Li et al. World Allergy Organization Journal (2024) 17:100980
http://doi.org/10.1016/j.waojou.2024.100980

WORLD ALLERGY ORGANIZATION JOURNAL

Open Access

Incidence and trends of anaphylaxis among inpatients from 2003 to 2023 in Wuhan, China: A multicenter retrospective study

Le Li, MD[a], Nan Huang, MD[a], Wenjing Li, MD[a], Yaqi Yang, MD[a], Dongxia Ma, MD[a], Hao Chen, MD, PhD[a]** and Rongfei Zhu, MD, PhD[a,b]*

ABSTRACT

Background: The incidence of a disease can help health professionals to identify risk factors and health-care policymakers to develop corresponding policies. The realization of both purposes depends on comprehensive studies, especially studies done on a large scale. However, comprehensive studies on the incidence of anaphylaxis among inpatients in China are still notably scarce. Hence we aim to explore the incidence and clinical characteristics of anaphylaxis among inpatients over a span of 21 years in Wuhan, China.

Methods: We retrieved data on anaphylaxis cases from the Data Platform Application Portal (DPAP) across 3 medical centers of Tongji Hospital, Wuhan, China from January 1, 2003, to December 31, 2023.

Results: The data encompassed a total of 362 anaphylaxis patients from 2,139,272 inpatients. Among them 204 (56.4%) were male, and the median age was 45 years old. Over the past 2 decades, the incidence rate of anaphylaxis at Tongji Hospital was 16.92 per 100,000 individuals. After adjusting for gender and age, the annual standardized incidence rate was 234.53 per 100,000 individuals. The incidence rate of anaphylaxis among the inpatients revealed a relatively stable but slowly rising trend over the 21-year observation period. As for the triggers of anaphylaxis, drugs were responsible for 73.6% of triggers, with antibiotics representing the highest proportion of these cases (38.4%). Drug triggers also showed age-specific features: chemotherapy (17.9%) had the highest proportions among children aged 0–3 years; blood products were more prevalent in school-age children. 13.5% of the cases had an unknown cause. In anaphylaxis cases, despite that only 36.0% received epinephrine treatment, the application of epinephrine still showed an ascending trend. Moreover, the mortality rate for anaphylaxis was relatively low (1.6%), displaying a consistent downward trend.

Conclusion: Our study provides insights into the incidence of anaphylaxis among inpatients in Wuhan over a 21-year period. Drugs are the most common triggers for anaphylaxis, and the use of epinephrine in anaphylaxis management is far from optimal.

[a]Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, China
*Corresponding author. Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology; Institute of Allergy and Clinical Immunology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 430030, Wuhan, China. E-mail: zrf13092@163.com
**Corresponding author. Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, 430030, Wuhan, China. Email: chenhao1019@126.com
Full list of author information is available at the end of the article

http://doi.org/10.1016/j.waojou.2024.100980
Received 22 July 2024; Received in revised from 3 September 2024; Accepted 3 October 2024
Online publication date xxx

Keywords: Anaphylaxis, Incidence, Inpatient, Trigger, China

Key messages

1. The incidence of anaphylaxis among inpatients was stable but slowly rising in Wuhan, China.
2. Drugs were the principal triggers of anaphylaxis, with antibiotics accounting for the majority.
3. Epinephrine was underused in this cohort, yet the mortality rate was still relatively low.

INTRODUCTION

Anaphylaxis is a severe systemic hypersensitivity reaction with acute onset that can potentially be fatal.[1] Its triggers are diverse and vary with age and geographical region , with common ones like food, medication, and insect venom.[2,3] Anaphylaxis is characterized by severe compromise of the airway, breathing, and/or circulation, which can pose a life-threatening risk, for these severe reactions may manifest without the presence of typical skin features or the onset of circulatory shock[4] and anaphylaxis recurs in 26.5–54.0% of patients, with a mortality rate ranging from 0.12 to 1.06 per million person-years.[5]

Depending on the definitions, methodologies, and regions, as well as the selected study periods, the incidence trends of anaphylaxis demonstrate diverse patterns.[6–8] The current global incidence of anaphylaxis is approximately 46 cases per 100,000 individuals annually, with rates fluctuating between 0.49 and 328.7 per 100,000 person-years.[6] For children, the incidence displays significant global variation, with rates for total anaphylaxis spanning from 1 to 761 per 100,000 person-years.[9]

The importance of understanding the incidence of anaphylaxis cannot be underestimated for diagnostic and preventive purposes. However, there is a paucity of research on the incidence of anaphylaxis in China. This is reflected in the lack of awareness regarding anaphylaxis as a disease, variations in diagnostic criteria, and the absence of large-scale databases. Besides, such constraining factors also make it understandable that, the majority of studies focus on the clinical characteristics and triggers of anaphylaxis.[10,11] This results in a substantial gap in knowledge regarding the incidence and current trends of anaphylaxis within the Chinese population.

The diagnostic benefits of incidence, coupled with timely and proper treatment, are crucial in reducing the life-threatening risk of anaphylaxis. Current guidelines[1,4,12] recommend epinephrine/adrenaline as the first-line treatment for anaphylaxis. However, the implementation of this rule is far from sufficient. Previous studies have shown that the global usage rate of epinephrine ranged from 17% to 98%.[13–18] In China, the application rate of epinephrine inpatients in Beijing is approximately 51.9%, compared to 25% in emergency settings.[10,19]

By employing the World Allergy Organization's (WAO) 2020 updated diagnostic criteria[12] and Data Platform Application Portal (DPAP) of Tongji Hospital, our research team has investigated the incidence, triggers, and treatment of anaphylaxis in outpatient settings by retrieving medical records.[20] This method has proven to be a viable approach for conducting epidemiological studies on anaphylaxis. Compared with outpatients, inpatients typically constitute a more severe patient group with comprehensive and precise medical records. These individuals often exhibit diverse triggers, which necessitates more intricate interventions, including advanced life support measures. A probe into the cases of the inpatients with the comparison in mind can reveal patterns that may have been overlooked in outpatient research and hopefully shed new light on previous findings.

Our study delves into the incidence of anaphylaxis among inpatients, utilizing both DPAP and WAO criteria. It marks the initial comprehensive analysis of anaphylaxis trends among inpatients at

3 medical centers affiliated to a university hospital over a 21-year span, encompassing clinical manifestations and treatment approaches. Furthermore, this research complements outpatient data with insights from an inpatient cohort, aiming to enhance the comprehension of the natural progression of anaphylaxis through horizontal comparisons. This endeavor seeks to clarify the epidemiology, as well as the current landscape of diagnosis and treatment, of anaphylaxis in the specified region.

MATERIALS AND METHODS

Patient

Data on anaphylaxis cases were extracted from the Data Platform Application Portal (DPAP) of Tongji Hospital's 3 medical centers in 3 different districts in Wuhan, specifically the Sino-French New City Branch in Caidian, the Qiaokou Branch in Hankou, and the Optics Valley Branch located in the Wuhan East Lake High-Tech Development Zone, spanning from January 1, 2003, to December 31, 2023. We identified potential anaphylaxis cases by searching for relevant diagnoses within the International Classification of Diseases, Tenth Revision (ICD-10), such as "anaphylactic shock" or "allergic reaction" within the platform (see Appendix 1 for details). These cases were subsequently confirmed manually by 5 doctors based on the 2020 WAO guidelines. The study received ethical approval from the Independent Ethical Committee of Tongji Hospital (NO.TJ-IRB202401061), and the requirement for informed consent was waived.

The identified patients with anaphylaxis in the study encompassed 2 categories. The first category of patients comprised those who were hospitalized at our institution for the treatment of diseases other than allergic conditions and developed anaphylaxis during their hospital stay for various reasons. Some patients in this group might have multiple medical records due to recurrent episodes of anaphylaxis. The second category included individuals admitted for extensive etiological exploration subsequent to syncopal episodes that preliminarily led to suspicions of cardiovascular or cerebrovascular disease diagnoses. Subsequent meticulous diagnostic workup culminated in the conclusive identification of anaphylaxis in these cases. These patients' symptoms of anaphylaxis had already been relieved at the time of their visit, but their episodes during the study period were still recorded and included in the statistical analyses.

Extraction process

We utilized PyCharm (2023.1.1 Community Edition) to clean and process the medical record data. We defined acute onset as occurring within 6 h after contact with the trigger, in line with the medical literature.[21]

We transformed the WAO 2020 guidelines into practical descriptions that clinicians had readily used in medical records, outlining the clinical symptoms and signs (see Appendix 2 for more information). Leveraging the symptomatology outlined in various guidelines, we assembled a comprehensive list that covers full terms, abbreviations, subject headings, keywords, synonyms, and near synonyms. Then, we adjusted our approach based on the search findings, utilizing hierarchical clustering of terms to distinguish between broader and narrower categories.

We extracted all pertinent data from the medical records. The process of extraction and the results obtained are depicted in Fig. 1. According to the guidelines, it is understood that not all patients with anaphylaxis will show symptoms of shock. This study aims to identify all patients who meet the diagnostic criteria, with or without a diagnosis of shock. As a result, patients diagnosed with anaphylactic shock were directly selected via manual screening. For patients without a diagnosis of anaphylactic shock but with other relevant diagnoses such as allergic reactions, an initial programmatic screening was conducted due to their larger numbers, before they were subjected to the manual screening process.

Statistical analysis

We calculated the crude incidence rate for anaphylaxis cases among inpatients. This rate was determined using the total number of new patient cases as the numerator, where each patient was counted only at their initial visit. The denominator was the total number of inpatient visits for each

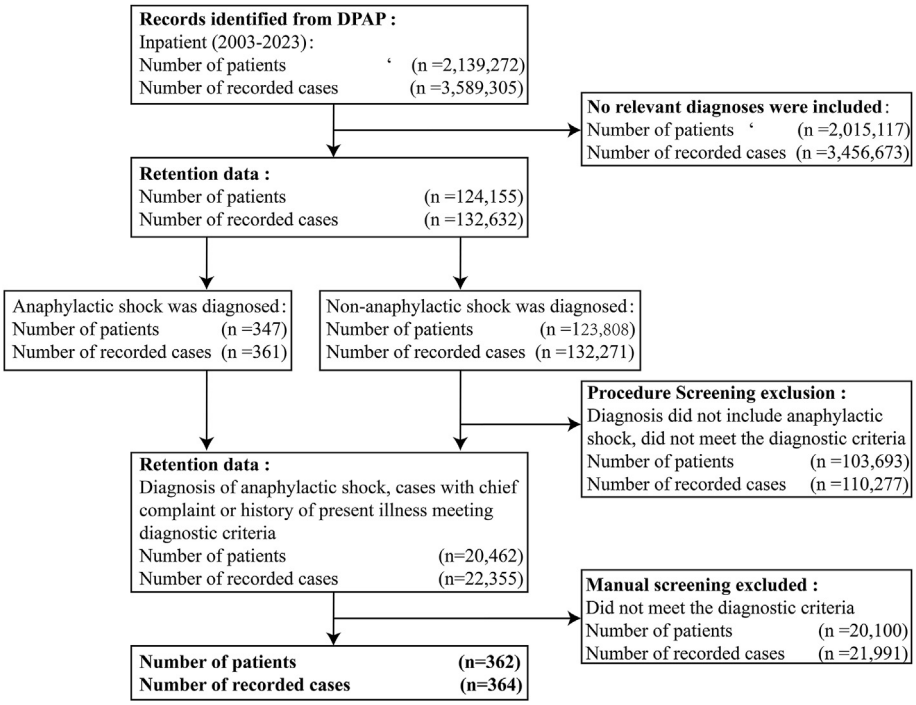

Fig. 1 Flow Diagram of anaphylaxis data extraction. The figure presents a flowchart detailing the process from database retrieval to automated and manual screening, with patient numbers and case inclusion/exclusion data at each step

corresponding year. For the adjusted incidence rate, we used a weighted average, factoring in the age group and gender distribution of our patient population. We estimated incidence rate ratios (IRR) and 95% confidence intervals (CI) employing negative binomial regression with Stata/MP 18.

RESULTS

Characteristics

Our study encompassed 362 anaphylaxis patients out of a total of 2,139,272 inpatients, with 364 recorded cases in the database. Among these anaphylaxis patients, 56.4% (204/362 patients) were male and the median age was 45 years. 8 patients (2.2%) experienced recurrent anaphylaxis.

Over the past 2 decades, the incidence rate of anaphylaxis at Tongji Hospital stood at 16.92 per 100,000 individuals. However, upon adjusting for factors such as age and gender, the annual incidence rate rose to 234.53 per 100,000 individuals. Over the course of these 21 years, we observed a relatively stable incidence of anaphylaxis, with a peak in 2008, followed by a rapid decline in 2009. Subsequently, an upward trend ensued (IRR 1.05, 95% CI 1.03–1.07, $P < 0.001$), as illustrated in Fig. 2.

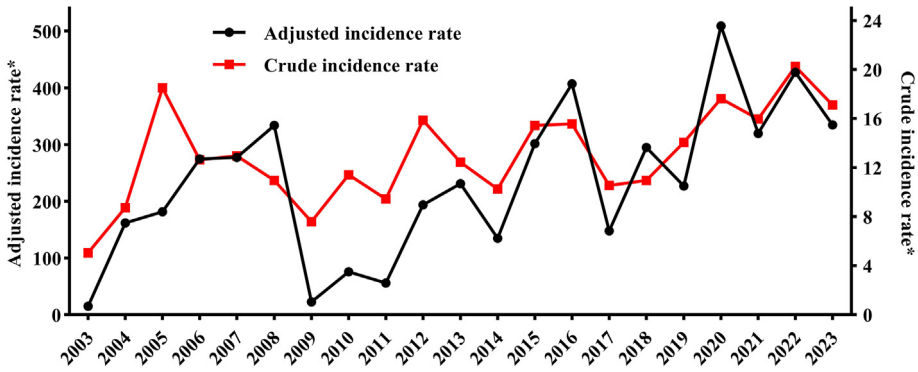

Fig. 2 Trend chart of crude and adjusted incidence of anaphylaxis among inpatients (*incidence rate per 100,000 person-years). The figure illustrates the trends of crude and adjusted incidence rates of anaphylaxis in a university hospital in Wuhan, China, from 2003 to 2023

The crude annual incidence data revealed that adults aged 19 to 64 exhibited the highest rate of anaphylaxis cases, constituting 53.9% (Fig. 3). However, when considering the adjusted incidence rates, the highest rates were observed in preschoolers within the age bracket of 4–6 years old. Consistent with the overall trend, the majority of age groups experienced a peak in incidence rates between 2005 and 2008, which was followed by an ascending trend commencing from 2009.

Triggers

Identifiable triggers were found in 315 cases, representing 86.5% (315/364) of all anaphylaxis. The preponderant cause was drugs, which accounted for 73.6% (268/364) of the cases, followed by foods at 8.5% (31/364). Other triggers included insect bites (1.6%, 6/364), with gases specifically referring to combustion smoke and argon gases used in welding (1.1%, 4/364) and medical devices (0.8%, 3/364), as well as exercise-induced reactions (0.5%, 2/364) and cosmetic products (0.3%, 1/364). Over the past 21 years, there has been a declining trend in the proportion of unspecified cases, whereas the incidence of drug-induced anaphylaxis (DIA) and food-induced anaphylaxis (FIA) has increased (Fig. 4).

In terms of age stratification, DIA emerges as a predominant trigger across all age groups. Notably, in the 55 recorded cases of individuals aged 65 years and above, DIA is found to have the highest prevalence at 90.9% (50/55). Following closely, in the 31 cases of school-age children between 7 and 12 years, DIA accounts for 87.1% (27/31), as illustrated in Table 1. Amongst drug allergen triggers (73.6% of the cases), antibiotics were the most common, accounting for 38.4% (103/268) of these instances. Antibiotic-induced anaphylaxis was the predominant trigger across all age groups (Table 1).

However, we also observed a decline in anaphylaxis cases triggered by antibiotics from

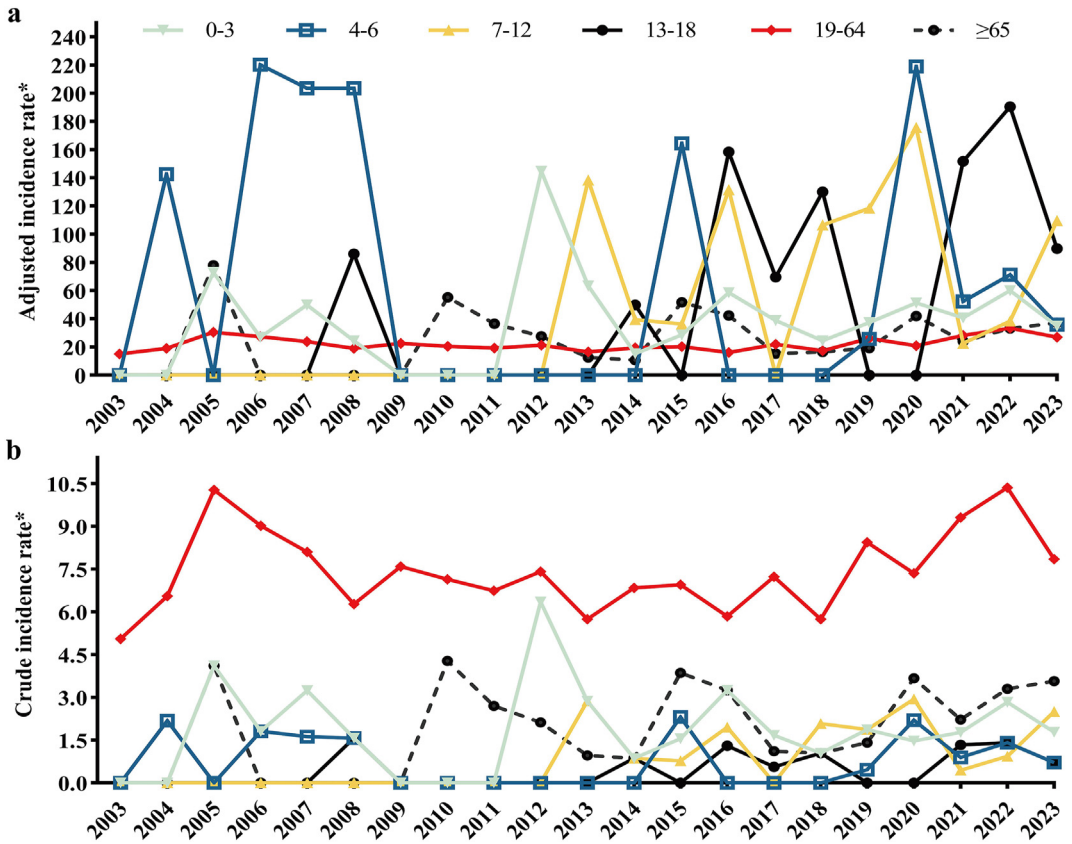

Fig. 3 Adjusted (a) and crude (b) incidence rate trends by age groups (*incidence rate per 100,000 person-years). Figure (a) presents the 21-year trends of adjusted incidence rates for anaphylaxis across 6 age groups. Figure (b) illustrates the crude incidence rate trends for anaphylaxis among different age groups

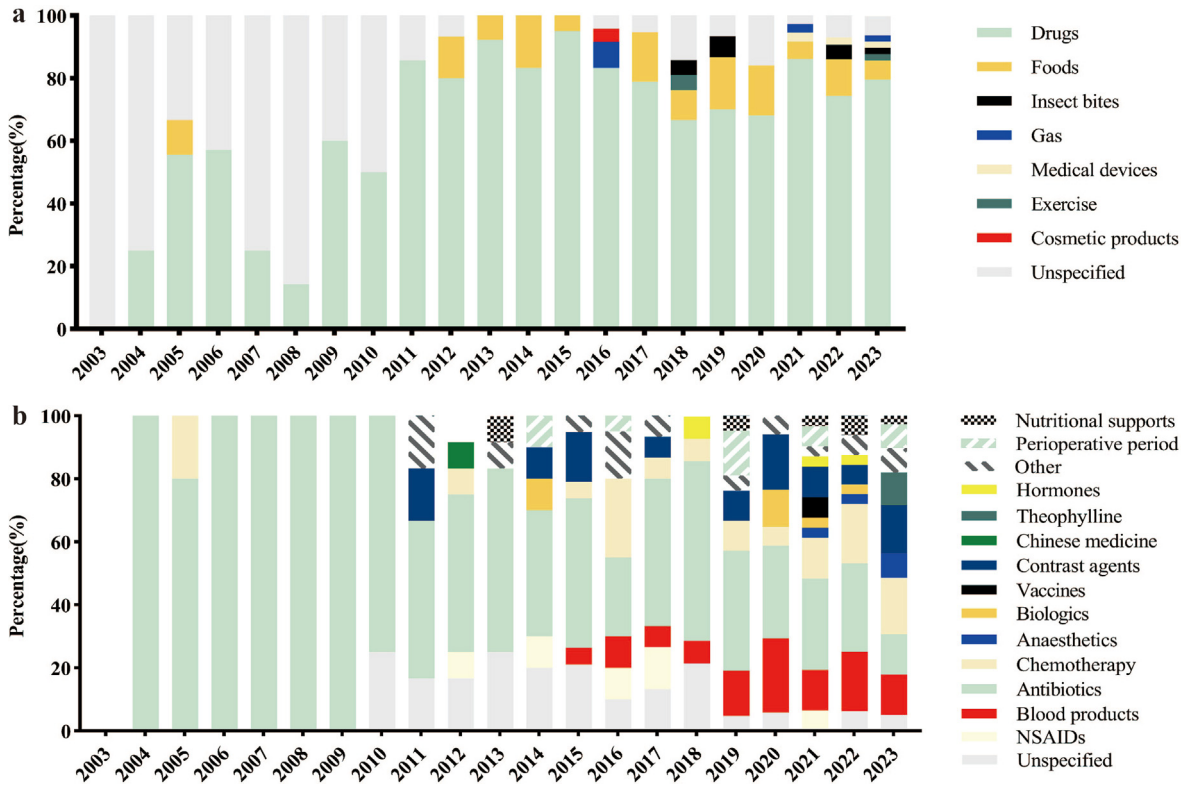

Fig. 4 Trend chart of anaphylaxis triggers (a) and drug trigger changes (b) from 2003 to 2023. Figure (a) shows the 21-year trend of anaphylaxis trigger proportions in a university hospital in Wuhan, China. Figure (b) depicts the 21-year trend of various drug trigger proportions for anaphylaxis

2003 to 2023. Instead, we noticed an uptick in cases induced by blood products, contrast agents, and chemotherapy. Notably, in the 28 cases of DIA among children aged 0–3 years, aside from antibiotics, chemotherapy and blood products exhibit the highest proportions, accounting for 17.9% (5/28) and 14.3% (4/28) respectively. Blood products also show the highest incidence among minors, particularly in the 27 cases of DIA among school-age children, where they constitute 29.6% (8/27) of cases. In contrast, contrast agents trigger anaphylaxis predominantly in individuals aged 65 and above. In the recent decade, hormones, biologics, and nutritional supports were also identified as triggers of DIA (Fig. 4).

Apart from drugs, another noteworthy trigger is food. Among the 49 cases of infants and toddlers aged 0–3 years, FIA demonstrates the highest prevalence at 28.6% (14/49), while in the 19 cases of preschool children aged 4–6 years, FIA represents a proportion of 21.1% (4/19). In the 31 reported cases of FIA, specific foods were implicated in 20 instances, while 11 cases were unspecified. Seafoods were identified as triggers in 6 cases, accounting for 19.4% (6/31) of the total, followed by dairy products (16.1%, 5/31). Health supplements and soy products each accounted for 2 cases (6.5%, 2/31), and the remaining categories including eggs, fruits, grains, meat, and vegetables were each associated with 3.2% (1/31) of the cases, as detailed in Table 1.

When it comes to specific age groups, dairy products have emerged as the primary trigger in 14 cases of FIA among infants and toddlers, accounting for 35.7% (5/14) of the reactions. In the 2 cases of FIA among preschool-age children, seafoods were the dominant trigger, causing 50% (2/4) of the anaphylaxis. Among elderly patients, there was only 1 FIA case, where the trigger was seafood.

Out of the 364 anaphylaxis cases, 6 cases (1.6%) were induced by insect bites , while 4 cases (1.1%) were due to chemical gases. Medical devices were responsible for 3 cases (0.8%), followed by cosmetic products and exercise each accounting

Age	0-3	4-6	7-12	13-18	19-64	≥65	total
Drug	57.1%	63.2%	87.1%	73.3%	71.8%	90.9%	73.6%
Antibiotics	39.3%	50.0%	48.1%	18.2%	41.4%	26.0%	38.4%
Chemotherapy	17.9%	16.7%	3.7%	9.1%	12.9%	8.0%	11.6%
Blood products	14.3%	8.30%	29.6%	18.2%	6.4%	6.0%	10.1%
Contrast agents	0.0%	0.0%	0.0%	9.1%	6.4%	24.0%	8.2%
NSAIDs	0.0%	0.0%	0.0%	9.1%	5.0%	0.0%	3.0%
Perioperative period	0.0%	0.0%	0.0%	9.1%	5.0%	4.0%	3.7%
Nutritional supports	10.7%	0.0%	3.7%	0.0%	1.4%	0.0%	2.2%
Biologics	0.0%	0.0%	0.0%	0.0%	1.4%	6.0%	1.9%
Theophylline	0.0%	0.0%	3.7%	0.0%	1.4%	2.0%	1.5%
Hormones	3.6%	8.3%	0.0%	0.0%	0.7%	0.0%	1.1%
Anesthetics	0.0%	0.0%	3.7%	0.0%	2.1%	2.0%	1.9%
Vaccines	0.0%	0.0%	0.0%	0.0%	1.4%	0.0%	0.7%
Chinese Medicine	0.0%	0.0%	0.0%	0.0%	0.7%	0.0%	0.4%
Other	10.7%	0.0%	0.0%	0.0%	5.0%	8.0%	5.2%
Unspecified	3.6%	16.7%	7.4%	27.3%	7.9%	14.0%	9.7%
Food	28.6%	21.1%	6.5%	0.0%	5.1%	1.8%	8.5%
Unspecified	7.1%	25.0%	100.0%	0.0%	70.0%	0.0%	35.5%
Seafoods	14.3%	50.0%	0.0%	0.0%	10.0%	100.0%	19.4%
Grains	7.1%	0.0%	0.0%	0.0%	0.0%	0.0%	3.2%
Dairy products	35.7%	0.0%	0.0%	0.0%	0.0%	0.0%	16.1%
Eggs	0.0%	25.0%	0.0%	0.0%	0.0%	0.0%	3.2%
Fruits	0.0%	0.0%	0.0%	0.0%	10.0%	0.0%	3.2%
Vegetables	7.1%	0.0%	0.0%	0.0%	0.0%	0.0%	3.2%
Meat	7.1%	0.0%	0.0%	0.0%	0.0%	0.0%	3.2%
Soy products	14.3%	0.0%	0.0%	0.0%	0.0%	0.0%	6.5%
Health supplements	7.1%	0.0%	0.0%	0.0%	10.0%	0.0%	6.5%
Insect bites	2.0%	0.0%	3.2%	0.0%	2.1%	0.0%	1.6%
Gases	0.0%	0.0%	0.0%	6.7%	1.5%	0.0%	1.1%
Medical devices	0.0%	0.0%	0.0%	0.0%	0.5%	3.6%	0.8%
Exercise	0.0%	0.0%	0.0%	6.7%	0.5%	0.0%	0.5%
Cosmetic products	0.0%	0.0%	0.0%	0.0%	0.5%	0.0%	0.3%
Unspecified	12.2%	15.8%	3.2%	13.3%	17.9%	3.6%	13.5%

Table 1. Triggers of anaphylaxis in different age groups

for 0.5% (2/364) and 0.3% (1/364) of the cases, respectively.

Treatment of anaphylaxis

Fig. 5 illustrates the treatment distribution across the 364 reported cases. All cases were managed in hospital settings. Treatment approaches varied, with glucocorticoids being the most frequently administered in 78.3% (285/364) of cases. This was followed by antihistamines (45.3%, 165/364), bronchodilators (41.5%, 151/364), respiratory support (36.3%, 132/364), vasopressors (26.9%, 98/364), and calcium gluconate (15.1%, 55/364). Notably, 36.0% (131/364) of the patients received epinephrine. Among this subset, 97.7% (128/131) were administered epinephrine in hospital, while 6.1% (8/131) received it at a primary care facility before being transferred to our institution for further management. Furthermore, the utilization of epinephrine displayed an ascending trend over the 21-year period examined. Additionally, other medications including glucose saline

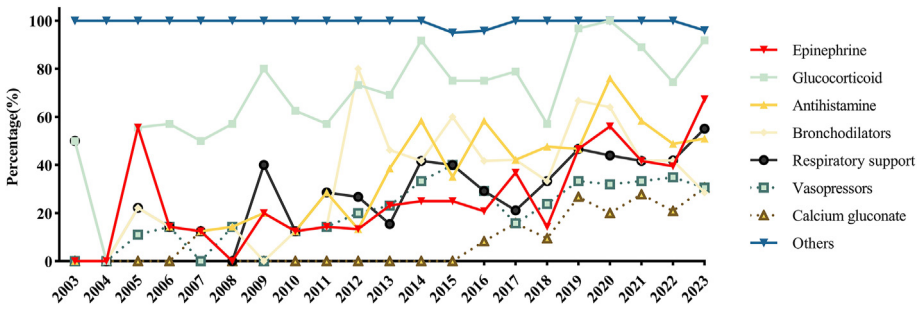

Fig. 5 Trend chart of various medications applications in anaphylaxis management from 2003 to 2023. The figure presents the 21-year trend of medications utilization among anaphylaxis patients

solutions (98.9%, 360/364) , acid-suppressing drugs (8.0%, 29/364) and water-soluble vitamins (2.2%, 8/364) were extensively employed in the management of anaphylaxis.

Duration

Outcomes were documented for all cases. Of these, 358 cases showed signs of improvement or complete recovery, while 6 resulted in death. Recurrent anaphylaxis was observed in 8 patients (2.2%). In summary, a total of 373 episodes of anaphylaxis were documented in 362 patients of 364 reported cases. Notably, there were 9 episodes for which no medical records were available.

The 6 fatalities occurred in the years 2003 (2 cases), 2005, 2015, 2019, and 2021. During the study period, the mortality rate of anaphylaxis was 0.28 per 100,000 individuals and demonstrated a declining trend. Of the 6 fatalities, 4 patients died due to DIA, while the triggers for the remaining 2 were unspecified. Among the 4 patients who died from DIA, 3 succumbed to anaphylaxis caused by antibiotics , specifically, 2 due to cephalosporins and 1 due to penicillin. The remaining fatality was triggered by a contrast agent.

DISCUSSION

Our study, carried out at Tongji Hospital—a renowned university hospital with 3 medical centers which draw patients from places all across Central China—revealed a relatively stable but slowly rising trend in the incidence of inpatient anaphylaxis over the past decades, totaling 364 cases. Drugs, with antibiotics in particular, emerged as the primary trigger. What paralleled this upward incidence trend was a year-on-year increase in the application rate of epinephrine and a remarkably low mortality rate of anaphylaxis patients over the past 2 decades. This study, which draws upon a database encompassing near 2.6 million inpatients, provides a robust perspective for our understanding of anaphylaxis in Central China, including its incidence, its triggers and its treatments.

The incidence rate of anaphylaxis from our study falls within the usual range of previously reported data in the global context. Over a 21-year period, it was recorded at 16.92 per 100,000 individuals, with an annual standardized incidence rate of 234.53 per 100,000 individuals. This rate is higher compared to other areas within China, such as Beijing, where crude incidence rates of inpatient anaphylaxis range from 3 to 6 per 100,000.[22] This variance might be due to differences in population characteristics, geographical locations, and the timeframes of the studies. It may also be associated with the different definitions of anaphylaxis used and the varying methods of diagnosing anaphylaxis in different studies. In our study, we utilized the current updated WAO guideline to identify anaphylaxis, thereby ensuring the robustness and credibility of our data.

Our study unveiled a generally steady, albeit slowly increasing trend in the incidence of inpatient anaphylaxis over the years. However, significant yearly variations were discernible, especially during the 2008 to 2009 period. While the precise causative factors remain to be identified definitively, a clear correlation is evident between these fluctuations and the considerable influence of case-weighting. This suggests that even a slight increase in a restricted number of cases can significantly disrupt the overall incidence rate. Moreover, the evolving nature of this pattern may

be attributed, at least in part, to the timing of the study and the selection criteria of the patient population. This observation mirrors previous findings from Thailand, where research on pediatric inpatient anaphylaxis from 2014 to 2021 indicated a downward trend[17] whereas studies from the same region focusing on adult inpatient anaphylaxis from 1992 to 2002 demonstrated an increasing trend.[18] However, given that our research is a three-center study in 1 city, there are significant regional limitations. We look forward to contributions from more institutions in the future to further enhance our understanding of the phenomenon.

As for the triggers, we found that drugs were the instigating trigger in 73.6% of anaphylaxis cases, with antibiotics being the primary culprit in 38.4% of these cases, particularly among adults, which coincides with several studies.[7,18,22,23] Given the rapid development and widespread use of new medications, especially antibiotics, as well as the common practice of prophylactic antimicrobial therapy in surgical patients, it is unsurprising that antibiotics have emerged as a principal cause of DIA.

Apart from antibiotics, other drug triggers also worked slightly differently in our study. Take chemotherapy for example. As the incidence of cancer has risen, chemotherapy has emerged as the second most frequent trigger of anaphylaxis, accounting for 11.6% of cases. Surprisingly, the highest proportion of these cases was found in the infant demographic aged 0–3 years. Although this subset may include infants misdiagnosed with anaphylaxis due to respiratory symptoms combined with viral exanthems, the definitions of triggers and timing of symptom onset in our study could mitigate potential bias to some extent. A parallel trend was observed with blood products, predominantly causing anaphylaxis in school-age children. Moreover, congruent Thai studies[17] have also reported a significant representation of chemotherapy and blood products within pediatric DIA, corroborating our results.

In addition to antibiotics and chemotherapy, contrast agents have been found to be predominantly implicated in triggering anaphylaxis among the elderly, which is consistent with findings from several studies.[18] With the evolving landscape of diseases, there has been a gradual increase in the incidence of cardiovascular and cerebrovascular disorders in this population, which has led to the widespread application of imaging techniques. This has augmented the probability of inducing anaphylaxis. Moreover, some research[24,25] indicates that 71% of DIA occur in individuals with pre-existing cardiovascular pathologies. This could be interpreted as an age-associated rise in the incidence of anaphylaxis triggered by these factors, along with an increased susceptibility to anaphylaxis in the elderly.

Perioperative and anesthetic-induced anaphylaxis accounted for 10 (3.7%) and 5 (1.9%) of cases, respectively. Compared to another multicenter perioperative study in China reporting an incidence of 200 per 100,000 individuals (2/1000 patients),[26] our figures are considerably lower. This stark contrast is undoubtedly influenced by the different definitions of anaphylaxis and methodological approaches between the 2 studies. It may also be related to the lack of a well-established management and reporting system for perioperative anaphylaxis in 3 medical centers.

One type of drug trigger whose performance differs slightly from our assumption is Traditional Chinese Medicine (TCM). It is implicated in only 0.4% of cases, a figure that is notably lower than the rates reported in Beijing.[10,11] This divergence is likely to have resulted partly from selection bias. As the medical hub of Wuhan, our institution preferentially treats complex cases that primary-level hospitals are unable to handle. Despite that our hospital has a department dedicated to TCM, Western medication remains the mainstay of our clinical practice as a comprehensive Western medical center.

When it comes to food triggers, our findings indicate that the incidence of FIA is higher during early life, with distinct age groups exhibiting unique food triggers. This is consistent with other research.[4,17] The maturation of the gastrointestinal immune system and the development of oral tolerance could potentially explain the early age peak observed for certain foods.[27] Differences of these triggers across various regional populations underscore the critical interplay between geography, lifestyle, and epigenetics.[3,5,15,28] As 1

study concluded,[29] the incidence rate of FIA among African American men rose from 0.06 per million during 1999–2001 to 0.21 per million in 2008–2010. Further research indicates that Asian children in Australia have a higher incidence of FIA compared to other ethnicities,[30,31] whereas their parents did not exhibit this trend.[9,31]

In our study, anaphylaxis related to insect bites was uncommon (1.6%), a rate lower than that reported in some foreign regions.[8,15] Literature suggests a higher susceptibility to insect bite-induced anaphylaxis among Caucasians, highlighting genetic influences on anaphylaxis development.[23,29,30] We tend to view this lower rate as resulting from that rural areas see a much higher prevalence of insects compared with urban areas whereas most of the patients in our study are urban dwellers who are less likely to encounter insects.

The last area of our study of anaphylaxis is its treatment. Our study revealed an epinephrine utilization rate of 36.0% during the study period among inpatients. This rate is not encouraging although there has been an upward trend in the use of epinephrine over the past 2 decades, especially when we compared it with similar studies in Asia. For example, the utilization rate of epinephrine for inpatients with anaphylaxis in Thailand was 87.3% (for adult)[18] to 98% (for child).[17] In Beijing, China, the rate of epinephrine use among inpatients reached 51.9%,[22] still higher than the rate found in our study. Interestingly, this contrasts with a study that showed 83.4% of perioperative anaphylaxis patients in China received epinephrine.[26] Our findings highlight a significant gap in anaphylaxis knowledge among medical practitioners. There's hesitancy to promptly administer epinephrine to non-shock anaphylaxis patients due to concerns about adverse reactions like malignant arrhythmias. Consequently, epinephrine use is often restricted to critical situations, which underscores the importance of further research in this area.

While we observed a relatively stable but slowly rising trend in inpatient anaphylaxis over the past decade, the mortality rate showed a slow downward trend. One possible explanation could be the enhanced standardization of anaphylaxis management among healthcare professionals, leading to a reduction in case fatality rates. Another explanation is that advancements in medical technology and a deeper understanding of anaphylaxis enable an increase in the accurate diagnosis of the disease by clinicians without an actual rise in incidence, an outcome facilitated by the enhanced level of record keeping by medical practitioners.

Whatever explanation we may come up with, it is crucial to promptly and correctly recognize, diagnose, and treat allergic reactions based on clinical presentation and knowledge of factors influencing anaphylaxis. Compared with the established Anaphylaxis Emergency Action Plan (AEAP) for out-of-hospital patients,[32] there is a greater need for a similar framework within the hospital setting to enhance both healthcare providers' and patients' awareness of anaphylaxis. This would facilitate the provision of advice on allergen avoidance and emergency interventions, optimize post-discharge management processes, including patient education and training.

Currently, our understanding of the natural progression of anaphylaxis is very limited, and it is unclear whether patients need to avoid allergens for life. Clearly, there is a necessity for the establishment of large international databases to aid in the collection and comparative analysis of observational data. This would support epidemiological studies, risk factor identification, and research analyses, thereby contributing to the continuous high-quality disease management of anaphylaxis patients.

LIMITATIONS

This study does have its limitations, which include potential patient recall bias and inconsistencies in medical record documentation by healthcare providers. These factors may introduce biases into our findings. Besides, serum tryptase detection kits have not yet received marketing approval in China, which precludes the possibility of using serum tryptase to further verify the diagnosis of anaphylaxis in patients initially identified by our physicians. Moreover, the composition of diseases among hospitalized patients varies across different regions and time periods, which may necessitate further validation of our observational findings in other areas. While the DPAP system is

limited to online use within the hospital and is not transferable to other regions or medical institutions, this large volume of data, with 4.2 million medical records from over 2.6 million inpatients, helps mitigate some of these biases.

CONCLUSION

Our study reveals the changes in the incidence of anaphylaxis among inpatients over a 21-year duration at 3 medical centers in Wuhan. Drugs emerge as the most common triggers for anaphylaxis. Moreover, despite a rising trend in its application during the study period, the use of epinephrine in managing anaphylaxis remains suboptimal. These findings underscore the pressing need for enhancements in the prevention and management strategies for anaphylaxis in China.

Abbreviations

DPAP: Data Platform Application Portal; WAO: World Allergy Organization; FIA: food-induced anaphylaxis; DIA: drug-induced anaphylaxis; TCM: traditional Chinese Medicine; IRR: incidence rate ratios; CI: confidence intervals.

Funding

This study did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors. Thus, there are no funding information to report.

Availability of data and materials

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Authors' contributions

RZ and HC conceived and designed the project. LL and HC set up the data screening procedure and generated the figures. LL wrote the first draft of the manuscript, RZ and HC revised the raw manuscript. LL, NH, WL, YY and DM manually screened and collected the patients' information. All authors critically revised the manuscript and approved the submitted manuscript.

Ethics approval

The study received ethical approval from the Independent Ethical Committee of Tongji Hospital (NO.TJ-IRB202401061), and the requirement for informed consent was waived.

Authors' consent for publication in WAO Journal

All authors have approved the submission of this manuscript.

Declaration of competing interest

There are no financial or other issues that might lead to conflicts of interest.

Acknowledgments

We would like to thank the Tongji Hospital affiliated with Huazhong University of Science and Technology for providing the data platform used in this study.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.waojou.2024.100980.

Author details

[a]Department of Allergy, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, 430030, China. [b]Institute of Allergy and Clinical Immunology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

REFERENCES

1. Muraro A, Worm M, Alviani C, et al. EAACI guidelines: anaphylaxis (2021 update). *Allergy*. 2022;77(2):357–377.
2. Robinson LB, Arroyo AC, Faridi MK, Rudders S, Camargo Jr CA. Trends in US emergency department visits for anaphylaxis among infants and toddlers: 2006-2015. *J Allergy Clin Immunol Pract*. 2021;9(5):1931–1938.e1932.
3. Lee S, Hess EP, Lohse C, Gilani W, Chamberlain AM, Campbell RL. Trends, characteristics, and incidence of anaphylaxis in 2001-2010: a population-based study. *J Allergy Clin Immunol*. 2017;139(1):182–188 e182.
4. Greenhawt M, Gupta RS, Meadows JA, et al. Guiding principles for the recognition, diagnosis, and management of infants with anaphylaxis: an expert panel consensus. *J Allergy Clin Immunol Pract*. 2019;7(4):1148–1156.e1145.
5. Tejedor-Alonso MA, Moro-Moro M, Múgica-García MV. Epidemiology of anaphylaxis: contributions from the last 10 years. *J Invest Allergol Clin Immunol*. 2015;25(3):163–175.
6. Pühringer V, Jilma B, Herkner H. Population-based incidence of all-cause anaphylaxis and its development over time: a systematic review and meta-analysis. *Frontiers in allergy*. 2023;4, 1249280.
7. Tejedor-Alonso MA, Moro-Moro M, Mosquera Gonzalez M, et al. Increased incidence of admissions for anaphylaxis in Spain 1998-2011. *Allergy*. 2015;70(7):880–883.
8. Decker WW, Campbell RL, Manivannan V, et al. The etiology and incidence of anaphylaxis in Rochester, Minnesota: a report from the Rochester Epidemiology Project. *J Allergy Clin Immunol*. 2008;122(6):1161–1165.
9. Wang Y, Allen KJ, Suaini NHA, Mcwilliam V, Peters RL, Koplin JJ. The global incidence and prevalence of anaphylaxis in children in the general population: a systematic review. *Allergy*. 2019;74(6):1063–1080.
10. Jiang N, Yin J, Wen L, Li H. Characteristics of anaphylaxis in 907 Chinese patients referred to a tertiary allergy center: a retrospective study of 1,952 episodes. *Allergy Asthma Immunol Res*. 2016;8(4):353.

11. Li X, Thai S, Lu W, et al. Traditional Chinese medicine and drug-induced anaphylaxis: data from the Beijing pharmacovigilance database. *Int J Clin Pharm*. 2018;40(4):921–927.
12. Cardona V, Ansotegui IJ, Ebisawa M, et al. World allergy organization anaphylaxis guidance 2020. *World Allergy Organ J*. 2020;13(10), 100472.
13. Hanache E, Hassan Perennec T, Beaumont P, et al. Food anaphylaxis in the elderly: analysis of allergy vigilance network data from 2002 to 2021. *Clin Exp Allergy : J British Soci Allergy Clinic Immunol*. 2023;53(5):561–572.
14. Pur Ozyigit L, Khalil G, Choudhry T, Williams M, Khan N. Anaphylaxis in the emergency department unit: before and during COVID-19. *Allergy*. 2021;76(8):2624–2626.
15. Gaspar Â, Santos N, Faria E, et al. Anaphylaxis in children and adolescents: the Portuguese anaphylaxis registry. *Pediatr Allergy Immunol*. 2021;32(6):1278–1286.
16. Galleani C, Dieguez MC, Cabanillas B, Martin-Arriscado Arroba C, Enriquez-Matas A, Crespo JF. Sunflower (helianthus annuus) seed allergy. *J Invest Allergol Clin Immunol*. 2025;35(1).
17. Wong-Onta N, Sawatchai A, Kanchongkittiphon W, Manuyakorn W. Anaphylaxis in children: effect of age and atopic status. *Asian Pac J Allergy Immunol*. 2024.
18. Techapornroong M, Akrawinthawong K, Cheungpasitporn W, Ruxrungtham K. Anaphylaxis: a ten years inpatient retrospective study. *Asian Pac J Allergy Immunol*. 2010;28(4):262–269.
19. Jiang C, Li H, Wang L, Liu C, Hao X. Gaps between actual initial treatment of anaphylaxis in China and international guidelines: a review and analysis of 819 reported cases. *Allergy*. 2020;75(4):968–971.
20. Li L, Chen H, Huang N, et al. Anaphylaxis in outpatients: a 5-year retrospective study on incidence and clinical characteristics at a university hospital in Wuhan, China. Allergy.n/a(n/a).
21. Demoly P, Adkinson NF, Brockow K, et al. International Consensus on drug allergy. *Allergy*. 2014;69(4):420–437.
22. Tang R, Xu HY, Cao J, et al. Clinical characteristics of inpatients with anaphylaxis in China. *BioMed Res Int*. 2015;2015, 429534.
23. Tanno LK, Molinari N, Annesi-Maesano I, Demoly P, Bierrenbach AL. Anaphylaxis in Brazil between 2011 and 2019. *Clin Exp Allergy : J British Soci Allergy Clinic Immunol*. 2022;52(9):1071–1078.
24. Turner PJ, Jerschow E, Umasunthar T, Lin R, Campbell DE, Boyle RJ. Fatal anaphylaxis: mortality rate and risk factors. *J Allergy Clin Immunol Pract*. 2017;5(5):1169–1178.
25. Mullins RJ, Wainstein BK, Barnes EH, Liew WK, Campbell DE. Increases in anaphylaxis fatalities in Australia from 1997 to 2013. *Clin Exp Allergy : J British Soci Allergy Clinic Immunol*. 2016;46(8):1099–1110.
26. Che L, Li X, Zhang X, et al. The nature and reported incidence of suspected perioperative allergic reactions: a cross-sectional survey. *J Clin Anesth*. 2021;74, 110404.
27. Meyer T, Ullrich R, Zeitz M. Oral tolerance induction in humans. *Exp Mol Pathol*. 2012;93(3):449–454.
28. Nocerino R, Leone L, Cosenza L, Berni Canani R. Increasing rate of hospitalizations for food-induced anaphylaxis in Italian children: an analysis of the Italian Ministry of Health database. *J Allergy Clin Immunol*. 2015;135(3):833–835.e833.
29. Jerschow E, Lin RY, Scaperotti MM, McGinn AP. Fatal anaphylaxis in the United States, 1999-2010: temporal patterns and demographic associations. *J Allergy Clin Immunol*. 2014;134(6):1318–1328.e1317.
30. Buka RJ, Crossman RJ, Melchior CL, et al. Anaphylaxis and ethnicity: higher incidence in British South Asians. *Allergy*. 2015;70(12):1580–1587.
31. Koplin JJ, Peters RL, Ponsonby AL, et al. Increased risk of peanut allergy in infants of Asian-born parents compared to those of Australian-born parents. *Allergy*. 2014;69(12):1639–1647.
32. Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update–2014. *J Allergy Clin Immunol*. 2014;134(5):1016–1025.e1043.