

Original Article

Anaphylaxis admissions to UK critical care units between 2005 and 2009

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Summary

Anaphylaxis is a life-threatening emergency that may necessitate admission to a critical care unit. There are no reports of the frequency of admission to critical care units for patients with anaphylaxis or indeed any description of their demographic characteristics or outcomes. We analysed all physician-diagnosed cases of anaphylaxis over a 5-year period in national audit data from critical care units across the UK. Over the period 2005–2009, there were 81 paediatric and 1269 adult admissions with anaphylaxis admitted to UK critical care units (0.1% of admissions to paediatric units and 0.3% of admissions to adult units). Absolute numbers in both children and adults rose year on year. There were comparable proportions of admissions in female and male children (female = 47% and male = 53%; rate ratios (RR) = 0.88, 95% CI 0.64–1.20), but a greater proportion of adult female admissions (female = 65% and male = 35%; RR = 1.83, 95% CI 1.68–1.99). Survival to unit discharge was 95% (77/81) for children, and survival to hospital discharge was 92% (1166/1269) for adults. Each UK critical care unit is likely to see at least one anaphylaxis case per year. The number of admissions has risen in both children and adults. Although admission ratios between the sexes were comparable in children, there was a female preponderance in adult life. Survival rates were high at over 90%.

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Accepted: 11 March 2012

Anaphylaxis is a serious allergic reaction that is rapid in onset and may cause death [1]. It is characterised by rapidly developing life-threatening airway, breathing, or circulatory problems, usually associated with skin or mucosal changes [2]. The incidence of anaphylaxis is thought to be increasing [3, 4]. Given the rapid onset and relatively short duration of reactions, anaphylaxis is inherently difficult to study. Although this results in under-diagnosis, there has been significant international

effort to characterise its epidemiology in recent years by standardising definitions [1], drawing together multiple measures to estimate incidence and prevalence [3] and providing a standard approach to assessment and treatment [5]. The incidence of anaphylaxis is relatively well characterised at around 10–20 per 100 000 population [6], but only around 3–4 per 100 000 [7] are hospitalised. Data from death certificates show that there are about 20 anaphylaxis deaths a year in the UK,

although this is probably an underestimate [8]. There is, however, an important knowledge gap in relation to the disease burden posed by anaphylaxis on critical care units. Such data are important as these units provide care to the most severely affected patients. We report the first national study of anaphylaxis admissions to critical care units over a 5-year period.

Methods

There are three national audits of critical care units in the UK: the Intensive Care National Audit and Research Centre's (ICNARC) Case Mix Programme (CMP) is the largest and between 2005 and 2009 covered admissions to 65–70% of the 230 adult general critical care units in England, Wales and Northern Ireland; the Scottish Intensive Care Society Audit Group (SICSAG) covers all critical care units in Scotland (24 units); and the Paediatric Intensive Care Audit Network (PICANet) collects data from all NHS paediatric critical care units (33 units) from all areas of the UK. All three audits collect both mandatory and discretionary data fields for each patient, with approval from the National Information Governance Board for Health and Social Care (NIGB) to hold patient identifiable information without consent under Section 251 of the NHS Act 2006.

The ICNARC CMP is a national comparative audit of adult, general critical care units based in NHS hospitals spread geographically across England, Wales and Northern Ireland and co-ordinated by ICNARC. The CMP data are prospectively recorded and abstracted on to standard forms by trained data collectors according to precise definitions and rules. Abstraction is usually retrospective and based on chart review. Data are validated, first at a local and then at a national level for completeness, illogical data and inconsistencies. This process is repeated until all queries are dealt with. Data are then incorporated into the CMP. The ICNARC coding method is a five-tiered hierarchical method specifically designed for coding reasons for admission to critical care units. Admissions were identified as associated with anaphylaxis if they had 'anaphylaxis' coded as either the primary or secondary reason for admission to the critical care unit. Identification of cases was dependent on complete recording of the relevant condition as either the primary reason for admission (mandated for all admissions) or the secondary reason for admission (optional).

The SICSAG data are collected prospectively from critical care units comprising all general adult critical care units and held on a bespoke electronic database. Validation queries relating to patients' age, treatment, outcomes and discharge are checked with contributing units by local and regional audit coordinators. Inter-mittent extensive review of the historical databases is also undertaken with missing data input and consistent analytical methods applied. Cases were included if 'anaphylaxis' or 'anaphylactic shock' were entered in the diagnosis fields or reason for admission.

PICANet is one of the national clinical audits supported by the Health Quality Improvement Programme (HQIP) and provides a clinical audit of paediatric critical care unit activity. Although PICANet collects data from all areas of the UK and the Republic of Ireland, data from the Republic of Ireland were excluded from this analysis. PICANet uses a paper data collection form and bespoke data entry software. Validation visits to individual units are carried out by a PICANet research nurse to ensure that data are accurately transcribed from medical notes. PICANet software provided to the individual units allows real-time range and internal logical consistency checking and provides an on-screen summary of outstanding validation checks on the completion of a record. Clinical diagnoses and procedures are coded using Clinical Terms 3 (The Read Codes). Admissions were associated with anaphylaxis if they had the condition 'anaphylaxis' coded in either the primary or secondary reason for admission or they had the phrase 'anaphyl' in the notes section of the data collection form.

Data from 1 January 2005 to 31 December 2009 were extracted from these national audit databases. These data were then analysed to establish the patterns of admission with anaphylaxis to critical care units in the UK. Length of stay was collected in days (PICANet and SICSAG) and hours (ICNARC) using the dates and times of admission and discharge. Hours were then converted to days. The source of admission and data on whether the patient required cardiopulmonary resuscitation (CPR) before their admission to a critical care area were also collected. Survival data were extracted at discharge from the CMP unit and at ultimate discharge from an acute hospital (ICNARC and SICSAG) and

survival at discharge from the paediatric critical care unit (PICANet).

Descriptive analyses were undertaken using STATA v10.1 (StataCorp LP, College Station, TX, USA) and PASW Statistics v18 (IBM Ltd, Feltham, UK). Chi-squared tests were used to look at changes in admission rates over time. Rate ratios (RR) and 95% CI were calculated using the Newcombe-Wilson method without continuity correction to examine sex-related variations in both children and adults.

Results

Adult and paediatric data from all geographical areas of the UK were included. Five cases from the adult datasets (four from ICNARC and one from SICSAG) were excluded in the under-15 age bracket to prevent any possibility of a case appearing in both the adult and paediatric datasets. The UK critical care system for children means that patients are often stabilised and treated in the (adult) critical care unit of their local district general hospital and then transferred to the specialist paediatric critical care unit. Therefore the same patient may appear on both paediatric and adult audits. In addition, one case was removed from the paediatric database, as although the diagnosis was coded as 'anaphylaxis', it was clear from the record that the actual cause of admission was malignant hyperthermia.

There were 77 392 admissions to 28 dedicated paediatric critical care units in the UK over the 5-year period and there were 460 213 adult admissions to approximately 175 critical care units (68% of all adult units). There were 81 paediatric admissions with anaphylaxis (0.1% of admissions, Table 1). Absolute numbers of admissions increased fourfold from six to 24 per year during this period ($p = 0.087$). There were 1269 adult admissions (0.3% of admissions to adult units) with anaphylaxis to UK critical care units during this

Table 2 Source of admissions to UK critical care units of patients with a diagnosis of anaphylaxis between 2005 and 2009.

Source of admission	Children (n = 81)	Adults (n = 1269)
Emergency department	34 (42.0%)	474 (37.3%)
Operating theatre	26 (32.1%)	482 (38.0%)
Wards	12 (14.8%)	291 (22.9%)
Others	9 (11.1%)	21 (1.6%)

time period (Table 1). Adult admissions also increased, with absolute numbers almost doubling over the 5-year period ($p < 0.001$).

The most common sources of referral are shown in Table 2. In children, during the 5-year period studied 47% (38 cases) were female and 53% (43 cases) were male (RR = 0.88, 95% CI 0.64–1.20). In adults, 65% (820) of admissions were female and 35% (449) of admissions were male (RR = 1.83, 95% CI 1.68–1.99). The numbers of admissions varied with age, peaking in the seventh decade of life (Fig. 1).

Nine children (11%) and 174 (13.7%) of adults required CPR before their admission to the critical care unit. The percentage of children surviving anaphylaxis at unit discharge was 95% (77/81), and the mean length of stay on the critical care unit for survivors was 2.4 days and for non-survivors was 2.7 days. In adults, 95.3% (1209/1269) of patients survived to leave the critical care unit, and 91.9% (1166/1269) survived to hospital discharge. The mean length of stay in survivors was 1.2 days, and in non-survivors was 2.1 days.

Discussion

This is the first national overview of anaphylaxis admissions to critical care units, showing that each critical care unit is likely to manage at least one case of anaphylaxis each year. Key strengths of this work

Table 1 Admissions to UK critical care units with a diagnosis of anaphylaxis between 2005 and 2009. Values are number (proportion).

	2005	2006	2007	2008	2009
Total paediatric admissions	14 062	14 327	15 608	16 284	17 111
Paediatric admissions with anaphylaxis	6 (0.04%)	17 (0.1%)	14 (0.1%)	21 (0.1%)	23 (0.1%)
Total adult admissions	84 115	86 561	93 567	100 774	95 196
Adult admissions with anaphylaxis	183 (0.2%)	186 (0.2%)	290 (0.3%)	279 (0.3%)	331 (0.3%)

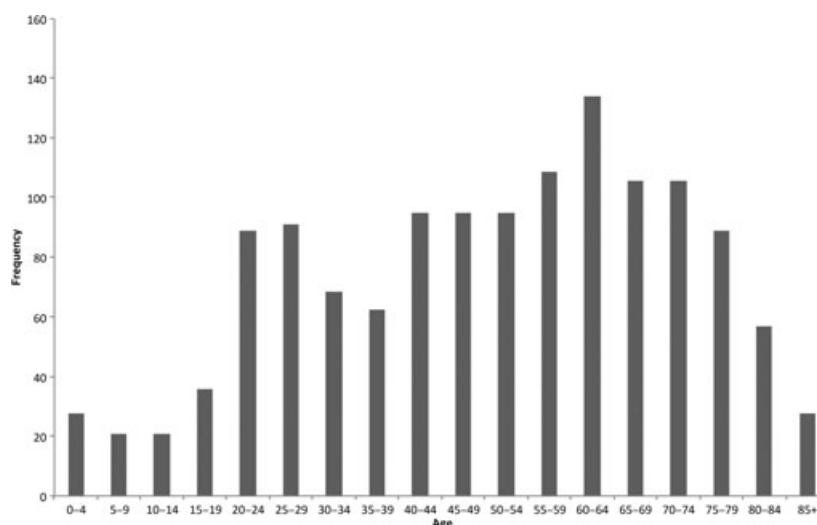


Figure 1 Admissions with anaphylaxis to UK critical care units by age between 2005 and 2009.

include the fact that all geographical areas of the UK were covered, and that data from ICNARC, SICSAG and PICANet are robust, validated and likely to be representative. A further important strength is that many critical care admissions will not have been included in previous studies, as these usually rely on hospital episode statistics (HES; a database of all NHS admissions in the UK), which record only the primary reason for hospital admission. Two thirds of critical care admissions come from within the hospital itself (excluding the emergency department) and it is likely that the primary reason for admission of these patients was not anaphylaxis. Our cases therefore include a high proportion of episodes of anaphylaxis that will not have been previously reported.

It is also important to consider potential limitations of this analysis. Whilst it is unlikely that these national audits have missed a large number of cases, it is not possible to verify if all cases of physician-diagnosed anaphylaxis were recorded in these audits. We did not include admissions to specialist stand-alone critical care units, such as for cardiac surgery or neurosurgery, although these represent only a small proportion of critical care beds in the UK. We have no information on the more than 30% of general critical care units in the UK not included in any of the audits. Finally, the diagnosis of anaphylaxis was based solely on physician-recorded diagnosis at discharge and we have no

information on any investigations (such as serum mast cell tryptase levels) to confirm the diagnosis. All three audits were designed to provide epidemiological data on generic critical care activity in the UK and not specifically on anaphylaxis. There is, therefore, no way to track the trigger for each case.

Studying the epidemiology of anaphylaxis has, historically, been difficult. There has previously been no suitable ICD-10 definition and many studies are based on hospital admissions [9] (which do not include emergency department visits without admission), adrenaline auto-injector prescriptions [10] (which may under- or overestimate incidence), and case series [11]. There have also been attempts to study the community-based prevalence of anaphylaxis. There have been no previous attempts, as far as we are aware, to study critical care unit admissions for anaphylaxis [12].

This work has shown that anaphylaxis represents a relatively small burden of the total work of critical care units when compared with other diseases such as community-acquired pneumonia (5.9% of total adult workload) [13]. Nevertheless, it is still important; our figures suggest that each unit sees, on average, at least one case a year and absolute numbers are rising. At the same time, overall rates of hospital admission with anaphylaxis have increased sevenfold in the last two decades [7]. The 'step' increase in adult critical care admissions between 2006 and 2007 probably represents

a natural fluctuation in admissions, as the number of units covered by the audits remained constant.

The variation in admission to critical care units with age is due, probably, to a number of factors: increasing rates of surgery with age; population decline in the older age brackets; and reduced physiological reserve and physicians' decisions about who should be offered critical care. The main source of admission to critical care units is the operating theatre; older patients are more likely to present for surgery. Drug-triggered reactions are more common in older people [14], in contrast to the predominantly food-triggered reactions in children. This may provide some explanation as to why adults are more likely to present with anaphylaxis from within the hospital. Operating theatres provide an environment where there is exposure to multiple triggering agents, particularly intravenous antibiotics and the neuromuscular blocking agents, which have a high risk of anaphylaxis [15]. These factors may tip the response towards anaphylaxis rather than other, less severe forms of allergy [16]. Indeed, over a quarter of previously reported UK deaths were related to either anaesthetics or antibiotics [7].

Our figures are also in keeping with the sex differences that have previously been reported in the general population in relation to anaphylaxis. In adults, females present more frequently with anaphylaxis [9, 12] whereas in children, the ratio is more evenly balanced [10]. One explanation is thought to be the effect of progesterone enhancing histamine release and sensitising end-organ tissues to inflammatory mediators [17, 18], although this has not been proved *in vivo*.

The fact that one in seven adults and one in nine children required CPR before admission justifies the inclusion of anaphylaxis in resuscitation guidelines [2], and its teaching on Advanced Life Support courses. We have no information on the cause of cardiac arrest in these cases, for example whether it was due to hypoxia or cardiovascular collapse. The proportion of patients surviving was high compared with other disease processes treated by the similar critical care units (pneumonia 50.6% [13], head injury 66.5% [19] and sepsis 55.3% [20]), with > 90% of both adults and children who arrived on the critical care unit with a diagnosis of anaphylaxis surviving to hospital discharge. This equates to around 20–30 people per year dying of anaphylaxis on critical care units in the UK.

This is similar to the total annual number of anaphylaxis deaths reported by Pumphrey et al. based on an analysis of UK death certificates [8]. However, fewer than one third of the deaths in Pumphrey's series occurred 'late' (in other words, not at the time of the initial anaphylactic reaction), whereas all of the cases in our series occurred 'late'. This difference would imply that there are a significant number of under-reported anaphylaxis deaths in the UK. The greatest proportion of 'late' deaths in Pumphrey's series was seen in iatrogenic reactions, which is consistent with our data, where two thirds of the patients came from within the hospital and are, therefore, likely to have been iatrogenic.

In both children and adults, patients who survived had a shorter length of stay on the critical care unit than the patients who died. The high rate of survival weighted the mean overall length of stay in favour of survivors and was, therefore, relatively short. Adults who survived stayed approximately a day less on the critical care unit than the non-survivors. This was different in children, where the survivors not only stayed a day longer than adult survivors, but the non-survivors stayed only a fraction of a day longer than the survivors. The reasons for this are unclear, but are probably in part due to different organisational factors such as retrieval and admission and discharge factors, rather than the unwell-to-well time interval.

In conclusion, we have shown that anaphylaxis, although not a large component of the workload of critical care units, remains important as each unit is likely to see at least one case per year. The numbers of admissions did not vary significantly in children, but there was a variation in adults with absolute numbers rising year-on-year. Admissions are equally common between the sexes in early life, but there is a female preponderance in adult life. Survival was high and actual numbers of deaths are similar to the overall number of deaths from anaphylaxis per year reported from death certificates.

Acknowledgements

We are grateful to Dr AT Lovell (Consultant Cardiac Anaesthetist, University Hospitals Bristol NHS Foundation Trust) and Dr David Harrison (Senior Statistician, ICNARC) for their helpful advice and data retrieval.

Competing interests

Dr Sheikh is a member of the Anaphylaxis Working Group, Resuscitation Council (UK), a member of the World Allergy Organization's Anaphylaxis Special Committee, a Royal College of General Practitioners (UK) Clinical Champion in Allergy, and a consultant to ALK-Abello and Phadia. Dr Soar is Chair of the Anaphylaxis Working Group, Resuscitation Council (UK), and Chair of the Resuscitation Council (UK). No external funding declared.

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