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Original Article

A retrospective registry-based study into the proportion of patients admitted to intensive care who have anaphylaxis as a principal diagnosis and their outcomes in Australia and New Zealand

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ABSTRACT

Objective: To describe the proportion of patients admitted to intensive care who have anaphylaxis as a principal diagnosis and their subsequent outcomes in Australia and New Zealand.
Design: Retrospective observational study of ICU admissions for severe anaphylaxis.
Setting: ICU admissions recorded in the Australian and New Zealand Intensive Care Society Adult Patient Database between 2012 and 2022.
Participants: Adults 16 years or older with severe anaphylaxis admitted to the ICU.
Interventions: None.
Main outcome measures: Proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis, mortality rate, ICU and hospital length of stay.
Results: 7189 of the 7270 ICU admissions for severe anaphylaxis recorded between 2012 and 2022, were included in the analysis. This represented a proportion from 0.25% in 2012 to 0.43% in 2022. ICU and hospital mortality were 0.4% and 0.8%, respectively. The proportion of ICUs reporting at least one severe anaphylaxis each year increased from 61.7% in 2012 to 83.0% in 2022. Most of the patients were discharged home (92.6%, n = 6660). Increasing age (OR = 1.055; 95%CI: 1.008–1.105) and SOFA scores (OR = 1.616; 95%CI: 1.265–2.065), an immunosuppressive chronic condition (OR = 16.572; 95%CI: 3.006–91.349) and an increasing respiratory rate above 16 breaths/min (OR = 1.116; 95%CI: 1.057–1.178) predicted in-hospital mortality in patients with anaphylaxis, while higher GCS decreased in-hospital mortality (OR = 0.827; 95%CI: 0.705–0.969).
Conclusions: The overall proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis has increased. In-hospital mortality remains low despite the need for vital organ support.

Abbreviations: ANZ, Australia and New Zealand; ANZICS, Australia and New Zealand Intensive Care Society; ANZROD, Australia and New Zealand a risk of death; APACHE, Acute Physiology and Chronic Health Evaluation; APD, Adult Patient Database; BMI, body mass index; BP, blood pressure; C, centigrade; COPD, chronic obstructive pulmonary disease; COVID-19, coronavirus disease 2019; CFS, Clinical Frailty Scale; ECMO, extracorporeal membrane oxygenation; ED, emergency department; GCS, Glasgow coma scale; HR, hazard ratio; ICU, intensive care unit; IQR, interquartile range; LOS, length of stay; MET, medical emergency team; MI, myocardial infarction; NIV, non-invasive ventilation; n, number; OR, odds ratio; RRT, renal replacement therapy; SD, standard deviation; UK, United Kingdom; USA, United States of America.

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Further studies should investigate these identified factors that may predict in-hospital mortality among these patients.

Trial registration: Not applicable.

SUMMARY BOX

Known: Severe anaphylaxis may require ICU admissions and these admissions may be increasing.

New: In this retrospective observational study of 7189 ICU admissions for severe anaphylaxis, we found an increasing proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis. The number of ICUs reporting severe anaphylaxis annually has also increased. Most patients were discharged home.

Implications: Although a larger proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis has increased, in-hospital mortality remains low despite vital organ support.

1. Introduction

Anaphylaxis is a multisystemic, severe acute allergic disease that occurs following exposure to an antigen.[1,2] The prevalence of anaphylaxis worldwide has increased, although studies have suggested overall mortality has remained constant at 0.5–1.0%.[3] Among patients requiring intensive care unit (ICU) support, higher mortality up to 5.0% has been reported.[4]

The risk factors associated with severe anaphylaxis requiring critical care support and fatal anaphylaxis have yet to be fully elucidated. Previous cohort studies have not investigated the potential factors contributing toward severe critical illness or mortality.[5,6]

In this study, we aimed to investigate the proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis and their associated outcomes in Australia and New Zealand.

2. Methods

2.1. Ethics approval

The study was approved by The Alfred Health Human Research Ethics Committee (Project number 679/22).

2.2. Study design and setting

This was a retrospective multicentre cohort study, which analysed all ICU admissions reported to the Australian and New Zealand Intensive Care Society (ANZICS) Adult Patient Database (APD) between 1st January 2012 and 31st December 2022. This 10-year period was chosen for recency to review the demographics and outcome trends relevant to current practice. Information including data on frailty status, ICU therapies and complications was available and collected for patients from 2017 onwards. Consequently, the patients admitted between 1st January 2017 and 31st December 2022 were studied in further detail.

2.3. ANZICS-APD

The ANZICS-APD is a binational database collected by the ANZICS Centre for Outcomes and Resources Evaluation that contains information on all admissions to 98% of adult ICUs in Australia and 67% of adult ICUs in New Zealand. ANZICS-APD prospectively collects high-quality de-identified patient information, including demographics (such as age and sex), chronic health status, and physiological and biochemical variables within the first 24 h of admission required for the Acute Physiology and Chronic Health Evaluation (APACHE)-III and IV illness severity scoring systems and the Australian and New Zealand Risk of Death (ANZROD), as well as ICU and hospital outcomes. Each patient is allocated a single admission diagnosis which reflects the primary cause of admission to the ICU using the ANZICS modification of the APACHE-IV diagnosis coding system. The data is maintained through the regular training of data collectors with a standardised data dictionary.[7] Quality assurance reviews and automatic data checks occur periodically to maintain data validity.[8]

2.4. Study population

Patients aged 16 years or older with an ICU admission diagnosis of anaphylaxis were included. These data were then analysed to determine the frequency of anaphylaxis during our study period. Patients were excluded if they were admitted to ICU without curative intent, such as for palliation or organ donation. To prevent replication of patient data, only the index ICU admission was included. As such, transfers from other ICUs were also excluded.

2.5. Data extraction

Data extraction included patient demographics, such as age, sex, comorbidities, goals of care, obesity status (body mass index $\geq$30 kg/m^2), the prevalence of delirium (during the current ICU admission), ICU and hospital mortality, and respective length of stays. The biochemical and physiological parameters within the first 24 h of admission were also extracted. Interventions including receipt of invasive mechanical ventilation, non-invasive ventilation, tracheostomy, vasopressors, renal replacement and extracorporeal membrane oxygenation (ECMO) therapies were also recorded.

2.6. Outcomes

The primary outcome was the proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis. The secondary outcomes included ICU and hospital length of stay, ICU complications (ICU readmission and delirium) and discharge destination.

2.7. Subgroup analysis

A predefined subgroup of patients termed “critically unwell” was used to describe the impact of anaphylaxis (predictors of becoming critically unwell or risk of in-hospital mortality among

critically unwell patients) from 1st January 2017 to 31st December 2022. For the purposes of this study, "Critically unwell" patients were defined if they were in receipt one or more specific cardiorespiratory ICU organ support, that included invasive mechanical ventilation, vasoactive medications, renal replacement therapy, or ECMO. This subgroup of patients represented patients who required significant healthcare resource use and longer treatment in ICU beyond the initial resuscitative management.

2.8. Statistical analyses

The overall trends of anaphylaxis were presented for all patients between 1st January 2012 and 31st December 2022. Categorical variables were reported with percentage (n (%)) and continuous data as mean (standard deviation) or median (interquartile range [IQR]) as appropriate depending on data distribution. Comparisons were made using Chi-square, student's *t,* or Log-rank tests as appropriate depending on the type and distribution of data. Multivariable regression analysis was performed to identify predictors of in-hospital mortality, with age, SOFA, physiological variables (heart rate, respiratory rate, mean arterial pressure, temperature and Glasgow coma scale [GCS]) and worst biochemical and ABG values (pH, PaO_2, $PaCO_2$, lactate) treated as continuous linear variables. We aimed to perform the sensitivity analyses by categorising covariates such as age and physiological variables (heart rate, respiratory rate, mean arterial pressure and GCS). A further multivariable regression analysis was performed to identify predictors of becoming critically unwell and in-hospital mortality in the subgroup of patients between 2017 and 2022. The variables that were statistically significant in the baseline comparison were included in the multivariable regression model, along with frailty status, as measured by the clinical frailty scale (CFS, as this was routinely collected from 2017 onwards; frailty defined as CFS = 5–8). These results were reported as an odds ratio (OR) with a 95% confidence interval (95%CI). SPSS Statistics version 27.0 (IBM, Armonk, NY) was used for all statistical analyses. A two-sided p-value <0.05 was considered statistically significant.

3. Results

7270 patients with anaphylaxis were admitted to ICU among 1,861,686 patients. After applying the exclusions, 7189 patients were included in the final analysis (Supplementary Fig. 1). The number of hospitals contributing to the APD increased from 154 to 196 between 2012 and 2022. The proportion of ICUs reporting at least one severe anaphylaxis annually increased from 61.7% in 2012 to 83.0% in 2022 (Fig. 1).

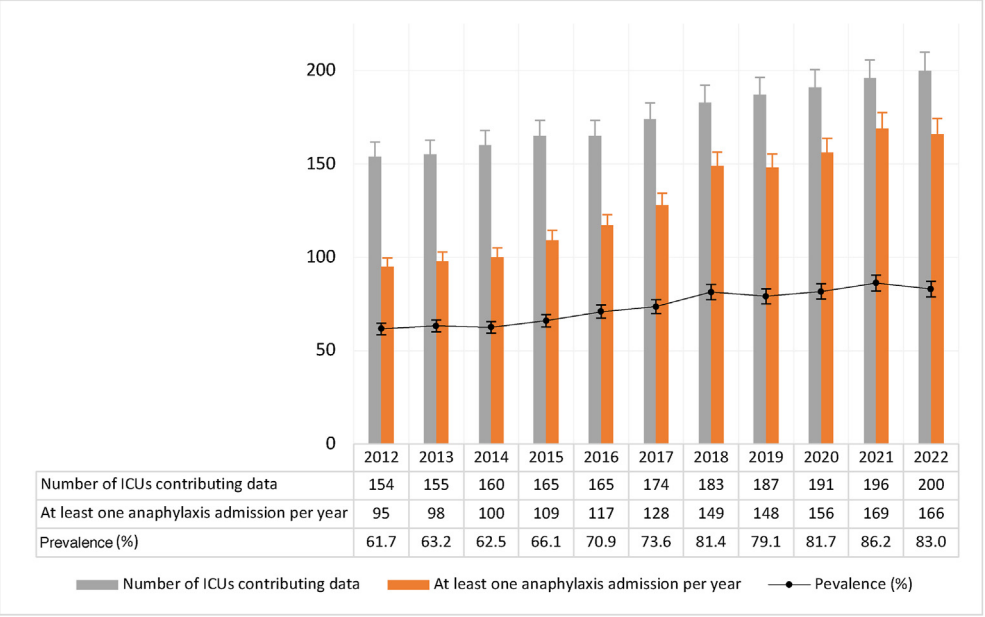
The baseline characteristics, physiological parameters and worst acid-base status within the first 24 h of the included patients are presented in Table 1. There was a female preponderance (61.7%). The median age for patients was 51.2 (IQR: 35.0–66.2) years. A small proportion of patients had comorbidities, and their median sequential organ failure assessment (SOFA) score was 1 (IQR: 0–3). The source of admission was most frequently the emergency department (47.6%), followed by general wards (33.2%) and operating theatres (7.7%).

3.1. Primary outcome

The proportion of severe anaphylaxis requiring ICU admission increased from 0.25% in 2012 to 0.43% in 2022 (Fig. 2). The median annual ICU and in-hospital mortality rates following severe anaphylaxis were 0.3% (range: 0.0–0.7%) and 0.7% (range: 0.1–1.1%), respectively (Fig. 2). Among all 7189 patients, overall ICU mortality was 0.4% (n = 27) and in-hospital mortality was 0.8% (n = 57) (Table 2). Increasing age (OR = 1.055; 95%CI: 1.008–1.105) and SOFA scores (OR = 1.616; 95%CI: 1.265–2.065), having an immunosuppressive chronic condition (OR = 16.572; 95%CI: 3.006–91.349) and an increasing respiratory rate (OR = 1.116; 95% CI: 1.057–1.178) predicted in-hospital mortality in patients with anaphylaxis, while an increasing GCS score was associated with a lower in-hospital mortality (OR = 0.827; 95%CI: 0.705–0.969). Lactate was not predictive of in-hospital mortality (Table 3).

3.2. Secondary outcomes

The outcomes following ICU admission are described in Table 2. The median ICU and hospital length of stays were 0.9 (IQR: 0.7–1.5)



	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022
Number of ICUs contributing data	154	155	160	165	165	174	183	187	191	196	200
At least one anaphylaxis admission per year	95	98	100	109	117	128	149	148	156	169	166
Prevalence (%)	61.7	63.2	62.5	66.1	70.9	73.6	81.4	79.1	81.7	86.2	83.0

Fig. 1. Number of hospitals reporting at least one case of severe anaphylaxis requiring intensive care admission. Error Bars represent standard error.

Table 1
Baseline characteristics for all included patients with severe anaphylaxis between 2012 and 2022.

	All patients (n = 7189)
Female Sex	4436 (61.7%)
Indigenous status	399/6310 (6.3%)
BMI ≥30 kg/m^2	1311/3015 (43.5)
Clinical frailty scale[c]	2 (2–3)
Age, years[c]	51.2 (35.0–66.2)
Hospital classification	
Tertiary	2347 (32.6%)
Metropolitan	1847 (25.7%)
Private	1457 (20.3%)
Rural/regional	1538 (21.4%)
Location of anaphylaxis	
Emergency department	3421 (47.6%)
General ward	2387 (33.2%)
Operating rheatre/recovery	554 (7.7%)
Transfer from other Hospital	757 (10.5%)
Other[a]	70 (1.0%)
Cardiac arrest	200 (2.8%)
Pre-ICU (hours)[c]	4.3 (1.88–9.8)
Treatment limitations	132 (1.3%)
Emergency response admission	1852 (25.8%)
Comorbidities	
Chronic respiratory condition	303 (4.2%)
Chronic cardiovascular condition	254 (3.5%)
Chronic liver condition	23 (0.3%)
Chronic renal failure	130 (1.8%)
Immunosuppressive condition	318 (4.4%)
Diabetes Mellitus	526 (7.3%)
Lymphoma	65 (0.9%)
Leukaemia	66 (0.9%)
Metastatic cancer	179 (2.5%)
Pregnant	46 (0.6%)
Postpartum	92 (1.3%)
Illness severity scores	
SOFA Score[c]	1 (0–3)
APACHE II score[c]	10 (7–15)
APACHE III score[c]	33 (23–46)
ANZROD (%)	1.8 [2.2]
ANZROD (%)[c]	0.4 (0.2–0.7)
Vital organ supports	
At least one vital organ support	2745/7189 (38.2%)
Mechanical ventilation	1533 (21.3%)
Mechanical ventilation on Day 1[b]	1010/1069 (94.5%)
Duration of MV, hours[c]	11.5 (2.0–20.0)
Inotropes/vasopressors[b]	1879 (26.2%)
Renal replacement therapy[b]	24 (0.3%)
Non-invasive ventilation[b]	138 (1.9%)
Tracheostomy[b]	2 (0.0%)
Extracorporeal membrane oxygenation therapy[b]	1 (0.0%)
Worst physiological parameters in the first 24 h	
Heart rate, per minute[c]	101 (82–115)
Systolic BP, mmHg[c]	100 (90–110)
Mean arterial pressure, mmHg[c]	70 (63–87)
Diastolic BP, mmHg[c]	55 (48–61)
Respiratory rate, per minute[c]	14 (12–25)
Temperature, °C[c]	36.1 (35.8–36.5)
Worst GCS[c]	15 (15–15)
Worst Acid-base status in the first 24 h	
pH[c]	7.34 (7.27–7.40)
$PaCO_2$, mmHg[c]	39 (34–45)
PaO_2, mmHg[c]	96 (75–134)
Bicarbonate, mmol/L[c]	22 (19–25)
Lactate, mmol/L[c]	3.0 (1.7–5.5)
Worst FiO_2[c]	0.32 (0.21–0.50)

ANZROD – Australia New Zealand risk of death, APACHE – Acute Physiology and Chronic Health Evaluation, ARDS – acute respiratory distress syndrome, BMI – body mass index, BP – blood pressure, C – centigrade, CFS – clinical frailty scale, ED – emergency department, ICU – intensive care unit, IQR – interquartile range, SD – standard deviation, SOFA – sequential organ failure assessment score.
[a] Other – direct admission, other hospital transfer.
[b] Information available only from 2017.
[c] Variables are described in median (interquartile range).

and 2.0 (IQR: 1.1–4.3) days, respectively. The frequency of ICU complications such as ICU readmission and delirium were 2.1% and 0.3%, respectively. Most of the patients were discharged home (92.6%, n = 6660).

3.3. Subgroup analysis

The cohort of patients included in the subgroup analysis between 2017 and 2022 was comparable to those between 2012 and 2016 (Supplementary Table 1). Between 2017 and 2022, there were a total of 994,763 ICU admissions; of these, 4861 patients had anaphylaxis. After excluding 771 patients with incomplete data on ICU organ support, 4090 patients were analysed. Although there were some baseline differences, the illness severity of the included patients was no different to 771 excluded patients (Supplementary Table 2). The baseline characteristics and outcomes of the included 4090 patients are described in Supplementary Table 3. These patients infrequently had comorbidities, with low illness severity scores (e.g. Median SOFA score 1 (IQR: 0–3). More than half of the patients admitted to ICU were critically unwell (55.8%, n = 2281). Baseline characteristics and outcomes for the subgroup of patients admitted between 2017 and 2022 are presented in Supplementary Table 3. A quarter (26.1%, n = 1069/4090) received invasive mechanical ventilation; of these patients, most (94.5%) were received mechanical ventilation on day 1 of ICU admission. Vasoactive medications were used in 1879 (47.4%) patients. Critically unwell patients had a higher ICU and hospital mortality compared to their non-critically ill counterparts ($p = 0.002$ and $p = 0.020$, respectively). Although critically unwell patients had a longer ICU stay ($p < 0.001$), the hospital length of stay was similar between both groups ($p = 0.64$). Increasing SOFA scores (OR = 1.67; 95%CI: 1.58–1.76), presence of chronic liver failure, diabetes mellitus and leukaemia were predictive of becoming critically unwell. Anaphylaxis in the emergency department and ward did not increase the risk of being critically unwell. Increasing age (OR = 0.99; 95%CI: 0.98–0.99), patients in private ICUs (OR = 0.13; 95%CI: 0.05–0.36), or those admitted to the ICU following an emergency response review were less likely to be critically unwell (OR = 0.62; 95%CI: 0.50–0.77) (Supplementary Table 4). Furthermore, SOFA scores (increment of 1) and frailty (CFS treated as a continuous variable) along with patients with immunosuppressive conditions or those who had a cardiac arrest were associated with increased in-hospital mortality in critically unwell patients (Supplementary Table 5). Due to the low hospital mortality observed in our findings, categorisation of respiratory rate and other physiological variables could not be performed.

4. Discussion

4.1. Key findings

This multicentre retrospective study found that the proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis in Australia and New Zealand was low. The location of anaphylaxis varied, with most admissions arising from the emergency department and general wards. This proportion has increased with more hospitals reporting at least one severe anaphylaxis episode requiring ICU admission each year. The overall in-hospital mortality was low. Similarly, the burden of severe anaphylaxis was low, with short ICU and hospital length of stay and most patients being discharged home. In the subgroup analysis that included patients between 2017 and 2022, over half the admitted patients were critically unwell requiring at least one vital organ support. These patients had statistically higher ICU and in-hospital

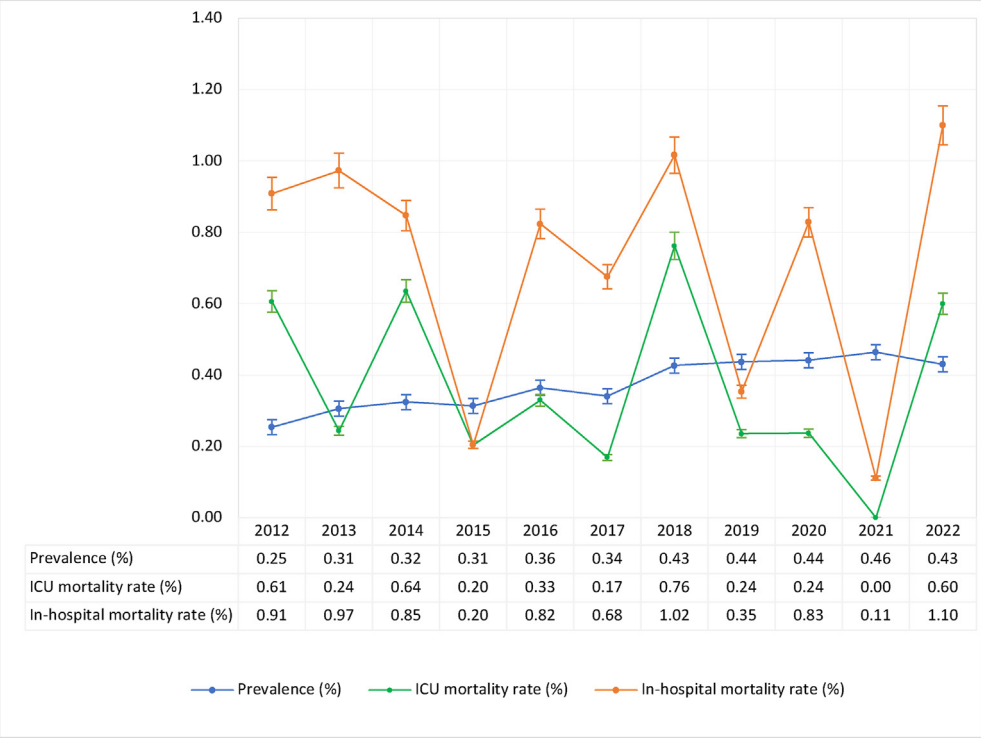


Fig. 2. Primary Outcome: Prevalence and mortality rates of anaphylaxis over time. Error Bars represent standard error.

Table 2
Secondary outcomes following ICU admission for severe anaphylaxis.

	All patients (n = 7189)
Primary Outcome	
Hospital mortality	57 (0.8%)
Secondary Outcomes	
1. ICU Mortality	27 (0.4%)
2. Duration of stay	
ICU length of stay, days[d]	0.9 (0.7–1.5)
Hospital length of stay, days[d]	2.0 (1.1–4.3)
3. ICU complications	
ICU readmission	136 (2.1%)
Delirium[a]	24/3335 (0.3%)
4. Hospital outcome	
Discharge to usual residence	6660 (92.6%)
Discharge to a nursing home[b]	72 (1.0%)
Discharge to rehabilitation[b]	54 (0.8%)
Transfer to other hospital	325 (4.5%)
Other[c]	21 (0.3%)

ICU – intensive care unit.
[a] Information available only from 2017.
[b] Before 2017 this was termed 'discharge to chronic care/nursing home/rehabilitation'.
[c] Other – discharge to Mental Health, or other destination not specified.
[d] Variables are described in median (interquartile range).

mortality. Increasing SOFA score and chronic conditions such as liver failure, diabetes mellitus and leukaemia were associated with critical illness Predictors for hospital mortality among the critically unwell included increasing age, SOFA score, frailty, immunosuppression and ICU admission following a cardiac arrest.

4.2. Comparison to other studies

This is the first study in Australia and New Zealand investigating severe anaphylaxis requiring ICU admission. Several large-scale national studies have previously been conducted within a similar time period in the United Kingdom (UK) by Gibbison et al. (2005–2009), France by Guerci et al. (2012–2017) and in the United States of America (USA) by Motosue et al. (2005–2014).[4–6]

4.3. Definition, frequency and location of anaphylaxis

The definition of anaphylaxis varied across the studies. Gibbison et al. and Motosue et al. utilised data from national audit databases, which was similar to our method of using the admission diagnosis from the ANZCIS-APD. Anaphylaxis severity stratified by grade was only available in Guerci et al. The prevalence of severe anaphylaxis requiring ICU admissions reported by Gibbison et al. was 0.2–0.3% across a five-year period in 175 ICUs and 460,123 patients,[6] which was comparable to our finding of 0.25–0.43% out of 1,861,686 patients. This was not reported by Motosue et al. and Guerci et al. Over the study period, there were newer ICUs that started reported to the ANZICS APD with an increase in both available and physical ICU beds over time. This could have resulted in an increased proportion of anaphylaxis cases.

The location of severe anaphylaxis was frequently observed to be from the operating theatre and emergency department. Gibbison et al. reported that the emergency department was the second highest source of admission (37.3%) after the operating theatre (38.0%). Guerci et al. reported that the highest source of admission was the operating theatre (56.0%), followed by "out of hospital" (18.9%) and radiology (11.8%). This was different from our findings where most patients came from the emergency department (47.6%) and only a minority from operating theatres (7.7%). The difference may be attributed to our different modes of data entry, as any anaphylaxis that occurred before a surgical start (such as induction of anaesthesia) would not be classified as anaphylaxis in the operating theatre but their source of admission (emergency department or general ward).

Table 3
Multivariable logistic regression to identify the predictors for hospital mortality in all patients.

Predictors for hospital mortality[b]	Multivariable Analysis	
	OR (95%CI)	p-value[a]
Patient factors		
Age	1.055 (1.008–1.105)	**0.022**
SOFA score	1.616 (1.265–2.065)	**<0.001**
Female sex	2.361 (0.707–7.888)	0.16
Comorbidities		
Chronic respiratory condition	0.712 (0.095–5.002)	0.71
Chronic cardiovascular condition	2.983 (0.406–21.920)	0.28
Chronic liver condition	7.541 (0.400–142.10)	0.18
Chronic renal failure	0.792 (0.067–9.378)	0.85
Diabetes mellitus	0.725 (0.171–3.072)	0.66
Immunosuppressive condition	16.572 (3.006–91.349)	**0.001**
Lymphoma	0.806 (0.034–19.120)	0.89
Leukaemia	0.484 (0.028–8.251)	0.62
Metastatic cancer	0.396 (0.026–5.950)	0.50
Obesity	2.677 (0.563–12.738)	0.22
Hospital classification		
Metropolitan	reference	
Private	0.152 (0.020–1.157)	0.07
Rural/regional	0.165 (0.009–3.018)	0.22
Tertiary	0.579 (0.140–2.387)	0.45
Other factors		
Cardiac arrest	2.227 (0.307–16.902)	0.42
Worst acid-base status in the first 24 h		
pH	0.001 (0.000–0.418)	**0.026**
$PaCO_2$, mmHg	1.032 (0.982–1.084)	0.21
PaO_2, mmHg	1.002 (0.996–1.009)	0.50
Lactate, mmol/L	0.870 (0.678–1.117)	0.28
Worst physiological parameters in the first 24 h		
Heart rate, per minute	0.996 (0.976–1.016)	0.69
Mean arterial pressure, mmHg	1.005 (0.986–1.024)	0.60
Respiratory rate, per minute	1.116 (1.057–1.178)	**<0.001**
Temperature, °C	0.804 (0.430–1.505)	0.50
Worst GCS	0.827 (0.705–0.969)	**0.019**

CFS – clinical frailty scale, ICU – intensive care unit, SOFA – sequential organ failure assessment score.
[a] Numbers in bold imply statistical significance in the final model.
[b] Numbers were very small for ICU admission source, indigenous patients and patients with metastatic cancer and leukaemia to analyse.

4.4. Outcomes following ICU admission

Within the study period, both ICU and in-hospital mortality were observed to fluctuate between each year. The exact reason for this fluctuation is unclear and may be reflective of the low mortality that occurs following anaphylaxis. Annual hospital mortality rates were not published in similar national anaphylaxis audits.

Guerci et al. reported a higher mortality (5.0%) in patients admitted to ICU with severe anaphylaxis.[4] Similarly, Gibbison et al. reported a mortality of 4.7% during their study period.[6] In contrast, we observed a lower ICU and hospital mortality rate reported in our study. This was despite an increasing incidence of severe anaphylaxis. This has been observed in previous studies, where mortality has not increased despite a 7-fold increase in anaphylaxis over a 20-year period.[9] Multiple reasons for this difference exist, including having different management approaches and ICU admission criteria for severe anaphylaxis across different studies. Notably, ICU and hospital length of stay observed in our study remain similar to those reported by Guerci et al. (Median [IQR] of 2 [2–3] and 5 [3–12], respectively) and Gibbison et al. (Mean range of 2.4–2.7 days in ICU).[4,6]

Guerci et al. reported that lactate concentration at ICU admission was a predictor of mortality following severe anaphylaxis. However, the study was limited by a small convenience sample size.[4] Our study was unable to replicate this observation, where lactate levels did not predict hospital mortality. While the exact reason for the different findings is unclear, hyperlactatemia continues to be associated with in-hospital mortality in ICU patients due to how critically unwell these patients are, or the cumulative doses of adrenaline used to achieve resuscitation endpoints.[10] Lactate levels may have been lower in our study, which may have diminished the association between lactate and mortality.

Studies evaluating the risk factors associated with in-hospital mortality after severe anaphylaxis are scarce. Studies such as the National Audit Project in the UK identified increasing age and mild systemic disease (equivalent to a score of 2 on the American Society of Anaesthesiologists Physical Status score) as predictors for critical care admission but focused on anaesthetic and surgical anaphylaxis.[11,12] Likewise, although a recent study found that older age, cardiac procedures and specific comorbidities increased the risk of fatal outcomes following anaphylaxis, the authors only explored perioperative and periprocedural anaphylaxis.[13] While our study shared similar findings such as increasing age being associated with in-hospital mortality, our study did not specifically investigate perioperative anaphylaxis and thus clear similarities cannot be drawn.

4.5. Implications

The findings of our study on the frequency and outcomes following severe anaphylaxis are broadly consistent with findings from other nationwide studies. The increased proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis and the increased number of ICUs admitting patients with severe anaphylaxis across Australia and New Zealand underscores the importance of early identification and management of anaphylaxis.[2] Future studies are required to investigate these causative antigens to potentially minimise exposure risk.

4.6. Strengths and limitations

Our study has several notable strengths. Firstly, our study spans most ICUs that admitted patients across Australia and New Zealand. Secondly, the relatively large sample of high-quality data increased the precision of our estimates. Thirdly, we incorporated several pre-specified subgroup analyses to assess the predictors of critical illness and in-hospital mortality.

This study had several limitations. As a retrospective study, data collection was reliant on pre-existing medical records and proper data entry. Similar to other national databases, a degree of human error from data entry and misinterpretation of information can be expected. The ability to admit a patient to ICU for the management of severe anaphylaxis can be subject to ICU bed availability. This study was unable to provide information on the causative agents for anaphylaxis or information on investigations relevant to anaphylaxis such as tryptase levels, which were reported in other papers.[4] The severity of anaphylaxis by grade was not available in this retrospective study, and hence vital organ support was used to determine if the patient was critically unwell. Patients who might have had anaphylactic shock and died before ICU admission were not included in this study. We did not have the precise timing of when various ICU supports were needed during their admission. The multivariate data analysis presented is limited to the available retrospective data and thus may not present the actual factors that predict in-hospital mortality.[14]

4.7. Conclusion

The overall proportion of patients admitted to ICU who have anaphylaxis as a principal diagnosis has increased steadily in Australia and New Zealand, with an increasing number of ICUs

seeing a case every year. These patients have a low burden of co-morbidities and in-hospital mortality remains low even when vital organ support is required. Further studies should investigate these identified factors that may predict in-hospital mortality among these patients.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

CRediT authorship contribution statement

Conceptualisation: Z.L., D.K., C.F., D.P. and A.S.; Data curation: Z.L., D.P. and A.S.; Formal analysis: Z.L., D.P. and A.S.; Investigation: Z.L., D.K., H.K., C.F., D.P. and A.S.; Methodology: Z.L., D.K., H.K., C.F., D.P. and A.S.; Project administration: Z.L., D.P. and A.S.; Resources: Z.L., D.P. and A.S.; Software: Z.L. and A.S.; Supervision: D.P. and A.S.; Validation: Z.L. and A.S.; Visualisation: Z.L., D.P. and A.S.; Writing – original draft: Z.L. and A.S.; Writing - review & editing: Z.L., D.K., H.K., C.F., D.P. and A.S.

Conflict of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Ashwin Subramaniam and David Pilcher are associate editors for critical care and resuscitation. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ccrj.2024.06.002.

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