

ORIGINAL ARTICLE

Paediatric emergency department anaphylaxis: different patterns from adults

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Background and Aims: Data on acute paediatric anaphylaxis presentations to the emergency department (ED) are limited. All allergic presentations to one Australian paediatric ED were studied to determine epidemiological, clinical, and outcome data.

Methods: Retrospective, case based study of patients under 16 years attending one metropolitan, paediatric teaching hospital ED in Australia over three years. The medical records of patients presenting with generalised allergic reactions and anaphylaxis satisfying relevant ICD-9-CM diagnostic codes were studied. The incidence, age, sex ratio, co-morbidities, likely aetiology, clinical features, management, and disposal were determined.

Results: A total of 526 children with generalised allergic reactions, and 57 with anaphylaxis were included in the study. This represented incidences of 9.3:1000 ED presentations for generalised allergic reactions and 1:1000 for anaphylaxis. There were no fatalities. In anaphylaxis cases, a cause was recognised in 68.4%. Cutaneous features were present in 82.5%. A past history of asthma was reported in 36.8%. Adrenaline was used in 39.3% of severe anaphylaxis cases. The ED alone definitively cared for 97.8% of all patients. Follow up was inadequate in cases of anaphylaxis.

Conclusions: This is the first reported incidence figure for paediatric anaphylaxis ED presentations in Australia, and is less than that reported in adults in the same local population. However, the incidence of generalised allergic reactions of 9.3:1000 was greater than in the adults. Virtually all paediatric allergic cases may be managed in the ED alone, provided that the importance of specialist follow up, particularly for severe anaphylaxis, is recognised.

Although the term anaphylaxis was introduced as far back as 1902 by Portier and Richet,¹ the definition continues to be contentious. A recent guideline from the Anaphylaxis Working Party of the Australasian Society of Clinical Immunology and Allergy Inc. (ASCIA) defined anaphylaxis as "a rapidly evolving generalised multi-system allergic reaction characterised by one or more symptoms or signs of respiratory and/or cardiovascular involvement, and involvement of other systems such as the skin and/or gastrointestinal tract".² ASCIA also defined a generalised allergic reaction as "one or more symptoms or signs of skin and/or gastrointestinal tract involvement without respiratory and/or cardiovascular involvement".²

There are few data on the emergency department (ED) incidence of this potentially fatal condition, especially in the paediatric population. Most previous paediatric anaphylaxis studies have been based on hospital admissions or in outpatient allergy clinics rather than children presenting to the ED.^{3,4}

We describe the epidemiology, aetiology, clinical features, and management of patients presenting with generalised allergic reactions or anaphylaxis to one Australian paediatric emergency department during a three year period. The purpose of the study was to describe how undifferentiated paediatric patients present with acute allergic and systemic hypersensitivity reactions and to determine if they differ from allergic reactions and anaphylaxis in adult emergency patients.

METHODS

A retrospective, case based study was conducted on all patients presenting to a single paediatric ED in a three year period from 1 July 1998 to 30 June 2001 with final ED ICD-9-CM (International Classification of Diseases, 9th Revision

Clinical Modification) discharge diagnostic codes listed under the four major headings of allergy, allergic (reaction); anaphylactic shock or reaction; angioedema; and urticaria. The same complete list of codes under these four major headings was used as in the adult study performed previously in the same geographical location in Brisbane.⁵

The study hospital was a university affiliated paediatric tertiary referral teaching hospital in Brisbane, Australia, a city of 1.7 million. This is the only general hospital serving, on recent census, a local catchment population of 71 000 persons aged 15 years or younger; 56 655 ED attendances were recorded in total during the study period. The patients studied were referred to the emergency department by their general practitioner or were self-referrals; there were no inter-hospital transfers for tertiary care. The study was approved by the Royal Children's Hospital Executive.

Exclusions

Two trained data collectors (SCB, DRLM) reviewed all relevant patient notes, and collected information onto standardised forms, with missing data recorded as negatives. Patients were excluded if there was insufficient documentation to clearly define an allergic or anaphylactic reaction, or if patient medical records were missing or unavailable.

Definitions

Presentations were separated into two distinct groups based on the recent ASCIA definitions utilised in their guidelines paper for the prescription of the EpiPen:²

Abbreviations: ED, emergency department; GAR, generalised allergic reaction

Box 1: Definitions of generalised allergic reaction and anaphylaxis

(1) Generalised allergic reaction (GAR)

Evidence of generalised mediator release restricted to:

Cutaneous features

- Generalised rash
- Pruritus
- Rhinitis/conjunctivitis
- Urticaria
- Local oedema
- Angioedema

and/or Gastrointestinal tract features

- Vomiting
- Loose stools
- Abdominal pain

without any other systemic symptoms or signs.

(2) Anaphylaxis

Respiratory features

- Shortness of breath (SOB) or dyspnoea
- Wheeze
- Bronchospasm
- High respiratory rate corrected for age
- Laryngeal oedema (stridor or hoarseness)*
- Accessory respiratory muscle use (intercostal recession or tracheal tug)*
- Cyanosis*
- Any one or more of a history of SOB, wheeze/bronchospasm plus a respiratory rate greater than the age adjusted upper limit of normal*

Cardiovascular features and/or neurological dysfunction (from hypoperfusion or hypoxia) with or without features of generalised allergic reaction above

- Loss of consciousness*
- Syncope*
- Dizziness or light-headedness*
- Systolic blood pressure of less than the age adjusted lower limit of normal*
- Glasgow Coma Scale (GCS) score of less than 15*

*Considered to represent severe, immediately life threatening features (see text)

Based on ASCIA guidelines²

- (1) **Generalised allergic reaction (GAR)** confined to cutaneous and/or gastrointestinal symptoms
- (2) **Anaphylaxis**, with multi-system involvement (see box 1).

We defined a further subgroup of the anaphylaxis patients as having severe, or potentially life threatening features as highlighted in box 1. This additional grouping is consistent with disease severity grading as used in a previous local adult study of anaphylaxis in Brisbane,⁵ and the US epidemiological study by Yocum and colleagues.⁶

Further data as reported by patients and or their carers were abstracted for each group including the causative agent, a previous history of asthma or a previous history of allergy to the causative agent, pre-hospital treatment, in-hospital

treatment, discharge treatment, and follow up arrangements. Descriptive statistics were calculated with the results expressed as medians with ranges, or as percentages. Excel (Microsoft Corp) was used to compare continuous variables between multiple groups.

RESULTS

During the study period, 607 patient presentations met the inclusion criteria. The patient medical records were missing or unavailable in 15 cases and a further nine cases were excluded because of insufficient documentation. A total of 583 patient presentations with generalised allergic reactions (GAR) or anaphylaxis remained for analysis.

Five hundred and twenty six of these patients presented with GAR, giving an incidence of 9.3 per 1000 ED presentations, which represented a population prevalence of 7.4 cases per 1000 children over the three year study period.

There were 57 children seen with anaphylaxis, giving an incidence of 1 per 1000 ED presentations and a population prevalence of 0.8 cases per 1000 children over the study period. Thirty six of the 57 anaphylaxis patients were male; the ratio of males to females was 1.7:1. The median age for patients with GAR was 3.9 years (range 0.1–14.5 years) and for patients with anaphylaxis was 4.1 years (range 0.2–14.1 years). Seventeen (30%) of those with anaphylaxis were under 2 years, 16 (28%) were aged 2–4 years, and 24 (42%) were 5 years or older, compared to 36.5%, 26.6%, and 36.9% in those respective age ranges of all ED presentations during the study period. Twenty eight patients had severe, potentially life threatening anaphylaxis. Their median age was 5.9 years (range 0.3–14.1 years).

Clinical features

Cutaneous features were present in 96% of all patients: 98% of those with GAR, but only 82% of those with anaphylaxis. The frequency of cutaneous, mucosal, and gastrointestinal features is recorded in table 1, and of the respiratory, cardiovascular, and neurological features in table 2.

Causative agents

The reported causative agent was recorded in 40.5% of patients with generalised allergic reactions and 68.4% of patients with anaphylaxis (table 3). The most common suspected cause of anaphylaxis was food items.

Co-morbid conditions

The prevalence of asthma in patients with anaphylaxis was 36.8%. Twenty one per cent of patients with severe

Table 1 Incidence of cutaneous, mucosal, and gastrointestinal features of patients presenting with generalised allergic reaction and anaphylaxis

	Generalised allergic reaction (n = 526)	Anaphylaxis (n = 57)
Cutaneous features		
Pruritus	329 (63%)	23 (40%)
Local erythema	275 (52%)	20 (35%)
General erythema on history	196 (37%)	15 (26%)
General erythema on examination	156 (30%)	14 (25%)
Urticaria	407 (77%)	31 (54%)
Angioedema	175 (33%)	18 (32%)
Total (any cutaneous feature)	515 (98%)	47 (82%)
Mucosal features		
Rhinitis/conjunctivitis	29 (6%)	6 (11%)
Gastrointestinal features		
Nausea/vomiting	32 (6%)	12 (21%)

Table 2 Additional respiratory, cardiovascular, and/or neurological features of patients presenting with anaphylaxis

	All anaphylaxis (n = 57)	Severe anaphylaxis (n = 28)
Respiratory features		
Dyspnoea	32 (56%)	15 (54%)
Wheeze	22 (39%)	10 (36%)
Hoarseness	9 (16%)	9 (32%)
Stridor	1 (2%)	1 (4%)
Bronchospasm	11 (19%)	3 (11%)
Tachypnoea	25 (44%)	15 (54%)
Laryngeal oedema	10 (18%)	10 (36%)
Cyanosis	0	0
Total (any respiratory feature)	54 (95%)	25 (89%)
Cardiovascular features		
Hypotension	0	0
Capillary refill >2 seconds	1 (2%)	1 (4%)
Total (any cardiovascular feature)	1 (2%)	1 (4%)
Neurological features		
Loss of consciousness	1 (2%)	1 (4%)
Syncope/dizziness	1 (2%)	1 (4%)
GCS <15	1 (2%)	1 (4%)
Total (any neurological feature)	2 (4%)	2 (7%)

GCS, Glasgow Coma Scale score (maximum 15, minimum 3).

anaphylaxis had a known pre-existing allergy to the causative agent.

Pre-hospital treatment

Twenty six patients (45.6%) with anaphylaxis had received H1-receptor antagonists (antihistamines), 13 patients (22.8%) had received steroids, and nine patients (15.8%) had been given adrenaline by various routes pre-hospital. No patients were given H2-receptor antagonists prior to arrival at hospital.

In-hospital treatment and combined treatments

In hospital, 29 patients (50.9%) with anaphylaxis were given H1-receptor antagonists, three (5.3%) H2-receptor antagonists, 28 (49.1%) steroids, and seven (12.3%) adrenaline. Seventeen patients with anaphylaxis (30%) received no H1-receptor antagonists either pre-hospital or in-hospital, 22 (39%) received no steroids, and 42 (73.7%) received no adrenaline at any stage. Overall, among patients with severe anaphylaxis, 11 (39.3%) received adrenaline and 17 (60.7%) none. No reported adverse events such as severe headache or cardiac dysrhythmias occurred in any of the 15 children receiving adrenaline for anaphylaxis.

Disposition of anaphylaxis patients

Thirty one patients (54.4%) with anaphylaxis were discharged directly from the ED after a period of monitoring, 22 (38.6%) were admitted to the ED observation ward, then discharged, and four (7%) were admitted to a general medical ward. None were admitted to the paediatric intensive care unit (PICU), although two patients with severe anaphylaxis were reviewed by the PICU team, but remained in the ED resuscitation area before being transferred to a medical ward. There were no biphasic reactions recorded.

On final hospital discharge, 54.4% of all patients with anaphylaxis were prescribed H1-receptor antagonists, 1.8% H2-receptor antagonists, 28.1% oral steroids, and 17.5% self-injectable adrenaline.

Follow up care was arranged for 16 patients (28.1%) by an allergist, seven (12.3%) at a general medical outpatient clinic, 14 (24.6%) by their GP, and nine (15.8%) had ED review. Eleven anaphylaxis cases (19.3%) and four severe cases

Table 3 Causes of generalised allergic reaction and anaphylaxis

	Generalised allergic reaction (n = 526)	Anaphylaxis (n = 57)
Food items		
Egg	11	7
Dairy	6	8
Peanut	10	3
Other nut	7	3
Fruit	9	0
Seafood	5	3
Composite foods*	6	8
Drug related		
Penicillins	18	1
Cephalosporins	47	0
Other antibiotics	11	1
Drugs other than antibiotics†	12	1
Insects		
Bee	10	1
Wasp	1	1
Ant	7	1
Other or unidentified insect	45	0
No cause identified‡	313 (59.5%)	18 (31.6%)
Miscellaneous§	8 (1.5%)	1 (1.7%)
Reaction to a previously known allergen	27 (5.1%)	12 (21.1%)
Total	526 (100%)	57 (100%)

*Items made up of several compounds, e.g. cakes, chocolates.

†None were non-steroidal anti-inflammatory drugs.

‡This included the single child with cardiovascular features of anaphylaxis.

§Miscellaneous items including plant material (3), marine exposure (2), medical tapes (2), cat (1), and latex (1), which was the one anaphylaxis case.

(16%) had no documented follow up arranged after ED discharge.

DISCUSSION

This is the largest series of cases presenting to a single paediatric ED with anaphylaxis or GAR, and is also the first comprehensive Australasian review of paediatric allergic presentations. The definitions used are consistent with the recent ASCIA consensus terminology for GAR and multi-system anaphylaxis.²

The severity of anaphylactic reactions was graded according to whether immediately life-threatening features were present. Grading was the same as that used in a similar descriptive review of 142 adult patients presenting with anaphylaxis to the co-located adult hospital in the same local catchment area, allowing direct epidemiological comparisons to be made.⁵

Several other anaphylaxis grading systems have been described, such as by Yocum and colleagues,⁶ Gavalas and colleagues,⁷ and Brown.⁸ Unfortunately, they show little concordance, and until this occurs, international prevalence figures may mislead. The recently published definition of anaphylaxis with a simple clinical grading system developed by Brown using logistic regression analysis appears the most promising tool yet for comparative studies.⁸

The annual incidence of paediatric anaphylaxis was 1:1000 total ED presentations. This compares with an incidence of 2.3:1000 adult ED presentations reported in the local adult study.⁵ The higher incidence of anaphylaxis in adults compared to children has been recognised previously.^{9, 10} The incidence of anaphylaxis appears to be increasing.^{3, 11} Moreover, this incidence is certainly an underestimate, as resolution, treatment, or even fatality pre-hospital, and misdiagnosis may have occurred. In addition, this study only addressed emergency department presentations, yet up to

one third of children with anaphylaxis referred to an immunology unit in Florence had not been treated in an emergency room or in hospital.¹² We were unable to determine our "missed" data rate.

The incidence of generalised allergic reactions was 9.3:1000 ED presentations for a population prevalence of 7.4:1000 children over the three year period. This is greater than the incidence of local adult acute allergic reactions reported at 2.6:1000 ED presentations for an 0.3:1000 population prevalence in the same geographical location.⁵

The fatality rate was zero for our study. Brown *et al* found a 0.7% fatality rate in the adult study.⁵ Pumphrey estimated a fatality rate of less than one case per year per million UK population and recorded no deaths in children under 13 years of age.¹³ Yocum *et al* found a fatality rate of 0.65% in the USA,⁶ and Sheikh and Alves 0.5% in another UK study including adults and children.¹⁰

Cutaneous features were absent in 18% (10/57) of anaphylaxis cases and 21% (6/28) of those considered severe. This is greater than in comparable adult studies that found well over 90% had cutaneous features.^{5, 6, 14} Respiratory abnormalities were more frequently recorded in the severe cases in children, whereas other studies have shown greater cardiovascular instability among adults with anaphylaxis, perhaps related to increasing age and co-morbid disease.^{8, 15} Alternatively, the predominance of respiratory features noted may be explained by food related causes being more common in children and tending to cause respiratory tract involvement, whereas drug and venom related reactions are more common in adults and tend to cause cardiovascular reactions.^{8, 15-18}

The reported causative agent was recorded in 40% of children with generalised allergic reactions and 68.4% of patients with anaphylaxis, by recognition from a prior reaction or by close temporal association with the onset of symptoms. This study did not seek to confirm these reports. The most common category for anaphylaxis was food items, followed by insect sting and drugs. The most common food items were dairy products and eggs. However, the lower figures for peanut and other nuts could be explained by them being represented as the predominant cause within the composite foods such as cakes and chocolate.

A prior history of asthma was reported in 36.8% of anaphylaxis patients compared with a background prevalence in 1993 of 17.5% in primary school children.¹⁹ Our study's increased prevalence is similar to the 33% in Yocum and colleagues' epidemiological study,⁶ and is higher than the rate of 23.2% in Brown and colleagues' local adult study.⁵ A history of poorly controlled asthma is significant as it is an independent risk factor for death from anaphylaxis.^{4, 20}

Twenty one per cent of anaphylaxis patients had a known pre-existing allergy to the same causative agent. This is consistent with previous findings and represents a potentially avoidable proportion. It emphasises the importance of taking a careful allergy history, and giving anaphylaxis patients clear discharge advice on what to avoid in the future.⁵ This is exemplified by the study of 32 fatal cases of food allergy reported in the USA, which found that all but one of the subjects were known to have existing food allergy before the fatal event.²¹

In our study, 39.3% of all severe anaphylaxis patients received adrenaline either pre- or in-hospital compared to 57% of patients in the local adult study by Brown and colleagues⁵ and 33% of ED patients in the study by Stewart and Ewan.²² Pumphrey, in another UK study of 164 fatalities, found that adrenaline was only used in 62% of all reactions, and in only 14% before cardiorespiratory arrest.¹³ Thus there is clearly a need in both children and adults for greater awareness of when and how to use adrenaline in

anaphylaxis, particularly as recovery from anaphylaxis is most likely if adrenaline is given within 30 minutes.⁴ Although our numbers were small, the absence of any reported side effects in the 15 children who received adrenaline pre- and in-hospital further emphasises its safety.

Most cases with anaphylaxis (93%) were managed in the ED alone, consistent with findings in the local adult study,⁵ and the 10 year retrospective clinical study of anaphylaxis in a mixed ED with 22% of cases aged 14 years or less (personal communication, Prof. Simon Brown, 2004).⁸ A period of 4-6 hours' observation is suggested before discharging a patient following an anaphylactic reaction.⁵ Biphasic reactions have been reported as significant in up to 3% of children, whereas we did not record any.²³ Allowing for this observation period, the vast majority of anaphylaxis patients may thus be definitively managed in the ED.

Only 28.1% patients with anaphylaxis were referred specifically to an allergy clinic, with 19.3% of anaphylaxis cases, including 17.9% of severe cases, having no follow up arranged. However, referral patterns changed during the study as initially there was no local paediatric allergist available to the hospital. This compares with referral rates of around 55% in previous studies.^{6, 22} Thus the importance of an anaphylactic reaction is still under-appreciated.

Specialist verbal and written management advice to paediatric patients and their parents on avoidance, and the selection of drugs for self-treatment, including training in their use, have been shown to be highly effective.^{18, 24} Current Australian guidelines suggest that all patients who have had an anaphylactic reaction should be assessed by an allergy specialist, advised on avoidance, and provided with an adrenaline auto-injector and an anaphylaxis plan.² Our discharge guideline for all children seen with anaphylaxis now mandates referral to a paediatric immunologist and three days' treatment with oral H1- and H2-receptor antagonists and steroids. Children with severe anaphylaxis, those with an unavoidable trigger, and those from isolated areas with limited transport are prescribed an EpiPen, and they and their carers are taught how to use it by trained ED staff prior to leaving.

Conclusions

The incidence of anaphylaxis presentations to ED in the paediatric population was 1:1000 cases and the incidence of generalised allergic reactions was 9.3:1000. The most common cause of anaphylaxis in children was food, and of generalised allergic reaction was drugs.

The prevalence of asthma in paediatric anaphylaxis cases is significantly higher than in the general population. Anaphylaxis may occur in the absence of alerting cutaneous features. In children with anaphylaxis, respiratory abnormalities are the predominant finding, in comparison to adults in whom cardiovascular instability appears more commonly.

The majority of patients with anaphylaxis and generalised allergic reactions may be definitively managed in the ED alone, provided that follow up is organised, including allergist referral when indicated, and that all patients are given clear and comprehensive discharge advice.

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Competing interests: none

What is already known on this topic

- The annual incidence of adult generalised allergic reactions presenting to the emergency department is 2.6:1000 presentations, and that of anaphylaxis is 2.3:1000 presentations, with prevalence figures of 0.3:1000 and 0.29:1000 adult population respectively
- The commonest causes of adult emergency department anaphylaxis are drugs, followed by insect venom and food, with mixed cardiovascular and respiratory clinical features

What this study adds

- The annual incidence of paediatric emergency department generalised allergic reactions was found to be 9.3:1000 presentations, and that of anaphylaxis was 1:1000 presentations, with prevalence figures of 2.47:1000 and 0.27:1000 paediatric population respectively
- The commonest cause of paediatric emergency department anaphylaxis was found to be food items, followed by drugs and then insect venom, with respiratory clinical features predominating

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