RISK FACTORS ASSOCIATED WITH FOOD-INDUCED ANAPHYLAXIS IN ATOPIC CHILDREN, AGED 0-5 YEARS: A CASE-CONTROL STUDY

A project submitted in partial fulfilment of the requirement for the award of the degree of

BACHELOR OF NUTRITION AND DIETETICS

UNIVERSITY OF WOLLONGONG

by

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DEPARTMENT OF CLINICAL IMMUNOLOGY

ROYAL PRINCE ALFRED HOSPITAL

October 2007

ACKNOWLEDGEMENTS

I would like to thank all the staff at the RPAH Allergy Unit for all their advice and encouragement throughout my project. You have all contributed immensely, not only to my project but my experience at RPAH.

A special thank you to Katherine, who was my primary source of stress and support throughout my project. Your time and knowledge was invaluable to me throughout.

Thank you to Velencia and Rob for giving me the opportunity to work with individuals as invaluable as yourselves, your knowledge and passion for your work is mind-blowing.

Many thanks to Anne for being so approachable and being the 'glue' when I became unstuck. Your cheerful smile and encouragement throughout was never unnoticed.

Thank you to our lecturers Karen Walton and Kelly Lambert who have guided us through the semester. I now have a sudden passion for research that I never had before.

A very special thank you also to my project partner Rachel, for all the laughs and fun. This project would not have been the same without the great company.

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ABSTRACT

Introduction: The incidence of food allergy and occurrence of food-induced anaphylaxis is increasing. Understanding the epidemiology of anaphylaxis has been challenged by inconsistencies in definition, and lack of a universal grading system. This study defined anaphylaxis as 'a severe, life threatening allergic reaction, characterised by signs of cutaneous, gastrointestinal, respiratory and cardiovascular compromise'. To date, literature concerning anaphylaxis has primarily researched clinical symptoms, risk factors (typically asthma) and management associated with the reaction. The primary aim of this study was to determine risk factors associated with food-induced anaphylaxis, within an atopic population.

Methods: This retrospective case-control study was carried out at the RPAH Allergy Unit in Sydney. Children were recruited if they were atopic and aged 0-5 years on presentation at the Allergy Unit. The medical records of 672 subjects were reviewed and cases were identified, that is, if the child had a history of anaphylaxis according to our definition (n=218). The following variables were analysed: age and sex of the child, presence or history of eczema and asthma, number of positive SPT's to food and airborne allergens, and family size and sibling order of the child. Binary logistic regression was used to determine risk factors associated with anaphylaxis according to statistical significance ($p<0.05$).

Results: Age ($p=0.033$), eczema ($p=0.036$), positive SPT to more than one food allergen ($p=0.012$) and presence of an airborne allergy ($p=0.055$) were all statistically associated with risk of anaphylaxis. Other variables analysed did not show to be significant ($p>0.05$). Sibling order and the number of food allergies were excluded as variables ($p>0.8$).

Conclusion: Establishment of a universal grading system would enable better comparison of the results of this study with other studies. Future research within this population is required to confirm statistical significance or non-significance of nominated variables, and to address potential confounding variables related to determined risk factors.

INTRODUCTION

Recent studies suggest that the incidence of food allergy is increasing (Brown et al, 2006; Sampson et al, 1992), possibly attributed to changes in the environment and human nutrition, including an increase in novel foods and use of food proteins as ingredients (DunnGalvin et al, 2006). The prevalence of food-induced anaphylaxis is also rising, especially among children in their first 2 years of life (Wang and Sampson, 2007). Highly significant increases in admissions for systemic allergic disease including anaphylaxis and food allergy in both Australia (Brown, 2004) and internationally (Gupta et al, 2003; Sampson, 2003) almost certainly reflect an increase in incidence.

Food allergy is the most common cause of anaphylaxis in children (Muraro et al, 2007). Food reactions account for one-third of all anaphylactic reaction cases in emergency departments in Australia (Brown, 2004) with similar results reported in the United States (Sampson, 2003), and United Kingdom (Pumphrey, 2004). A three year retrospective case study in a Brisbane hospital emergency department found that food (56%) was the principle cause of anaphylaxis in children, with respiratory symptoms commonly reported (Braganza et al, 2006). A similar study in Italy found that food caused 57% of anaphylaxis episodes in atopic children, 30% attributed to fish (Novembre et al, 1998).

Understanding of the epidemiology of anaphylaxis has been challenged by inconsistencies in definitions and minimal paediatric data available, leading to an underestimation of incidence and difficulty in diagnosis (Muraro et al, 2007). To date, there have been no population-based epidemiological studies examining the association between the prevalence of food-induced anaphylaxis, nor sufficient studies which identify risk factors associated with anaphylaxis and its potential reoccurrence.

The main aim of this study was to determine risk factors associated with food-induced anaphylaxis. Doing so will help to establish clinical criteria which will enable physicians and health professionals to distinguish between children who are sensitised to allergens known to trigger anaphylaxis, and who are at increased risk of developing clinical manifestations associated with anaphylaxis. The findings of this study should also improve our understanding of the nature of anaphylaxis as well as develop research agenda for risk assessment in anaphylaxis, leading to the development of an anaphylaxis registry.

An extensive literature search was undertaken using Medline, Meditext, Synergy, Expanded Academic and ProQuest databases with appropriate search terms (anaphylaxis, risk, food-induced, epidemiology, prevention, hypersensitivity, children, prevalence and prevention).

Definitions

Food induced anaphylaxis is a severe life-threatening allergic reaction in the form of an immunoglobulin E (IgE) mediated hypersensitivity reaction, manifested by an abrupt onset of symptoms resulting from exposure to an offending agent (Sampson, 2003). The ASCIA Anaphylaxis Working Party (2004) defined anaphylaxis as a 'rapidly evolving generalised multi-system allergic reaction'. A number of severity grading systems have been described throughout the literature, ranging from simple definition descriptions between generalised allergic reactions and anaphylaxis (Braganza et al, 2006), to a 'mild, moderate, severe' grading system (Brown, 2004; Brown and McKinnon, 2001; Clark et al, 2007), 'two or more' ruled grading criteria (Muraro et al, 2007) or a five levelled grading system as proposed by Sampson (2003). Lack of a universally accepted severity grading system for anaphylaxis has impacted on the degree to which the condition can be successfully diagnosed and managed.

For the purpose of this study, anaphylaxis has been defined as a 'severe, life threatening allergic reaction, characterised by signs of cutaneous, gastrointestinal, respiratory and cardiovascular compromise'.

Risk Factors for Anaphylaxis

Several factors may predispose an individual to anaphylaxis, including history of atopy (Roberts et al, 2003; Sampson, 2003), presence and a history of poorly controlled asthma (Sampson, 2003; Braganza et al, 2006; Brown et al, 2006), eczema (Lowe et al, 2007), sibling order and family size (Emmett et al, 1999; Wahn and von Mutius, 2001), being female (Brown, 2004), over four food allergies (Roberts et al, 2003), allergy specifically to peanut or tree nut (Wang and Sampson, 2007; Clark et al, 2007), and delayed administration of epinephrine (Wang and Sampson, 2007).

Clinical Manifestations of Anaphylaxis

Anaphylaxis encompasses a variety of symptoms and often affects multi organ systems including the skin, gastrointestinal tract, respiratory tract and cardiovascular system (Sampson, 2003). [Refer to Appendix 1 for clinical features of anaphylaxis, where Wang and Sampson (2007) list clinical observations associated with each body system].

Management of Anaphylaxis

Among individuals who are sensitised there are no completely reliable measures to determine those who are clinically tolerant from those at risk of an anaphylactic episode. However most frequently, clinical history, skin prick testing and IgE measures are taken to determine individuals who are sensitised (Simons et al, 2007). Management includes education about reading labels from commercial products, problems with cross-contamination with allergens in restaurants and other settings, and issues arising in schools (Sicherer et al, 2003). Emergency plans should be in place for treatment with medications, especially epinephrine in the event of accidental ingestion. Intramuscular epinephrine (adrenaline) is the drug of choice for treatment of anaphylaxis which should be prescribed to any individual at high risk of an anaphylaxis in the form of an EpiPen (Sampson, 2003).

METHODS

Study Design, Setting and Recruitment

This retrospective case-control study was undertaken at the Royal Prince Alfred Hospital (RPAH) Allergy Unit in Camperdown, Sydney. Subjects were recruited from a patient database of Dr Velencia Soutter if they were aged 0-5 years on presentation at the Allergy Unit, and if they were atopic. Of the initial study population of 904 patients, 672 subjects were recruited based on these inclusion criteria. Subjects were excluded if they were beyond 5 years of age at presentation, were non-atopic, and/or if their clinical information was incomplete.

The patient database included information on each case, including age and sex; history of asthma, eczema and gastro-intestinal symptoms; family size and sibling order; number of food allergies and presence of diagnosed food or airborne allergies. Patients' files were then referred to, to complete any missing information in the database, and to determine history of anaphylaxis according to observation of the physician. Patients were considered to have had an anaphylaxis if the physician had stated so, or if they met our definition of anaphylaxis, which was a 'severe, life threatening allergic reaction, characterised by signs of cutaneous, gastrointestinal, respiratory and cardiovascular compromise.' Subjects were therefore categorised into two groups, (1) atopic children who have had an anaphylaxis or recurrent anaphylactic reactions (cases), and (2) atopic children who had not had an anaphylaxis (controls).

Statistical Analysis

SPSS Software for Windows was used for statistical analysis (V12.0: 2000-5, SPSS Inc., Chicago II, USA). Variables including age, sex, asthma, eczema, gastro-intestinal symptoms, family size, sibling order, number of food allergies, and presence of an airborne allergy, were analysed using binary logistic regression models against cases and controls, to determine if the association between such variables and anaphylaxis was statistically significant ($p<0.05$), and therefore a risk factor. Results are reported as odds ratios and percentages based on a 95% confidence interval (CI).

RESULTS

Of the 672 subjects in this study, there were 218 cases and 454 controls (OR 1:2.1). The results in Table 1 specify the p-value and Exp (B) value for each variable, using history or no history of anaphylaxis as the dependent variable.

Table 1. P-values and Exp (B) for each variable using binary logistic regression analysis for significance.

Independent Variable	p-value	Exp (B)
Age	0.033*	1.423
Sex	0.501	0.894
Asthma	0.087	1.360
Eczema	0.036*	0.620
Gastro-intestinal symptoms	0.202	0.793
Family size	0.097	
1 child	0.622	1.422
2 children	0.655	0.541
3 children	0.330	0.247
4 children	0.495	0.357
5 children	0.999	0.000
1 child vs. Multi-child family	0.355	0.849
Sibling order	0.937	
1st child of *n*	1.000	0.000
2nd child of *n*	1.000	0.000
3rd child of *n*	1.000	0.000
4th child of *n*	1.000	0.000
5th child of *n*	0.999	0.000
6th child of *n*	1.000	0.998

7th child of *n*	0.999	0.000
No. of food allergies	0.254	
1	1.000	5.6E+008
2	1.000	7.8E+008
3	1.000	8.7E+008
4	1.000	8.7E+008
5	1.000	1.1E+009
6	1.000	6.2E+008
7	1.000	2.4E+009
8	1.000	1.2E+009
9	1.000	1.000
10	1.000	3.2E+009
11	0.999	2.6E+018
12	0.999	2.6E+018
13	1.000	1.000
1 vs. ≥ 2 food allergies	0.012*	1.582
No. of airborne allergies	0.366	
1	0.837	0.907
2	0.551	1.321
3	0.655	1.243
4	0.485	1.457
≥1 airborne allergies	0.055	0.537

*p<0.05 indicates statistical significance

On further analysis, the presence or history of asthma and eczema were used as dependent variables against the presence of an airborne allergy. Refer to Table 2 which outlines these results.

Table 2. Statistical analysis using binary logistic regression, comparing the presence of asthma and eczema against the presence of an airborne allergy.

Dependent Variable	Independent Variable	p-value	Exp(B)
Asthma vs. No Asthma	Airborne allergies	0.000*	3.861
Eczema vs. No Eczema	Airborne allergies	0.002*	2.032

* $p<0.05$ indicates statistical significance

Refer to Appendix 2 in which the number of cases and controls within each variable is expressed as a percentage of the group.

The main findings of these results are:

- Approximately 55% of controls were aged between 0-2 years, and the same percentage of cases were aged 2-5 years.
- There was no significant difference in the gender of subjects between case and control groups. 58% of the case group were male, compared with 55% in the control group. Likewise, females represented 42% of the case group and 44% of the control group.
- The prevalence of asthma in patients with anaphylaxis was 33%, compared to 26% in the control group.
- The majority of atopic children within case and control groups had eczema (80-90%).
- The percentage of subjects with and without gastro-intestinal symptoms did not differ statistically between the two groups.
- 66% of the case group and 70% of the control group were from multi-child families, i.e. two or more children.
- The majority of anaphylactic reactions (approximately 87%) occurred in families with 1 or 2 children.
- Half of anaphylactic reactions occurred in children who, at date seen, were the 1st child in the family.
- Cases and controls had an average of 3.1 and 2.7 food allergies respectively, with the majority of subjects having more than one food allergy (73% of cases; 64% of controls).
- Overall, 69.2% of the study population had an airborne allergy, the majority being dust mite (62.5%).
- Amongst cases and controls, the minority represented children with a history of anaphylaxis, with no airborne allergy.

DISCUSSION

This retrospective case-control study compared 218 children who had an anaphylactic reaction or recurrent reactions, with 454 controls. Based on the results of binary logistic regression, four variables significantly predicted risk of anaphylaxis – age, eczema, more than one food allergy, and presence of an airborne allergen. Even though these risk factors have been determined, there are no objective clinical markers of anaphylaxis in the paediatric population.

Prevalence of atopy in childhood in Australia rose dramatically from 1992 to 1997 (Downs et al, 2001). Children with food-induced anaphylaxis are highly atopic, as previously reported (Novembre et al, 1998). However, one scientific review identified that atopy does not necessarily predispose individuals to an increased risk of anaphylaxis, but more predispose them to a more severe reaction (Sampson, 2003).

Risk Factors for Anaphylaxis

Age

The mean age of anaphylaxis occurrence within the case group (2.1 years) was consistent with other studies. One report stated that 18% of allergic children reacted by the age of 1 year, and 56% by the age of 2 years (Emmett et al, 1999), with most children loosing sensitivity to the most allergic foods between 3-5 years of age (Dowdee et al, 2007). In this study, the association between age and history of anaphylaxis was statistically significant ($p=0.033$), suggestive that age is indicative of anaphylaxis risk. However due to the difference between the p-value and Exp (B) for this variable, we cannot exclude confounders.

Sex

Sex did not show to be a risk factor for anaphylaxis in this study ($p=0.501$). The incidence of anaphylaxis was higher in males than females (OR 1.4:1), however, females were reportedly found to suffer from more severe anaphylactic reactions than males (18% compared to 11%); this is consistent with recent literature findings (DunnGalvin et al, 2006).

Literature regarding differences in sex, corresponding to the prevalence and incidence of atopy and subsequent food allergy, has been inconsistent. Retrospective and prospective studies have reported that food anaphylaxis is more prevalent in females, with a substantially

higher prevalence of recurrence (Brown, 2004; Mullins, 2003; Webb and Lieberman, 2006). The results of population-based studies differ. One particular study amoungst emergency department paediatric patients reported a 1.7:1 male to female ratio (Braganza et al, 2006); these findings are more consistent with the result of this study.

Asthma

History of asthma was reported in 33% of anaphylaxis cases. This may be compared to the 36.8% prevalence of asthma reported in a recent retrospective case study of Australian children (Braganza et al, 2006) and a background prevalence of 17.5% in school children (Comino, 1993). One case-control study found that more than a third of children with food allergies have asthma and 8% of asthmatic children have a food allergy (Roberts et al, 2003).

This study found no statistical association between asthma as a potential risk for the development of anaphylaxis (p=0.087). Literature has suggested a direct relationship between asthma and anaphylaxis, however most suggest that it is not the presence of asthma, but a history of poorly controlled asthma or concurrent asthma that is a risk factor for anaphylaxis (Braganza et al, 2006; Wang and Sampson, 2007).

Eczema

The incidence of eczema is most commonly associated with allergic sensitisation (Lowe et al 2007). In this study, a positive relationship was found between eczema and risk of anaphylaxis, with a statistically significant association reported (p=0.036). Eczema was noted in 82% of anaphylaxis cases. However, these findings are not in agreement with previous literature, reporting eczema prevalence as low as 50% (Novembre et al, 1998). Increased prevalence found in this study may be due to the study population chosen, as all children had a history of atopy, which can be related to eczema.

Gastro-intestinal symptoms

The association between the presence of gastrointestinal (GI) symptoms and history of anaphylaxis was statistically non-significant (p=0.202). Most studies report that although the gastrointestinal tract is usually the initial sight of food contact, allergic manifestations usually spread rapidly, affecting other organs such as the skin, respiratory and cardiovascular systems such that cutaneous symptoms occur in 80% of paediatric patients (Wang and Sampson,

2007). Even though GI symptoms was not identified as a potential risk factor in this study, its significance may have arisen through other organs affected during the anaphylactic episode, and therefore reported symptoms.

Family size (One vs. Multi-child families)

The association between family size and history of anaphylaxis was found to be statistically non-significant (p=0.097), although there was a decrease in anaphylaxis episodes in families with two or more children, with the majority of anaphylactic reactions occurring in families with two children (55%). Both the structure and size of the family may be influential in regards to allergic sensitisation (Wahn and von Mutius, 2001). According to this study, children born into families with older siblings are at reduced risk of allergic sensitisation and asthma at school age. Other studies have reported otherwise, reporting that infants with a family history of allergic disease are at greater risk of asthma and allergic rhinitis, causing infants to become sensitised earlier in life, leading to a greater risk of allergic reactions (Lowe et al, 2007).

Sibling order

The results showed that the statistical association between sibling order - the first, second, third, fourth, fifth, sixth and seventh child of *n* children within the family - and history of anaphylaxis, was not significant (p=0.937). As the p-value exceeded 0.8, this variable was excluded as a potential risk factor following analysis. 50% of anaphylaxis cases occurred in sibling one, with 40% occurring in sibling two. Although genetic predispositions are present in regards to the development of food allergy, the findings of this study suggest that risk of anaphylaxis in a child is not dependent on the size of their family, nor the number or order in which they present within the family unit. However, one could assume that a second or third child etc, would be less likely to have an anaphylaxis, due to increased awareness of food allergy and its management. This study however, did not agree with such an assumption.

No. of food allergens (1 vs. >1 food allergy)

This study found that the majority (74%) of cases had more than one food allergy, and on analysis, this was statistically associated with anaphylactic risk (p=0.012). However, the strength of this statistical association was independent of the number of food allergies present (p=0.254). One case-control study identified that sensitisation to four or more allergens was a

significant risk factor for life-threatening asthma, directly correlating to severity of bronchial hypersensitivity causing allergic reactions (Roberts et al, 2003). Positive skin prick tests (a wheal diameter great than 3mm compared to a negative control), have been identified to indicate sensitisation, but not necessarily a casual relationship or clinical reactivity (Simons et al, 2007), with approximately 60% of individuals with detectable food-specific IgE levels considered as non-clinically reactive, as they experience no signs or symptoms on exposure to the offending allergen (Simons et al, 2007). According to the co-findings of this study (Rachel Myhill, 2007) SPT results could not be used as a predictor of the severity of anaphylaxis, as the median SPT (6-8mm) of both mild and moderate reactions, were similar to those reported in severe reactions. Therefore based on these findings, the number of food allergies a child has, and the SPT of the corresponding allergen, is not indicative of anaphylaxis risk. This has implications on the clinical approach undertaken by health professionals in identifying at-risk children, and educating their families regarding food allergen avoidance and management of anaphylaxis.

Airborne allergens

The association between the presence of an airborne allergen and history of anaphylaxis, was of borderline significance (p=0.055). 75% of the case group had an airborne allergy compared with 66% of the control group. Within the anaphylaxis population, the most prevalent airborne allergen was dust mite (57%), followed by cat (19%) and pollen (17%). The findings of this study are consistent with existing literature, with one study reporting that children sensitised under the age of 3 years have a more rapid loss of lung function on exposure to dustmite, cat, dog and other airborne allergens, leading to development of wheezing, eczema and asthma, preceeding and predicting allergic sensitisation (Lowe et al, 2007). On further analysis however, the number of airborne allergies was not statistically associated with anaphylaxis risk (p=0.366), therefore indicating that children with an airborne allergy are more likely to have an anaphylaxis, independent of how many airborne allergies they actually have.

This study also addressed potential confounders, which may have contributed to the significant and non-significant results found. Following analysis, a statistical association between the presence of asthma and the presence of an airborne allergy, was found (p=0.000). Consistent with the findings of this study, other studies have found associations

between sensitivities to airborne allergens – dust mite, cat, dog and cockroach – and the development of asthma in children (Dowdee et al, 2007; Wahn and von Mutius, 2001). 92% of anaphylaxis cases within this study had a history of asthma, as well as one or more airborne allergies.

Further to this, the association between the presence of eczema and the presence of an airborne allergy was also found to be statistically significant (p=0.002). 75% of the case group had both eczema and an airborne allergy compared with 69% in the control group. One case-control study identified that increasing sensitisation to aeroallergens correlates to eczema severity and atopy, and that children with atopic eczema had a greater risk of having an airborne allergy (OR 2.5:1) compared to children with no history of eczema (Roberts et al, 2003).

Therefore, analysing the presence of asthma and eczema against the presence of an airborne allergy has enabled us to identify potential confounders relating to the statistically significant association observed between the presence of an airborne allergy and history of anaphylaxis.

Other study findings

Previous studies have identified other factors which may put individuals at greater risk of an anaphylactic reaction, including allergy to peanuts and tree nuts, and delayed administration of adrenaline/epinephrine. This study found that an allergy to peanut was present in 81% of anaphylaxis cases. Studies have reported that tree nuts account for more than 90% of anaphylactic reactions, and allergy to tree nut and increasingly an allergy to cashew nut, are major risk factors for life-threatening anaphylaxis (Simons et al, 2007; Clarke et al, 2007).

Intramuscular adrenaline is the acknowledged first-line of therapy for anaphylaxis. According to the co-findings of this study (Rachel Myhill, 2007), adrenaline was only administered in 9% (n=20) of anaphylaxis cases, which is lower than previously reported by Novembre and colleagues (1998), in which 18% of anaphylactic children were administered adrenaline on first sign of manifestation.

LIMITATIONS

Studies which attempt to research allergic reactions and anaphylaxis are limited by the lack of a diagnostic gold standard definition of anaphylaxis and grading system. In some studies, mild skin reactions may not have been considered to be an anaphylaxis, but rather a generalised allergic reaction, and therefore this case study population may have been an overestimation of the incidence of anaphylaxis. The cases identified to have a mild reaction in this study may have been used as controls in other studies. Consequently, the results of this study could therefore not be accurately compared to previous study findings, based on the possible overestimation, or even underestimation of the results.

Other limitations may be related to misreporting and bias. This study relied on accurate and complete medical records taken by a physician, and all data presented was collected retrospectively and thus prone to reporting bias. We were unable to assess the accuracy of anaphylaxis diagnosis. Furthermore, many reaction characteristics are likely to have been undocumented, such as in severe reactions, mild skin involvement may have been missed or epinephrine treatment may have altered subsequent development of other symptoms, which may have affected the study findings.

This study included only patients who attended a single Allergy Unit, and therefore results may not be able to be generalised to the population as a whole. In addition, this particular study population may over-represent the incidence of food allergy, as all patients willingly attended the clinic, where in most cases they had already had a reaction.

The primary research focus of this study was anaphylaxis in a paediatric population, and therefore results may not be applicable to the adult population or to the general population. Differences in food allergy have been previously noted in adults compared to paediatrics, with food being the most common trigger of food allergy in children compared to drugs and insect vemon in adults (Braganza et al, 2006; Wang and Sampson, 2007). Children were often found to suffer from more respiratory symptoms, whereas adults were more frequently affected by cardiovascular compromise, which may be due to their increased age. Some studies believe the incidence of anaphylaxis is the same for both adults and children (Brown, 2004), other studies think otherwise (Braganza et al, 2006; Brown and McKinnon, 2001). Further studies would need to examine the risk of anaphylaxis in an adult population.

As previously reported, SPT results do not define clinical reactivity, and therefore these results may not necessarily relate to prevalence and severity of the condition. Using SPT results to assess severity of anaphylaxis is not a reliable biomarker. This study was limited as we did not obtain plasma IgE levels or undertake food challenges, which may have provided a more accurate diagnosis of the severity of anaphylactic episodes (Wickman et al, 2005).

Interpretation of these data also needs to take into consideration the retrospective nature of the study, including confounding effects.

RECOMMENDATIONS and CONCLUSION

Future studies should address risk factors associated with anaphylaxis in adulthood, and how they are similar to or differ from results found in this study for anaphylaxis in childhood. Future research should also focus on developing clinical biomarkers to distinguish between atopic children at risk of anaphylaxis to those who are food allergic but not as risk of anaphylaxis, and perhaps incorporate food challenges as a better predictor of risk. This report should raise awareness of the importance in physicians taking careful and detailed clinical histories of all children with allergic sensitisation, in order to monitor and manage anaphylaxis risk. No studies have been conducted to determine optimal dose of epinephrine in cases of anaphylaxis.

This research project was conducted with the aim of identifying risk factors associated with food-induced anaphylaxis, so as to establish clinical criteria which will enable physicians and health professionals to distinguish between children who are sensitised to allergens known to trigger anaphylaxis, and who are at increased risk of developing clinical manifestations associated with anaphylaxis.

Overall, it was found that the age of the child, history of eczema, more than one food allergy, and presence of an airborne allergy was statistically associated with anaphylaxis risk in atopic children aged 0-5 years. Currently there are no reliable indicators to predict who is more at risk of an anaphylactic episode, therefore ensuring a detailed medical history, and periodic follow-up with food allergy testing and food challenges would be appropriate, including consideration of the presence of atopy and airborne allergy.

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APPENDIX 1

Table 1. Clinical features of anaphylaxis

BODY SYSTEM	CLINICAL OBSERVATIONS
Cutaneous	Urticaria, angioedema, flushing, rash, pruritus
Gastrointestinal	Oedema of the lips/tongue, nausea, vomiting
Respiratory	Upper airway – congestion, sneezing, rhinorrhea Lower airway – cough, wheeze, chest tightness
Cardiovascular	Tachycardia, arrhythmia, hypotension
Neurologic	Anxiety, headache, seizure, loss of consciousness
Ocular	Pruritus, conjunctival injection, lacrimation

Source: Wang and Sampson (2007)

APPENDIX 2

Table 1. Age of Subjects

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
0 to 1	115	25.33	27	12.39
1 to 2	134	29.52	71	32.56
0 to 2	**249**	**54.85**	**98**	**44.95**
2 to 3	83	18.28	54	24.77
3 to 4	62	13.65	32	14.68
4 to 5	60	13.22	34	15.60
2 to 5	**205**	**45.15**	**120**	**55.05**
TOTAL	**454**		**218**	

Table 2. Male/Female vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Male	**253**	**55.73**	**127**	**58.26**
Female	201	44.27	91	41.74
TOTAL	**454**		**218**	

Table 3. Asthma/No asthma vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Asthma	119	26.21	72	33.03
No Asthma	**335**	**73.79**	**146**	**66.97**
TOTAL	**454**		**218**	

Table 4. Eczema/No Eczema vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Eczema	400	88.10	179	82.10
No Eczema	54	11.90	39	17.90
TOTAL	**454**		**218**	

Table 5. Gastro-intestinal symptoms/No Gastro-intestinal symptoms vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	*%*	*n*	*%*
Gastro	147	32.38	60	27.52
No Gastro	**307**	**67.62**	**158**	**72.48**
TOTAL	**454**		**218**	

Table 6. Multi-child family/Single child family vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	*%*	*n*	*%*
One child family	136	29.95	73	33.49
Multi-child family	**318**	**70.05**	**145**	**66.51**
TOTAL	**454**		**218**	

Table 7. Family Number vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	*%*	*n*	*%*
1	137	30.17	73	33.48
2	**219**	**48.24**	**119**	**54.59**
3	81	17.85	20	9.17
4	14	3.08	5	2.30
5	2	0.44		
7	1	0.22	1	0.46
TOTAL	**454**		**218**	

Table 8. Sibling Order vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	*%*	*n*	*%*
Sibling 1	**222**	**48.90**	**111**	**50.92**
Sibling 2	173	38.10	87	39.90
Sibling 3	50	11.01	16	7.34
Sibling 4	7	1.55	3	1.38
Sibling 5	1	0.22		
Sibling 6			1	0.46
Sibling 7	1	0.22		
TOTAL	**454**		**218**	

Table 9. No. of food allergies vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
1	163	35.90	57	26.15
>1	**291**	**64.10**	**161**	**73.85**
TOTAL	**454**		**218**	

Table 10. Airborne allergy/No airborne allergy vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Airborne allergy	**303**	**66.74**	**162**	**74.31**
No airborne allergy	151	33.26	56	25.69
TOTAL	**454**		**218**	

Table 11. No. of Airborne allergies vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
0	**151**	**33.26**	**56**	**25.69**
1	**172**	**37.89**	**92**	**42.20**
2	86	18.94	44	20.18
3	30	6.61	19	8.72
≥4	15	3.30	7	3.21
≥2	**131**	**28.85**	**70**	**32.11**
TOTAL	**454**		**218**	

Table 12. All airborne allergens vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Dustmite	**279**	**54.92**	**161**	**56.90**
Cat	87	17.13	53	18.73
Mould	53	10.43	22	7.76
Pollen	89	17.52	47	16.61
TOTAL	**508**		**283**	

Table 13. Peanut/No peanut allergy vs. Anaphylaxis/No Anaphylaxis

	NO ANAPHYLAXIS		ANAPHYLAXIS	
	n	***%***	***n***	***%***
Peanut	**329**	**72.47**	**178**	**81.65**
No peanut allergy	125	27.53	40	18.35
TOTAL	**454**		**218**	