organ involvement. The impact of asthma on severe food-induced allergic reactions is not completely understood. In the hypothesis that asthma increases the risk of severe food-induced allergic reactions, the aim of this study is to compare the incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma. **Methods.** We performed a systematic research on electronic databases, including PubMed, Scopus and Web of Science. Observational studies, studies reporting medical characteristics of patients diagnosed with food allergy and studies reporting medical history of patients with allergic reactions were included. The primary outcome was the incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma. **Results.** Eight studies with a total of 90,367 patients met the inclusion criteria and were included, with a total population of 28,166 of patients with food allergy. The incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma was increased (OR 1.28; 95% CI 1.03-1.59; $p = 0.03$; $I^2 = 59\%$). **Conclusions.** Individuals with both food allergy and asthma are at high risk of severe, potentially fatal allergic reactions. Healthcare professionals should prioritize prevention and management strategies for these subjects. Patients with asthma and food allergy are at increased risk of potentially fatal food-induced allergic reactions. Optimal management of both diseases is necessary to prevent potentially life-threatening events. **Study registration.** The protocol of this review was registered in PROSPERO (CRD42023448293).

Introduction

Food allergy is responsible for a variety of symptoms and disorders which can vary widely in severity ranging from mild to severe, potentially life-threatening reactions with multiple organ involvement (1). The prevalence of food allergy in the general population

ranges from approximately 1% to 10% and can vary depending on the specific geographical location or age group (2). Asthma is even more common, with approximately 262 million people worldwide suffering from this condition (3).

Despite the increasing prevalence of asthma and food allergy in general population, little is known about the coexistence of these

two diseases. In addition, there appears to be a significant rise in the incidence of asthma among individuals with severe food-induced allergic reactions (4). Understanding the potential link between asthma and food allergy is of paramount importance for several reasons. Indeed, there is growing evidence that asthma can potentially worsen severe food-induced allergic reactions through various immunoinflammatory mechanisms which can lead to more pronounced respiratory and systemic symptoms contributing to a high risk of life-threatening complications, including anaphylaxis (5). It is therefore necessary for clinicians to thoroughly investigate the simultaneous presence of both conditions in order to provide patients with the correct dietary indications and treatments for potentially life-threatening events.

In the hypothesis that asthma increased the risk of severe food-induced allergic reactions, the aim of this study is to compare the incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma in studies that investigate the characteristics of patients with severe food-induced allergic reactions.

Materials and methods

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (6). The review question was developed using the Population, Intervention or exposure, Comparison, Outcome framework (7): among patients with food allergy (P), those with history asthma (E), compared with patients without asthma (C), is increased the incidence severity reaction (O)? The protocol of this review was registered in PROSPERO (CRD42023448293).

Literature search

A systematic review of the literature was conducted to identify observational studies reporting medical characteristics of patients with food allergy. Electronic databases, including PubMed, Scopus and Web of Science were comprehensively searched to identify relevant studies up to July 2023. The search strategy involved using relevant keywords, Medical Subject Headings, and Boolean operators to capture relevant articles. The search string follows below:

((food[tiab]) OR (peanut [tiab]) OR (milk [tiab]) OR (wheat[tiab]) OR (seafood [tiab]) OR (crustac* [tiab]) OR (nut [tiab]) OR (fish [tiab])) AND ((allergic reaction [tiab]) OR (hypersensitivity [tiab]) OR (anaphyl* [tiab]))

No restrictions were applied regarding the publication date or languages.

Study selection

Two independent reviewers screened the titles and abstracts of the identified studies to assess their eligibility for inclusion. The full texts of potentially relevant studies were then retrieved and

further evaluated. Inclusion criteria for study selection were as follows: 1) observational studies (cohort studies, case-control studies, or cross-sectional studies); 2) studies reporting medical characteristics of patients diagnosed with food allergy; and 3) studies reporting medical history of patients with allergic reaction. Disagreements between the reviewers were resolved through discussion or consultation with a third reviewer.

Data extraction and synthesis

Data extraction was performed using a standardized data extraction form. Relevant information from each selected study was extracted, including study characteristics (*e.g.*, study design, sample size, and follow-up duration), participant characteristics (*e.g.*, age, gender, and food allergy diagnosis criteria), and outcomes of interest (*e.g.*, incidence of asthma in food allergy patients). Characteristics and reason for exclusion of major excluded studies were reported in **table IS**.

Data analysis

Data of the incidence of severe allergic reactions to food in patients with history of asthma was compared with patients without history of asthma in the entire cohort of selected studies. A qualitative analysis was also conducted to provide a comprehensive overview and synthesis of the findings from the included studies.

Ethical approval

As this study is a systematic review based on published literature, ethical approval was not required. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed during the conduct and reporting of this systematic review (6).

Outcomes

The primary outcome was the incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma.

Statistical analysis

Computations were performed with Review manager version 5.4.1. This meta-analysis was performed in compliance with PRISMA (8). We calculated pooled odds ratio (OR) for the primary and secondary outcomes and 95% confidence intervals (CI) using the Mantel-Haenszel method for dichotomous outcomes (9). The statistical heterogeneity hypothesis was evaluated with statistical significance set at the two-tailed 0.05 levels, whereas the extent of statistical consistency was quantified with Higgins and Thompson's I^2 . I^2 values around 25, 50, and 75% were considered respectively low, moderate, and severe statistical inconsistency ($I^2 > 50\%$ was used as a threshold indicating significant heterogeneity for individual studies) (10). Pooled data were analyzed using the inverse variance method with a fixed-effect model in case of low-moderate ($I^2 < 50\%$) statistical inconsistency or with a ran-

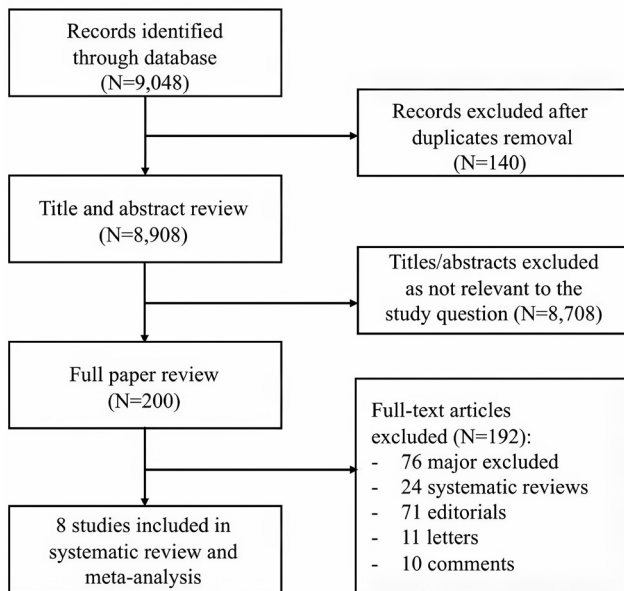
dom-effect model when the I^2 was above 50% (11). A P-value < 0.05 was considered statistically significant. The risk of bias was assessed by the tool Risk Of Bias In Nonrandomized Studies-of Interventions (ROBINS-I) (12). Results of pooled analyses were presented with forest plots. A sensitivity analysis was performed including only the studies that report unpooled data in the results.

Results

Characteristics of the studies

The research strategy of electronic databases detected 9,048 potentially relevant articles (figure 1).

Figure 1 - PRISMA flow diagram showing literature search results.



Eight studies with a total of 90,367 patients met the inclusion criteria and were included, with a total population of 28,166 of patients with food allergy (13-17). All studies were conducted between February 2005 and January 2022, including data of patients from 1990 and 2020. Five studies were conducted in Europe (13, 15, 18-20), three in United States (14, 16, 17). Six studies were retrospective observational studies (14, 15, 17, 18-20), two were prospective (13, 16). Five studies were multicentric (13, 15, 16, 18, 20). Three studies included only children (13, 17, 19), the other studies both adults and children (14-16, 18, 20). Five studies included only patients with food allergy (13, 15-17, 19), while three studies included patients with history of anaphylactic reactions also to other agents (14, 18, 20). Two studies defined severity of food-induced reaction according to Ring and Messmer grading scale for anaphylactic reactions (18, 20). One study used Sampson’s grading system to identify the level of severity of food-induced allergic reactions (13). One study used Mueller’s scale to identify the severity of anaphylaxis (19). One study defined severe anaphylaxis as an index event requiring hospitalization and identified severity of anaphylaxis as an index event resulting into cardiorespiratory failure or the need of cardiorespiratory/resuscitative intervention (14). Three studies defined the degree of severity of allergic reactions according to level of multisystem organ involvement (15-17) (table IIS). Majority of studies had a low risk of bias (figure 1S). Characteristics of the studies are reported in table I.

Outcome

The incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma was increased (OR 1.28; 95%CI 1.03-1.59; p = 0.03; $I^2 = 59%$, figure 2).

We performed a sensitivity analysis including only the studies that report unpooled data in the results (706/4,427 [15.9%] vs 2,558/18,589 [13.8%]; OR 1.26; 95%CI 0.98-1.63; p = 0.07; $I^2 = 66%$, figure 3).

Figure 2 - The incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma.

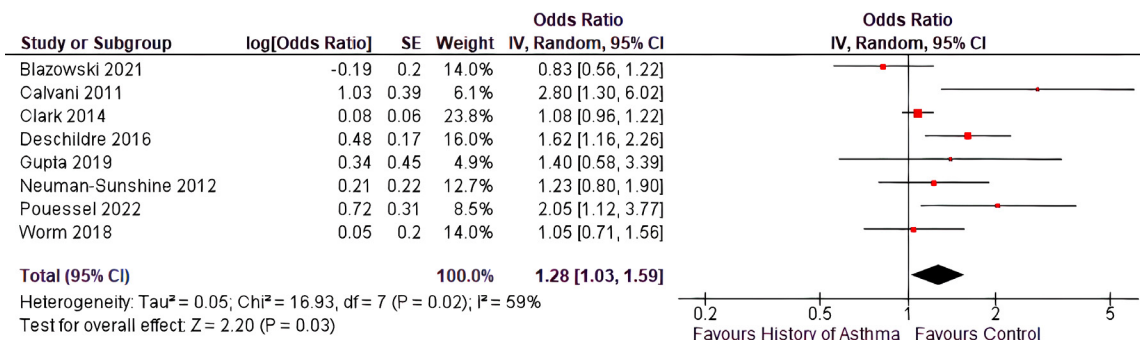


Table I - Characteristics of included studies.

Study	Country	Population	n of patients	Number of patients with food allergy (%)	Number of severe food-induced allergic reactions (%)	Number of patients with asthma (%)	Number of patients without asthma (%)
Calvani <i>et al.</i> (2011) (13)	Italy	Children with food allergy, 0-18 years	163	163 (100%)	36 (22%)	59 (36%)	104 (64%)
Clark <i>et al.</i> (2014) (14)	United States	Adults requiring hospitalization for anaphylaxis, no age limitation	36,943	11,972 (32%)	2,622 (7%)	1,822 (5%)	10,150 (27%)
Deschildre <i>et al.</i> (2015) (15)	France	Peanut-allergic children ≤ 6 years; school age children 6-12 years; teenagers, 12-16 years; adults ≥ 16 years	669	669 (100%)	202 (30%)	381 (57%)	288 (43%)
Gupta <i>et al.</i> (2019) (16)	United States	Adults with suspected food allergy ≥18 years	40,443	4,368 (11%)	2,228 (51%)	NR	NR
Neuman-Sunshine <i>et al.</i> (2011) (17)	United States	Children with peanut allergy, 0-16 years	782	782 (100%)	443 (57%)	436 (56%)	346 (44%)
Worm <i>et al.</i> (2018) (18)	Germany	Individuals with immediate hypersensitivity reactions, 0-93 years	7,316	7,316 (100%)	187 (3%)	1,125 (15%)	6,191 (85%)
Blazowski <i>et al.</i> (2021) (19)	Poland	Children with food-induced acute allergic reaction, 0-18 years	541	421 (78%)	175 (32%)	223 (41%)	198 (37%)
Pouessel <i>et al.</i> (2022) (20)	France	Children and adults patients with anaphylactic reactions	3,510	2,475 (71%)	42 (1.7%)	817 (33%)	1,658 (77%)

Funnel plot show less heterogeneity in both analyses in terms of size and effect estimates of included studies (figures 4, 5).

Discussion

The main finding of this study is that there is a significant association between history of asthma and the incidence of severe

food-induced allergic reactions. However, the results of the sensitivity analysis did not reach statistical significance. Individuals with asthma have an increased risk of 28% to experience severe food-induced allergic reactions compared to those without a history of asthma. The results of the sensitivity analysis, which included only studies reporting unpooled data, confirm the direction and the magnitude of the primary analysis, although they

Figure 3 - The incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma, including only the studies reporting unpooled data.

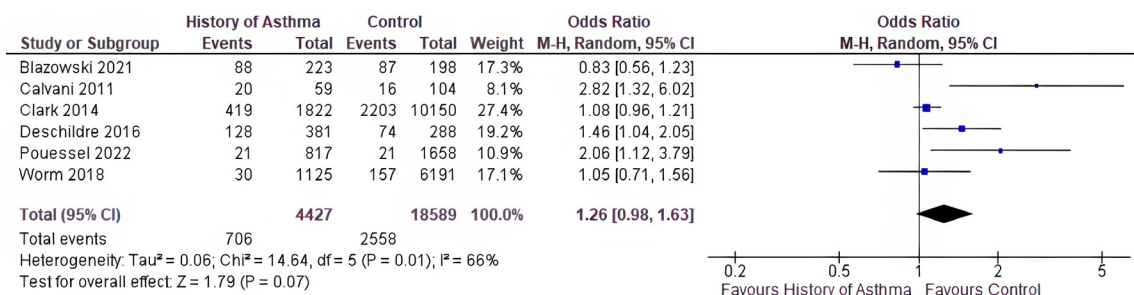


Figure 4 - Funnel plot of the primary outcome measure: incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma.

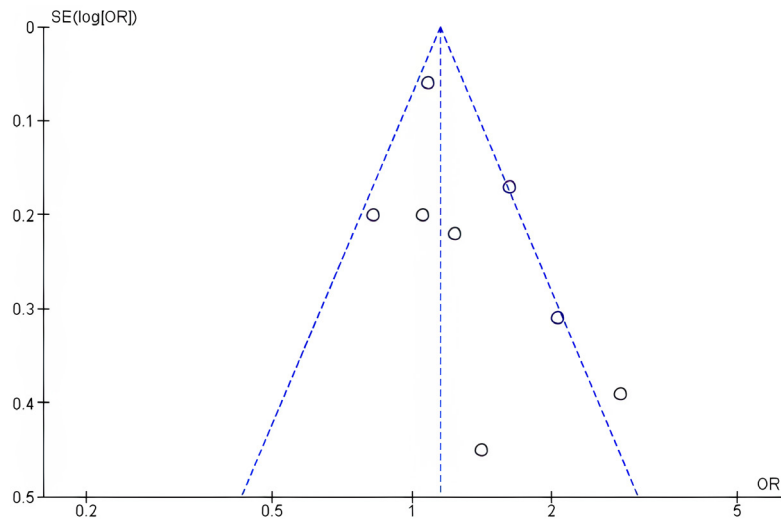
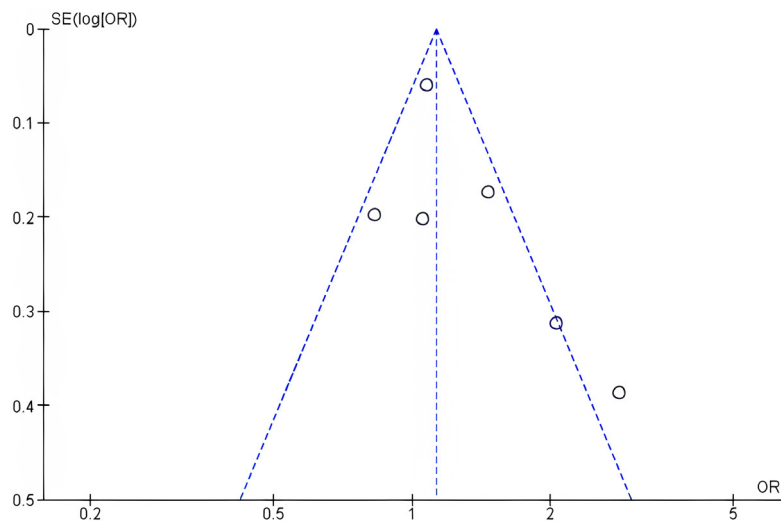


Figure 5 - Funnel plot of the sensitivity analysis: incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma, including only the studies reporting unpooled data.



report only a trend consistent with the initial finding. One of the main reasons for the mismatch between the main analysis and the sensitivity analysis is likely the inclusion of a heterogeneous population in terms of asthma control and severity. Included studies did not distinguish between controlled and uncontrolled asthma, resulting in a heterogeneous population. Although it is not possible to confirm this from our analysis results, it is plausible that uncontrolled asthma makes individuals more susceptible to severe reactions compared to controlled asthma. Another reason

was the reduction in sample size, which decreased the statistical power and led to non-significant results in the sensitivity analysis. The funnel plot analysis indicates less heterogeneity in terms of study size and effect estimates among studies included, providing additional support for the validity of the results.

Turner *et al.* in their meta-analysis reported that asthma increases the risk of severe allergic reactions to food, consistent with our analysis (21). However, they included studies that did not clearly report data specifically related to the population of interest. In-

deed, Motosue *et al.* did not report specific data on exclusively food-induced allergic reactions in asthmatic population (22). The same was observed for Olabbari and colleagues who considered history of asthma as a risk factor for all the anaphylactic events and not specifically food-induced reactions (23). Furthermore, Versluis *et al.* in their prospective cohort study did not include subjects with a clinically defined diagnosis of asthma (24). Finally, Gabrielli *et al.* did not report data on the prevalence of asthma in subjects with severe allergic reactions, but exclusively in individuals with mild and moderate reactions (25). In addition, Turner and colleagues did not report which of these individuals developed severe allergic reactions (21). We included these studies as major excluded studies, despite they could have empowered our message. A particularly impactful finding is that among a cohort of 32 children who died due to food-induced allergic reactions, 24 of them had a definitive diagnosis of asthma (26). Similarly, in a separate cohort of 12 children with fatal reactions, all of them had a history of asthma (27).

The present findings have important clinical implications. They highlight the need for increased awareness and vigilance among healthcare professionals in managing individuals with both asthma and food allergies. Patients with asthma should be closely monitored and educated about the potential risks of severe food-induced allergic reactions. Although not addressed in our review, the association between asthma and severe food-induced allergic reactions could be mediated by reduced respiratory reserve in asthmatic individuals. It can be assumed that patients with uncontrolled asthma may be more susceptible to experience severe allergic reactions to food. Indeed, the latest updated GA2LEN guideline 2022 on management and treatment of food allergy report that it is good practice to optimize asthma control in people with food allergy as this reduces morbidity and mortality due to asthma (28). However, they report that the evidence on optimizing asthma control to reduce the risk of severe food-induced allergic reactions is unclear with low level of evidence for all good practice statements. In addition, they did not address that all asthmatic patients have an increased risk of severe allergic reactions, but they only hypothesized that uncontrolled asthma could be related to severe allergic reactions. EAACI guidelines emphasize that asthma is a risk factor for experiencing anaphylaxis in the context of food allergy and that reactions in individuals with severe asthma are a factor to consider for prolonged observation following anaphylaxis (29). These recommendations may act as a confounding factor in observational studies, leading to increased vigilance among clinicians and patients. This heightened awareness could potentially result in a lower prevalence of severe allergic reactions in asthmatic individuals, masking their heightened susceptibility. The underlying mechanisms linking asthma and increased susceptibility to severe food-induced allergic reactions need further investigations. It is possible that chronic airway inflammation and bronchial

hyperresponsiveness in asthma contribute to the exaggerated immune response seen in food allergies (30). Understanding these mechanisms could potentially lead to the development of targeted interventions to mitigate the risk of severe reactions in individuals with both diseases. Targeting this specific population to prevent asthmatic exacerbations may have dual benefits by addressing the underlying mechanisms of both food reactions and asthma, given the bidirectional relationship between these two conditions (4). Indeed, pharmacological interventions, such as omalizumab, which have a dual impact on both food allergy and asthma, may elicit a synergistic effect in the treatment of these two conditions (30). Moreover, strategies for prevention, early recognition, and prompt treatment of allergic reactions should be emphasized in this high-risk population. One of the major clinical implication of our study is to emphasize the significance of ensuring that asthmatic patients with food allergies receive adequate chronic asthma treatment to effectively prevent severe allergic reactions. The current indications for oral immunotherapy for food allergy do not specifically mention individuals with asthma, indicating that the association between asthma and the high risk of severe food-induced allergic reactions is not yet fully understood (31). Further research and investigation are needed to better understand the potential benefits in terms of prevention for individuals with coexisting asthma. Moreover, the current algorithm for the administration of self-injectable adrenaline in patients with food allergies does not include individuals with concomitant diagnosis of asthma (32). These individuals may represent the ideal population for desensitization strategies and for the prescription of adrenaline auto-injectors in out-of-hospital setting, as these interventions play a crucial role in reducing the risk of life-threatening allergic reactions and improving their overall quality of life.

To the best of our knowledge, our review includes the latest available evidence regarding the impact of asthma on significant patient-centered outcomes. Notably, it includes recent and significant data that may contribute to a more precise estimation and interpretation of treatment effects. A notable strength of our study lies in its focused examination of a single outcome, the incidence of severe food-induced allergic reactions in patients with history of asthma compared with patients without history of asthma in studies that investigate the characteristics of patients with severe food-induced allergic reactions. This approach reinforces and emphasizes the crucial role and impact of asthma on the level of severity of these reactions. In this way, our study provides a clear and robust understanding of the association between asthma and the risk of potentially fatal food-induced allergic reactions. The methodological strengths of this review are attributed to its clear research question, specific population, defined interventions, and comparators. In addition, we performed a sensitivity analysis that exclusively considered studies with unpooled data, further enhancing the reliability of our findings.

However, it is important to acknowledge certain limitations associated with this review. First, the included studies used different classification systems to define the level of severity of food-induced allergic reactions, which could potentially influence the overall results. One important limitation is the lack of distinction between various levels of asthma severity in relation to the primary outcome. However, the data available in the included manuscripts did not allow for a distinction between patients with controlled and uncontrolled asthma. It is plausible that patients with uncontrolled asthma are more susceptible to severe allergic reactions; further research are needed to address this topic. Additionally, factors such as age, concomitant allergies, and specific food allergens were not considered in subgroup analysis, as the included manuscripts did not provide the necessary data. Further studies with larger sample sizes, different populations, and comprehensive patient characteristics would provide better understanding of the relationship between asthma and severe food-induced allergic reactions.

Conclusions

This study provides strong evidence that individuals with both food allergy and asthma might be at high risk of severe, potentially life-threatening food-induced allergic reactions. Healthcare professionals should be aware of this association and take appropriate measures to prevent and manage these potentially fatal reactions. Further studies are needed to investigate the underlying mechanisms and empower management and treatment strategies for individuals with both asthma and food allergy.

Fundings

None.

Contributions

MBC: conceptualization, writing – original draft, data curation, methodology, formal analysis, validation. GAR: writing – review & editing, visualization, validation. CA, AF, GB, SN, RMAH, CC: writing – review & editing, data extraction, validation. LD, MC, MRY: conceptualization, writing – review & editing, supervision, methodology, validation.

Conflict of interests

The authors declare that they have no conflict of interests.

References

- Anvari S, Miller J, Yeh CY, Davis CM. IgE-Mediated Food Allergy. *Clin Rev Allergy Immunol.* 2019;57(2):244-60. doi: 10.1007/s12016-018-8710-3.
- Warren CM, Jiang J, Gupta RS. Epidemiology and Burden of Food Allergy. *Curr Allergy Asthma Rep.* 2020;20(2):6. doi: 10.1007/s11882-020-0898-7.
- GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet.* 2020;396(10258):1204-22. doi: 10.1016/S0140-6736(20)30925-9.
- Emons JAM, Gerth van Wijk R. Food Allergy and Asthma: Is There a Link? *Curr Treat Options Allergy.* 2018;5(4):436-44. doi: 10.1007/s40521-018-0185-1.
- Foong RX, du Toit G, Fox AT. Asthma, Food Allergy, and How They Relate to Each Other. *Front Pediatr.* 2017;5:89. doi: 10.3389/fped.2017.00089.
- Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ.* 2021;372:n71. doi: 10.1136/bmj.n71.
- Higgins JP, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, et al. *Cochrane handbook for systematic reviews of interventions.* 2017. Hoboken, NJ: John Wiley & Sons. doi: 10.9781119536604.
- Moher D, Liberati A, Tetzlaff J, Altman DG; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *Ann Intern Med.* 2009;151(4):264-9, W64. doi: 10.7326/0003-4819-151-4-200908180-00135.
- Davies HT, Crombie IK, Tavakoli M. When can odds ratios mislead? *BMJ.* 1998;316(7136):989-91. doi: 10.1136/bmj.316.7136.989.
- Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. *BMC Med Res Methodol.* 2014;14:135. doi: 10.1186/1471-2288-14-135.
- Higgins JP, Thompson SG, Deeks JJ, Altman DG. Measuring inconsistency in meta-analyses. *BMJ.* 2003;327(7414):557-60. doi: 10.1136/bmj.327.7414.557.
- Sterne JA, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. *BMJ.* 2016;355:i4919. doi: 10.1136/bmj.i4919.
- Calvani M, Cardinale F, Martelli A, Muraro A, Pucci N, Savino F, et al. Italian Society of Pediatric Allergy and Immunology Anaphylaxis Study Group. Risk factors for severe pediatric food anaphylaxis in Italy. *Pediatr Allergy Immunol.* 2011;22(8):813-9. doi: 10.1111/j.1399-3038.2011.01200.x.
- Clark S, Wei W, Rudders SA, Camargo CA Jr. Risk factors for severe anaphylaxis in patients receiving anaphylaxis treatment in US emergency departments and hospitals. *J Allergy Clin Immunol.* 2014;134(5):1125-30. doi: 10.1016/j.jaci.2014.05.018.
- Deschildre A, Elegbédé CF, Just J, Bruyère O, Van der Brempt X, Papadopoulos A, et al. Peanut-allergic patients in the MIRABEL survey: characteristics, allergists' dietary advice and lessons from real life. *Clin Exp Allergy.* 2016;46(4):610-20. doi: 10.1111/cea.12681.
- Gupta RS, Warren CM, Smith BM, Jiang J, Blumenstock JA, Davis MM, et al. Prevalence and Severity of Food Allergies Among US Adults. *JAMA Netw Open.* 2019;2(1):e185630. doi: 10.1001/jama-networkopen.2018.5630.
- Neuman-Sunshine DL, Eckman JA, Keet CA, Matsui EC, Peng RD, Lenehan PJ, et al. The natural history of persistent peanut

- allergy. *Ann Allergy Asthma Immunol.* 2012;108(5):326-31.e3. doi: 10.1016/j.anai.2011.11.010.
18. Worm M, Francuzik W, Renaudin JM, Bilo MB, Cardona V, Scherer Hofmeier K, et al. Factors increasing the risk for a severe reaction in anaphylaxis: An analysis of data from The European Anaphylaxis Registry. *Allergy.* 2018;73(6):1322-30. doi: 10.1111/all.13380.
 19. Błażowski, Ł, Kurzawa, R, Majak P. The usefulness of molecular diagnosis in the assessment of the aetiology, clinical phenotypes and risk of food-induced anaphylaxis in children. *Pediatr Med Rodz.* 2021;17(2):121-31. doi: 10.15557/PiMR.2021.0020.
 20. Pouessel G, Alonzo S, Divaret-Chauveau A, Dumond P, Bradatan E, Liabeuf V, et al. Allergy-Vigilance® Network. Fatal and near-fatal anaphylaxis: The Allergy-Vigilance® Network data (2002-2020). *Allergy.* 2023;78(6):1628-38. doi: 10.1111/all.15645.
 21. Turner PJ, Arasi S, Ballmer-Weber B, Baseggio Conrado A, Deschil-dre A, Gerdtts J, et al. Global Allergy, Asthma European Network (GA2LEN) Food Allergy Guideline Group. Risk factors for severe reactions in food allergy: Rapid evidence review with meta-analysis. *Allergy.* 2022;77(9):2634-52. doi: 10.1111/all.15318.
 22. Motosue MS, Bellolio MF, Van Houten HK, Shah ND, Campbell RL. Risk factors for severe anaphylaxis in the United States. *Ann Allergy Asthma Immunol.* 2017;119(4):356-61.e2. doi: 10.1016/j.anai.2017.07.014.
 23. Olabbari M, Vazquez P, Gonzalez-Posada A, Sanz N, Gonzalez-Peris S, Diez N, et al. Risk Factors for Severe Anaphylaxis in Children. *J Pediatr.* 2020;225:193-97.e5. doi: 10.1016/j.jpeds.2020.06.021.
 24. Versluis A, van Os-Medendorp H, Blom WM, Michelsen-Huisman AD, Castenmiller JJM, Noteborn HPJM, et al. Potential cofactors in accidental food allergic reactions are frequently present but may not influence severity and occurrence. *Clin Exp Allergy.* 2019;49(2):207-15. doi: 10.1111/cea.13282.
 25. Gabrielli S, Clarke A, Morris J, Eisman H, Gravel J, Enarson P, et al. Evaluation of Prehospital Management in a Canadian Emergency Department Anaphylaxis Cohort. *J Allergy Clin Immunol Pract.* 2019;7(7):2232-38.e3. doi: 10.1016/j.jaip.2019.04.018.
 26. Bock SA, Muñoz-Furlong A, Sampson HA. Fatalities due to anaphylactic reactions to foods. *J Allergy Clin Immunol.* 2001;107(1):191-3. doi: 10.1067/mai.2001.112031.
 27. Pumphrey RS, Roberts IS. Postmortem findings after fatal anaphylactic reactions. *J Clin Pathol.* 2000;53(4):273-6. doi: 10.1136/jcp.53.4.273.
 28. Muraro A, de Silva D, Halken S, Worm M, Khaleva E, Arasi S, et al. GA2LEN Food Allergy Guideline Group; GALEN Food Allergy Guideline Group. Managing food allergy: GA2LEN guideline 2022. *World Allergy Organ J.* 2022;15(9):100687. doi: 10.1016/j.waojou.2022.100687.
 29. Muraro A, Worm M, Alviani C, Cardona V, DunnGalvin A, Garvey LH, et al. European Academy of Allergy and Clinical Immunology, Food Allergy, Anaphylaxis Guidelines Group (2022). EAACI guidelines: Anaphylaxis (2021 update). *Allergy.* 2022;77(2):357-77. doi: 10.1111/all.15032.
 30. Burman J, Palosuo K, Pelkonen A, Malmberg P, Remes S, Kukkonen K, et al. Bronchial hyperresponsiveness and asthma during oral immunotherapy for egg or peanut allergy in children. *Clin Transl Allergy.* 2022;12(10):e12203. doi: 10.1002/ct2.12203.
 31. Fiocchi A, Artesani MC, Riccardi C, Mennini M, Pecora V, Fierro V, et al. Impact of Omalizumab on Food Allergy in Patients Treated for Asthma: A Real-Life Study. *J Allergy Clin Immunol Pract.* 2019;7(6):1901-9.e5. doi: 10.1016/j.jaip.2019.01.023.
 32. Angier E, Choudhury D, Luyt D, Baker S, Warner A, Clark A, et al. Adrenaline auto-injector prescription for patients at risk of anaphylaxis: BSACI guidance for primary care. *Clin Exp Allergy.* 2023;53(9):951-54. doi: 10.1111/cea.14325.