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Contents

Editorial

The prevalence of food allergy was estimated to be 7%–8% in children.[1] Its prevalence has been increasing over the past two decades.[2] In this issue of Pediatric Respirology and Critical Care Medicine, Shaun Chad Lee presented an extensive review of existing literatures about food allergy in school children particularly in Asia.[3] Twenty-eight studies from 10 Asian countries published between 1994 and 2022 were included. The prevalence and kinds of food allergy varied widely among countries and age groups of the children. The alphabetical order list of common allergenic food reported in children were egg, fruits, milk, nuts, sea food, soy, and wheat. The author stated that the prevalence of food allergy in Hong Kong was higher than that in mainland China, Russia and India.[4] Moreover the incidence of food anaphylaxis, which was the most serious adverse reaction of food allergy, has doubled from 2009 to 2019 in Hong Kong.[5] One fifth of anaphylactic reactions occurred in day-care and school settings.[6] Since anaphylaxis was life threatening and could occur suddenly anytime, the author emphasized the crucial roles of school staff to prevent and give emergency management to anaphylaxis at the school. In addition, school staff should be trained to recognize anaphylaxis and administer intramuscular epinephrine to the children effectively in the event of anaphylaxis. Despite the increasing trend of food allergy and anaphylaxis, awareness and training on food allergy management were found to be lacking in the school settings in Asian countries. So far there were a small number of published articles from Japan and Korea focusing on the preparation and measures taken to prevent food-related adverse reactions at the school.[7,8] The author proposed a nice schematic diagram of potential interventions to improve schools' anaphylaxis management such as food allergens labeling, school epinephrine autoinjectors, etc. The author concluded that it would be more effective if the government of each country agreed and supported through policymaking and legislation.

Another interesting research in this issue was conducted by Sweta Sadani and Mrinalini Das from India which focused on empyema thoracis in children.[9] They found that *Staphylococcus aureus* was the major causative organism isolated from the culture of pleural fluid. This finding was similar to another 2 reports from Thailand[10] and India.[11] In this current series, 3 out of 42 patients died. Unfortunately, the authors did not report the causes of death. Four patients developed pneumothorax and one patient had bronchopleural fistula. Unfortunately, all patients were managed by only antibiotics and chest tube drainage. No patients received intrapleural fibrinolytics nor surgical interventions. In the future, it would be helpful to perform a well-designed, multicentered, randomized, clinical trial study to demonstrate scientifically whether the fibrinolysis and/or surgical interventions could decrease the mortality rate and complications of empyema thoracis.

Furthermore, Professor Moharmmad Ashkan Mosehi from Shiraz Univeristy of Medical Sciences, Iran suggested an excellent idea towards the progress of pediatric interventional bronchoscopy.[12] In recent years, newer advance techniques used in adults' fiberoptic bronchoscopy such as cryobiopsy, balloons, stents, lasers, electrocautery knives, cryotherapy have been successfully performed in children as well. The removal of airway foreign bodies, formerly needed rigid bronchoscopy, could be done through a fiberoptic bronchoscope's channel. Asian Paediatric Pulmonology Society (APPS) might be the best group to establish a collaboration among Asian pediatric pulmonologists in order to facilitate educational resource and training to broaden the beneficial role of fiberoptic bronchoscopy to younger and smaller patients.

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Conflicts of interest

There are no conflicts of interest.

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Original Article

Assessment of Bacteriological Profile and Outcome of Empyema Thoracis of Hospitalized Children: A Single Center Experience

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Abstract

Background: Empyema is often associated with the consequence of infection including pneumonia, tuberculosis, or lung abscess. This study was conducted to assess the clinico-etiological profile and outcomes of empyema thoracis cases. **Materials and Methods:** This was a prospective hospital-based observational study conducted from July 2019 to June 2020 which included patients of either sex, aged between 2 months to ≤12 years, with empyema thoracis confirmed by radiological evidence of pleural fluid. Clinico-etiological details were collected and presented using appropriate statistics. **Results:** A total of 42 patients were included in the study, of which 35.7% were aged between 4 and 7.99 years and 27 patients (64.3%) were male. Twenty (47.6%) patients had a history of cough for 7–14 days while eight had cough for >14 days; however, a total of 29 (87.9%) patients had breathing difficulty for ≤7 days. Chest pain was observed in 16.7% of patients. Chest X-ray showed that right side pleural effusion was more commonly affected than the left pleural effusion (69.0% vs. 31.0%). The most common micro-organism pleural fluid culture was *Staphylococcus aureus* (n = 8; 20.5%). The majority of patients with empyema thoracis had elevated levels of leukocytes (>11,000 cumm) and CRP levels (>10 mg/dL) [92.9% and 97.6%, respectively]. **Conclusion:** The present study showed that most of the children presented at the age of 4–7.99 years with a male predominance. *S. aureus* was the major organism associated with pediatric empyema in this region.

Keywords: Empyema thoracis, pediatric, single center, *Staphylococcus aureus*

Introduction

Thoracis empyema is usually caused by a lung infection and it is a pus accumulation within the pleural space in the thorax. Empyema is often associated with the consequence of infection including pneumonia, tuberculosis, or lung abscess.[1]

A wide range of microbes have been implicated in pleural infection in children. Common bacterial pathogens include *Staphylococcus aureus* (*S. aureus*), *Streptococcus milleri*, *Streptococcus pneumoniae* (*S. pneumoniae*), *Escherichia coli* (*E. coli*), *Pseudomonas*, *Haemophilus influenza*, *Klebsiella pneumoniae*, *Enterobacteriaceae* species.[2,3] Previous literature suggests that *S. pneumoniae* is the most common etiologic agent in empyema which has an important role in disease progression. However, in developing countries, *S. aureus* is one of the most important causes of thoracis empyema.[4,5]

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Major risk factors associated with thoracis empyema are male sex, parapneumonic PE, longer duration of illness, incomplete antibiotic course, leukocytosis, or neutrophilia.[6,7] In developing countries, malnutrition, history of measles, are infection with antibiotic-resistant organisms increase the risk of developing thoracis empyema.[8] These risk factors predominantly affect children which could lead to longer disease exposure and increase chronic complications. Hence the early

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identification of risk factors is necessary to avoid further complications related to the disease.

Chest tube drainage, intrapleural fibrinolytics, VATS (video-assisted thoracoscopic surgery), and open decortications alone or in combination with antibiotics are being explored in various studies for their efficacy and safety in alleviating infection, thereby improving the survival outcomes.[4,5,9]

Radiological investigation of pleural effusion is a key element in diagnosing and determining the management. Conventional chest radiograph (CXR) remains as the initial investigation of suspected pleural disease. Computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and thoracis ultrasound (US) can each play important roles in further investigation.[10]

With the above background, the present study was conducted to assess the clinico-etiological profile and outcome of empyema thoracis cases.

Methods and Materials

This was a prospective hospital-based observational study conducted in patients with empyema thoracis admitted in the Department of Pediatrics in Gauhati Medical College and Hospital, Bhangagarh, Guwahati, India from1st July 2019 to 30th June 2020.

Ethical consideration

The study was conducted in accordance with ethical principles that are consistent with the Declaration of Helsinki, ICH GCPs, and the applicable legislation on non-interventional studies. The study protocol was approved by the Institutional Ethics committees.

Inclusion and exclusion criteria

The inclusion criteria were patients of either sex, aged within the range of 2 months to ≤12 years, with empyema thoracis, radiological evidence of pleural fluid. Patients aged >12 years were excluded.

Treatment

Initially, intravenous antibiotics such as amoxicillin-clavulanic acid were started empirically in the dose of 100 mg/kg/day in three divided doses. Vancomycin was started as an infusion in the dose of 40 mg/kg/day in four divided doses if staphylococcal pneumonia was suspected. Later on, suitable antibiotics were further started according to culture sensitivity reports. After ICD insertion—a chest X-ray was done to confirm the exact place of the tube, also to document lung expansion and residual collection subsequently. Bedsides, an examination was done daily to look for vital signs, air entry, and the patency of the ICD tube. Whenever blockage was suspected, the intercostal tube was readjusted. Every day, the amount of pus draining each day via chest tube was noted. If drainage is nil, tube patency was checked by flushing the tube with normal saline. For those with persistent symptoms and no signs of recovery, an ultrasound of chest was done to look for any loculations following tube thoracostomy. Diet advice was given to all patients to maintain good nutritional status.

Chest physiotherapy was started at an earliest. Older children were advised to use a respirometer for good lung expansion. Younger children were encouraged to blow balloons. ICD was removed when the drainage was less than 50 mL/day with radiological and clinical improvement. Proper antibiotics were started and were continued depending on the clinical condition of the patient and the organism isolated. After verifying good lung expansion and absence of fever, patients were discharged. However, children with continual clinical symptoms, not showing improvement with medications, incomplete lung expansion after ICD insertion and antibiotics, ultrasound chest suggestive of multiple locations, and thick pleural peel were planned for surgery. The criteria for discharge for all patients were absence of fever for at least 5 days, good oral acceptance, chest tube removal, absence of respiratory distress, and clinical well-being.

Data collection

After detailed clinical examination, all children were subjected to baseline investigations such as age, month of admission, duration of fever, cough, breathing difficulty, chest pain, history of contact with TB patient, type of infection, predisposing factor, immunization status, history of prior antibiotic use, symptoms, nutritional status [Table 6], incidence of anemia [Table 7], socio-economic status [Table 8], side of chest involvement, Mantoux test, blood culture, pleural fluid culture, leukocyte count, CRP, pleural fluid protein, pleural fluid glucose, LDH, duration of chest tube in situ, complications, lung expansion, outcome, and hospital stay. The patients suspected of pleural effusion were subjected to a chest X-ray.

Follow up

On discharge, advice was given to all children for follow-up at regular interval in pediatrics OPD, GMCH for check-up. The clinical examination was done to assess for lung expansion and deformities of the chest wall and chest X-ray was performed if required.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL). Categorical variables were presented as frequency and percentages. A comparison of quantitative variables between the groups was done using the χ^2 test and Fisher's exact test. A $P < 0.05$ was considered statistically significant.

Results

Demographic characteristics

Out of 42 patients studied, at admission majority of patients belonged to age group of 4 to 7.99 years (35.7%) followed by the age group 1 to 3.99 years (31.0%), age group <1 year (19.0%), and age group 8 to 12 years (14.3%). In total, 27 patients (64.3%) were male and 15 patients (35.7%) were female. Twenty children (47.6%) with empyema had a history of cough for 7–14 days while eight children had a cough for more than 14 days and the remaining 14 children had a cough history of less than 7 days. Total 29 (87.9%) patients had breathing difficulty for ≤7 days and the remaining 4 patients had breathing difficulty for 8–14 days. Chest pain was observed in 16.7% of patients. Pneumonia was majorly observed in 90.5% of patients while pulmonary tuberculosis and the hepatic abscess were observed in 7.1% and 2.4% of patients, respectively. A number of children with complete, partial, and no immunization were 41.4%, 44.8%, and 13.8%, respectively. The most common presenting symptoms were tachypnea (95.2%; *n* = 40), nasal flaring (33.3%; *n* = 14), followed by grunting (21.4%; *n* = 9). Signs of respiratory discomfort such as subcostal retractions (45.2%) were common in patients with empyema thoracis. In the overall study population, 57.1% of children were underweight, 38.1% were stunted, and the remaining 14.3% were wasted [Table 1].

Biochemical and radiological parameters and outcome

Chest X-ray showed that right side pleural effusion was more commonly affected than the left pleural effusion (69.0% vs. 31.0%). Only two (5.1%) patients showed induration for the Mantoux test. The most common micro-organism isolated on the culture of pleural fluid was *S. aureus* which was present in eight cases (20.5%) followed by *E. coli* in two cases (5.1%). The majority of patients with empyema thoracis had elevated levels of leukocytes (>11,000 cumm) and CRP levels (>10 mg/dL) [92.9% and 97.6%, respectively]. Six patients (14.3%) had chest tube indwelling for more than 8 days while 33 patients (78.6%) had chest tube indwelling for 5–8 days. Incidence of bronchopleural fistula (*n* = 1) and pneumothorax (*n* = 4) was developed among patients with empyema thoracis. Out of 38 patients, 36 (94.7%) had complete lung expansion, while two patients (30%) had only partial expansion. Total of 90.5% (*n* = 38) of patients improved; while 7.1% (*n* = 3) of patients died [Table 2].

Culture and clinicopathological parameters

The majority of children with empyema without any growth in blood culture had a fever for 7–14 days [Table 3].

Clinical parameters and outcome

Three patients with empyema who died lie between 1 to 3.99 years of age. Majority of patients who improved

Table 1: Demographic characteristics

Parameters	Number of patients (*N* = 42)*
Age groups [years]	
<1	8 (19.0)
1–3.99	13 (31.0)
4–7.99	15 (35.7)
8–12	6 (14.3)
Sex	
Male	27 (64.3)
Female	15 (35.7)
Month of admission	
January–March	4 (9.5)
April–June	15 (35.7)
July–September	14 (33.3)
October–December	9 (21.4)
Socio-economic status	
Lower income	19 (45.2)
Lower middle	13 (31.0)
Upper lower	10 (23.8)
Duration of fever [days]	
<7	7 (16.7)
7–14	21 (50.0)
>14	14 (33.3)
Duration of cough [days]	
<7	14 (33.3)
7–14	20 (47.6)
>14	8 (19.0)
Duration of breathing difficulty (*n* = 33)	
≤7	29 (87.9)
8–14	4 (12.1)
Chest pain	7 (16.7)
Pain in abdomen [days], (*n* = 5)	
1–6	3 (60.0)
>14	2 (40.0)
History of contact with TB patient	3 (7.1)
Type of infection	
Pneumonia	38 (90.5)
Pulmonary tuberculosis	3 (7.1)
Hepatic abscess	1 (2.4)
Predisposing factor (*n* = 8)	
Measles	2 (25.0)
Poor dental hygiene	6 (75.0)
Immunization status (*n* = 37)	
Complete	20 (54.1)
Incomplete	17 (45.9)
History of prior antibiotic use	34 (81.0)
Symptoms	
Tachypnea	40 (95.2)
Nasal flaring	14 (33.3)
Grunting	9 (21.4)
Chest retractions	
SCR and ICR	10 (23.8)
SCR	19 (45.2)
Temperature [F]	
<100	7 (16.7)
>100	35 (83.3)

Table 1: Continued

Parameters	Number of patients (*N* = 42)*
Air entry	
Decrease in left side	14 (33.3)
Decrease in right side	28 (66.7)
Nutritional status	
Underweight	24 (57.1)
Stunted	16 (38.1)
Wasted	6 (14.3)
Incidence of anemia [*n* = 20]	
Mild	7 (16.7)
Moderate	10 (23.8)
Severe	3 (7.1)

ICR = intercostal recession, SCR = subcostal recession
Data shown as *n* (%).*N = 42, unless otherwise specified

(39.5%) were of less than 1 year of age. It was noted that the patients who expired had pneumonia as the foci of infection. A total of 35 (92.1%) patients who improved had pneumonia as the foci of infection, 19 patients who improved were completely immunized, and only 10.5% of children who improved were not at all immunized [Table 4].

Discussion

The present study prospectively determined the prevalence of thoracis empyema and bacteriological profile and outcome including pediatric patients diagnosed with thoracis empyema. The salient observations were: (i) majority of population were presenting age group of 4–7.99 years; (ii) male preponderance in the overall study population; (iii) the most common micro-organism isolated was *Staphylococcus aureus*; (iv) majority of patients with empyema thoracis had elevated level of leukocytes and CRP levels; (v) incidence of improved status in 90.5% of patients; (vi) incidence of bronchopleural fistula and pneumothorax was developed among patients with empyema thoracis [Table 5].

In this study, the common age of presentation of empyema thoracis was 4–7.99 years followed by age group 1–3.99 years, age group <1 year, and age group 8–12 years. This result was in concordance with a prospective study carried out by Kumar *et al.* which showed a median age of presentation of 3 years.[11] It is more common in younger patients, higher incidence of empyema has been reported in 52% of children younger than 5 years.[11] Another evidence-based study reported the prevalence of thoracis empyema and 37.5%of patients were below 2 years of age. Similarly previous longitudinal study showed that the mean age of patients with thoracis empyema was 3.89 years with a male predominance.

The present study also shows that thoracis empyema occurs in both sexes with a male predominance. The study correlated well with the studies done by Narayanappa *et al.* and Borade *et al.*[12,13]

Table 2: Biochemical parameters and outcome

Parameters	Number of patients (*N* = 42)*
Side of chest involvement	
Right	29 (69.0)
Left	13 (31.0)
Mantouxtest (*n* = 39)	
10 mm induration	2 (5.1)
Blood culture (*n* = 39)	
Staphylococcus aureus	2 (5.1)
No growth	37 (94.9)
Pleural fluid culture (*n* = 39)	
Escherichia coli	2 (5.1)
Staphylococcus aureus	8 (20.5)
No growth	29 (74.4)
Leukocyte count (cumm)	
<4000	1 (2.4)
4000–11,000	2 (4.8)
>11,000	39 (92.9)
CRP [mg/dL], (*n* = 41)	
<10	1 (2.4)
>10	40 (97.6)
Pleural fluid protein [gm/dL], (*n* = 40)	
<3	14 (35.0)
≥3	26 (65.0)
Pleural fluid glucose [mg/dL], (*n* = 40)	
<40	28 (70.0)
>40	12 (30.0)
Pleural fluid LDH [U/L], (*n* = 40)	
<1000	27 (67.5)
>1000	13 (21.5)
Duration of chest tube in situ [days]	
0–4	3 (7.1)
5–8	33 (78.6)
>8	6 (14.3)
Complications	
Bronchopleural fistula	1 (2.4)
Pneumothorax	4 (9.5)
Lung expansion (*n* = 38)	
Complete	36 (94.7)
Partial	2 (5.3)
Outcome	
Expired	3 (7.1)
Improved	38 (90.5)
LAMA	1 (2.4)
Hospital stay [days]	
<7	3 (7.1)
7–14	17 (40.5)
>14	22 (52.4)

Data shown as *n* (%). *N = 42, unless otherwise specified
CRP = c-reactive protein, LAMA = leave against medical advice

Among the culture positive cases, *S. aureus* was the most common organism isolated among 20.5% of patients. Similarly, other studies also reported corroborating findings indicating *S. aureus* as the most common organism to be observed in patients with thoracis empyema.[14] Toppo *et al.* evaluated the bacteriological

Table 3: Association between culture and clinicopathological parameters

Parameters	Organism			*P* value
	No growth (*n* = 29)	*E. coli* (*n* = 2)	*S. aureus* (*n* = 8)*	
Blood culture				
Age groups [years]			[*n* = 2]	0.002
1–3.99	11 (29.7)	–	–	
4–7.99	15 (40.5)	–	–	
8–12	3 (8.1)	–	2 (100.0)	
Duration of fever [days]			[*n* = 2]	0.049
<7	6 (16.2)	–	–	
7–14	21 (56.8)	–	–	
>14	10 (27.0)	–	2 (100.0)	
Pleural fluid culture				
Foci of infection				0.010
Hepatic abscess	–	1 (50.0)	–	
Pneumonia	27 (93.1)	1 (50.0)	8 (100.0)	
Pulmonary TB	2 (6.9)	–	–	

Data shown as *n* (%)

**n* = 8, unless otherwise specified

Table 4: Association between clinical parameters and outcome

Parameters	Outcome			*P* value
	Expired (*n* = 3)	Improved (*n* = 38)	LAMA (*n* = 1)	
Age group [years]				
<1	–	8 (21.1)	–	0.040
1–3.99	3 (100.0)	10 (26.3)	–	
4–7.99	–	15 (39.5)	–	
8–12	–	5 (5.3)	1 (100.0)	
Month of admission				
January–March	–	3 (7.9)	1 (100.0)	0.047
April–June	1 (33.3)	14 (36.8)	–	
July–September	1 (33.3)	13 (34.2)	–	
October–December	1 (33.3)	8 (21.1)	–	
Foci of infection				
Hepatic abscess	–	1 (2.6)	–	0.009
Pneumonia	3 (100.0)	35 (92.1)	–	
Pulmonary TB	–	2 (5.3)	1 (100.0)	
Immunization status				
Complete	1 (33.3)	19 (50.0)	–	0.045
Incomplete	2 (66.7)	15 (39.5)	–	
Not immunized	–	4 (10.5)	1 (100.0)	
Pleural fluid stain				
Normal	–	30 (79.0)	–	0.041
Gram positive *Cocci*	1 (100.0)	6 (15.8)	–	
Gram negative *Bacilli*	–	2 (5.3)	–	

Data shown as *n* (%)

profile of children with empyema thoracis. The authors concluded that *S. aureus* was the most common causative. Organism present in 70.0% of children.[15] Similar outcome was also seen in several other studies carried out by Kumar *et al.* and Barnawal *et al.* where *S. aureus* was the most common organism isolated from pleural fluid culture, and the percentage being 83% and 77%, respectively.[11,16] Therefore, all these evidences along with the present study allude that the predominance of *S. aureus* in patients with thoracis empyema. In contrast to studies previous noteworthy study from Malaysia, Ho *et al.*, showed *S. pneumoniae* as the most common isolated pathogen.[17] This wide variation in different countries might be due to the mandatory vaccination policy, or presence of malnutrition and low social-economic status.

The evaluation of a single CRP measurement is a useful prognostic marker in the diagnosis of thoracis empyema. Recently, CRP has become more widely used to evaluate the activity of inflammatory diseases and following its evolution over the duration of a hospital stay can be more helpful in the monitoring of the response to therapy.[18] The higher incidence of elevated levels of leukocytes and CRP among the present study patients with thoracis empyema is in accordance with the previous studies.[19] Dielbar *et al.* and Watanabe reported high incidence of elevated CRP levels in patients with thoracis empyema.[20] Therefore, all these evidences along with the present study allude that the predominance of leucocytes and CRP in patients of thoracis empyema.

In the present study, all patients with thoracis empyema were managed by chest tube drainage. The present study reported incidence of improved status in 90.5% of patients. It is interesting to note that a study by Akanksha *et al.* that included 52 patients with thoracis empyema, showed 94% survival.[14] Seema *et al.* showed that the incidence of the clinical improvement was 100%.[21] In a previous study by Baranwal *et al.*, two patients died due to tension pneumothorax, one more expired with uncontrolled septicemia and one child due to postoperative shock.[16] In concordance with the Baranwal *et al.* study, the present study also reported incidence of bronchopleural fistula and pneumothorax among patients with empyema thoracis.[16]

Authors acknowledge few limitations of this study. This study did not record the type of socio-economic status of the patients which could have added valuable data while inferring the observations. This has considerably limited the result interpretation and indicates a need of well-designed prospective studies to validate these results.

Also, in this setup, antigen test was not available. So, authors could not use pleural fluid antigen test, urine pneumococcus antigen test, and pleural fluid PCR to exclude the possibility of *Streptococcus pneumoniae* co-infection. *Streptococcus pneumoniae* is the most common cause of pneumonia in children which can lead to pleural effusion and later empyema. And lastly, small sample size has restricted its applicability to a general population.

Table 5: Association between foci and complication

Culture	Complications			*P* value
	Bronchopleural fistula (*n* = 1)	Pneumothorax (*n* = 2)	No complication (*n* = 36)	
Blood culture				
No growth	1 (100.0)	1 (50.0)	35 (97.2)	0.013
Staphylococcus aureus	–	1 (50.0)	1 (2.8)	
Pleural fluid culture				
Escherichia coli	–	–	2(5.6)	
Staphylococcus aureus	1 (100.0)	2 (100.0)	5(13.9)	0.013
No growth	–	–	29(80.6)	
Pleural fluid stain				
Normal	–	2 (100.0)	4 (11.1)	
Gram positive *Cocci*	1 (100.0)	–	2 (5.6)	0.005
Gram negative *Bacilli*	–	–	30 (83.3)	
Blood culture				
No growth	1 (100.0)	1 (50.0)	35 (97.2)	0.013
Staphylococcus aureus	–	1 (50.0)	1 (2.8)	
Pleural fluid culture				
Escherichia coli	–	–	2 (5.6)	
Staphylococcus aureus	1 (100.0)	2 (100.0)	5 (13.9)	0.013
No growth	–	–	29 (80.6)	

Data shown as *n* (%)

Table 6: Nutritional status

Underweight- < –2SD weight for age of WHO chart
Wasted-< –2SD weight for height of WHO chart
Stunted- < –2SD height for age of WHO chart

Table 7: Hemoglobin levels for anemia

Population	Mild anemia	Moderate anemia	Severe anemia
	Hemoglobin (g/dL)		
2–59 months	10.0–10.9	7.0–9.9	<7.0
5–11 years	11.0–11.4	8.0–10.9	<8.0
11–14 years	11.0–11.9	8.0–10.9	<8.0

Table 8: Modified Kuppuswamy scale for socio-economic status

	Score
Education	
Professors or honors	7
Graduates or postgraduates	6
Intermediates or Posthigh school diploma	5
High school certificate	4
Middle school certificate	3
Primary school certificate	2
Illiterate	1
Occupation	
Profession	10
Semi-profession	6
Clerical, shop owner, farmer	5
Skilled worker	4
Semi-skilled worker	3
Unskilled worker	2
Unemployed	1
Family income per month (in rupees)	
>30,375	12
15,188–30,374	10
11,362–15,187	6
7594–11,361	4
4556–7593	3
1521–4555	2
<1520	1
Total score	
26–29	Upper
16–25	Upper middle
11–15	Lower middle
5–10	Upper lower
<5	Lower

Conclusion

The present study showed that most of the children presented at the age of 4–7.99 years with a male predominance. *S. aureus* was the major organism associated with pediatric empyema in this region. All the patients were treated chest tube drain. Majority them (90.5%) responded well to the treatment. While the incidence of bronchopleural fistula and pneumothorax complications was developed among patients with thoracis empyema. Early diagnosis and management are crucial in reducing the mortality, morbidity, and associated complications in pediatric empyema thoracis cases.

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Conflicts of interest

There are no conflicts of interest.

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Review Article

Pediatric Anaphylaxis Management in Schools: Current Issues and Challenges in Asia and Hong Kong. A Scoping Review

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Abstract

Hong Kong has the highest prevalence of food allergies compared with Mainland China, Russia, and India. There has been a twofold increase in anaphylaxis incidence between 2009 and 2019, of which 20% occur in day-care and school settings. A scoping systemic search was performed with the aim of reviewing existing literature in the Asia-Pacific region regarding food allergy management in the school setting. Current loopholes and inadequacies on governmental policy regarding school anaphylaxis management were explored. 28 articles from MEDLINE-OVID were compared with a PRISMA scoping review published in 2022 having similar search terms but focusing on Western countries. Furthermore, current loopholes and inadequacies on governmental policy regarding school anaphylaxis management in Hong Kong were explored. An Internet search was later conducted to supplement the information on governmental policies for school anaphylaxis management. Most publications identified focused on assessing food allergy prevalence and causative agents. However, there is an evident lack of literature on emergency action plans and school training programs. Existing governmental policies regarding school anaphylaxis were reviewed and compared. Hong Kong currently lacks legal protection for bystanders and policies, encouraging school staff training for anaphylaxis management. Governmental regulations and subsidization are also absent in encouraging schools to purchase backup stocks of unassigned epinephrine autoinjectors. Raising awareness and improving guidelines and policies in schools are integral in the management of food-induced adverse events and anaphylaxis. Governmental support through policymaking and legislation can significantly enhance and hasten the process, thus minimizing the impact adverse food reactions bring to the pediatric population.

Keywords: Action plans, anaphylaxis, Asia, epinephrine autoinjector, food allergy, Hong Kong, hypersensitivity, management, pediatric, schools, training

Introduction

Food allergy is a common problem globally, affecting 7%–8% children worldwide.[1] In other words, two children in each classroom of 25 students have food allergies. Hong Kong's local incidence of food allergy is not low, with parent-reported, and parent-reported, doctor-diagnosed adverse food reactions (AFRs) being 9.7% and 4.6%, respectively, according to two local studies.[2,3] The EuroPrevall-INCO survey conducted in 2019 also concluded that Hong Kong had the highest prevalence of food allergies compared with Mainland China, Russia, and India.[4]

The most severe form of AFR is anaphylaxis, which is defined as a "serious allergic reaction that is rapid in onset and can cause death.[5] It is a medical emergency that can be unpredictable and life-threatening. In Hong Kong, there has been more than a twofold increase in anaphylaxis incidence between 2009 and 2019.[6] The most common food allergens include milk, eggs, nuts, seafood, soy, and wheat, all of which are commonly found in school meals and snacks.[7] A total of 20% of pediatric anaphylactic reactions occur in day-care and school settings, environments that are integral to a child's life, and poses a significant problem in Hong Kong, where policies

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on food allergy management and its implementation lack sufficient support from the government.[1]

Materials and Methods

A scoping systemic search was performed on MEDLINE-OVID with the aim of reviewing existing literature and studies conducted in the Asia-Pacific region regarding food allergy management in the school setting. Current loopholes and inadequacies on governmental policy regarding school anaphylaxis management were explored.

Keywords and search terms are provided below, and the screening and selection process is summarized in Figure 1. The search revealed 90 registers, of which 28 were included in the review after screening and assessment for relevance to the school setting and food allergy. There were no restrictions to the study design, and Chinese, Japanese, and Korean-language articles were included in addition to English. Results were later compared with a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) scoping review published in 2022 having similar search terms but focusing on Canada, America, Australia, and European countries. An Internet search was also conducted to supplement the discussion on governmental policies for school anaphylaxis management.

Search terms

Ovid MEDLINE(R) <1946 to August 23, 2022>

1 Food Hypersensitivity/
2 (food hypersensitivit* or food intoleran* or food allerg* or food hyper sensitivit*).tw,kw.
3 1 or 2
4 Schools/ or schools, nursery/

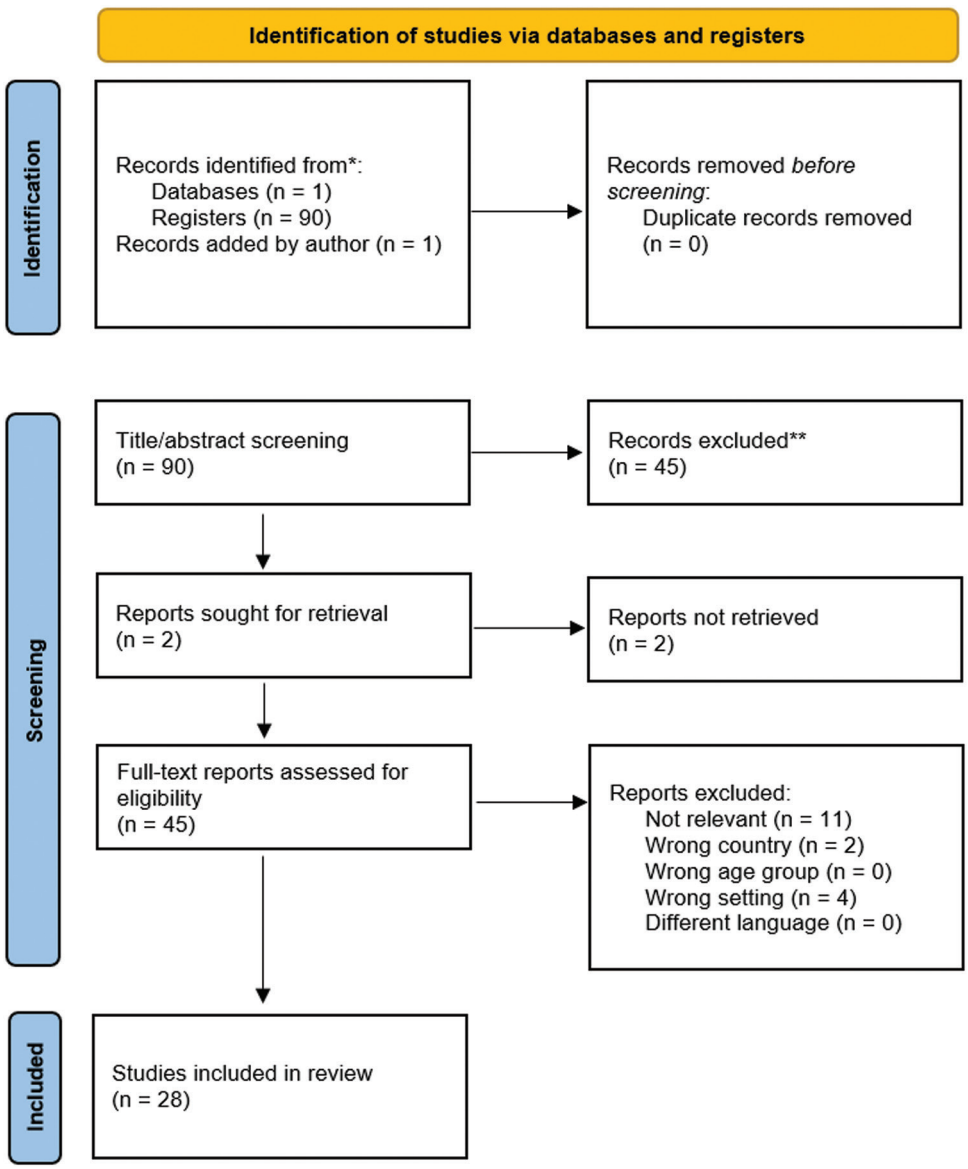

Figure 1: PRISMA flow diagram depicting the selection process articles and reports in the current scoping review

5 exp Child Day Care Centers/
6 (school* or daycare* or day care* or preschool*).tw,kw.
7 4 or 5 or 6
8 3 and 7
9 (Asia or Asia Pacific or China or Hong Kong or Japan or Korea or Singapore or Taiwan or Thailand or Philippines).mp.
10 8 and 9

Results

Out of the 28 publications, which have been summarized in Table 1 below, the majority focused on assessing prevalence of food allergies and identification of common causative agents in schools.[2,8-34] Only four articles (from Japan and Korea) investigated school's preparedness and measures taken to prevent food-related adverse reactions.[8,16,18,22] A survey conducted regarding food-dependent exercise-induced anaphylaxis found insufficiencies with level of understanding of the allergies, collection of precise information from students, and lack of implementation of measures to prevent incidence and recurrence.[18] Approximately 35% of schools did not know how to implement safeguards.

Notably, no Asian studies identified mentioned about emergency action plans nor educational training programs in schools for staff, regarding anaphylaxis management. In contrast, a PRISMA scoping review published this year in 2022 by Santos *et al.*,[1] with identical search terms but focusing on Canada, USA, Australia, and European countries, found at least 12 publications in the recent 5 years reporting on school staff management of food allergies. These studies investigated teacher's past experience, presence and effectiveness of training programmes, as well as in-school emergency preparedness such as guidelines and policies on food allergy emergency action plans. The distribution of articles is summarized in Figure 2.

Discussion

The lack of relevant studies and publication may point toward an inadequate awareness and training on food allergy management in Asian countries, including Hong Kong. It is important that the government steps in to take up a leading role regarding food allergy adverse event prevention in the community and schools. Some suggestions are made in the following section on how governmental intervention could greatly improve food allergy management in schools and have been summarized in Figure 3 and Table 2.

Food allergy action plans

Although food-induced allergic reactions are not uncommon, preparation for management is often inadequate in the school setting. It is essential that carers and school staff are on alert for anaphylaxis and can recognize signs of food allergic reactions. They should also understand the indication for epinephrine, have rapid and convenient access to the autoinjectors, and be capable in its administration.

Patients in Hong Kong are now given anaphylaxis action plans by physicians, detailing confirmed food allergens, as well as providing information on signs to be aware

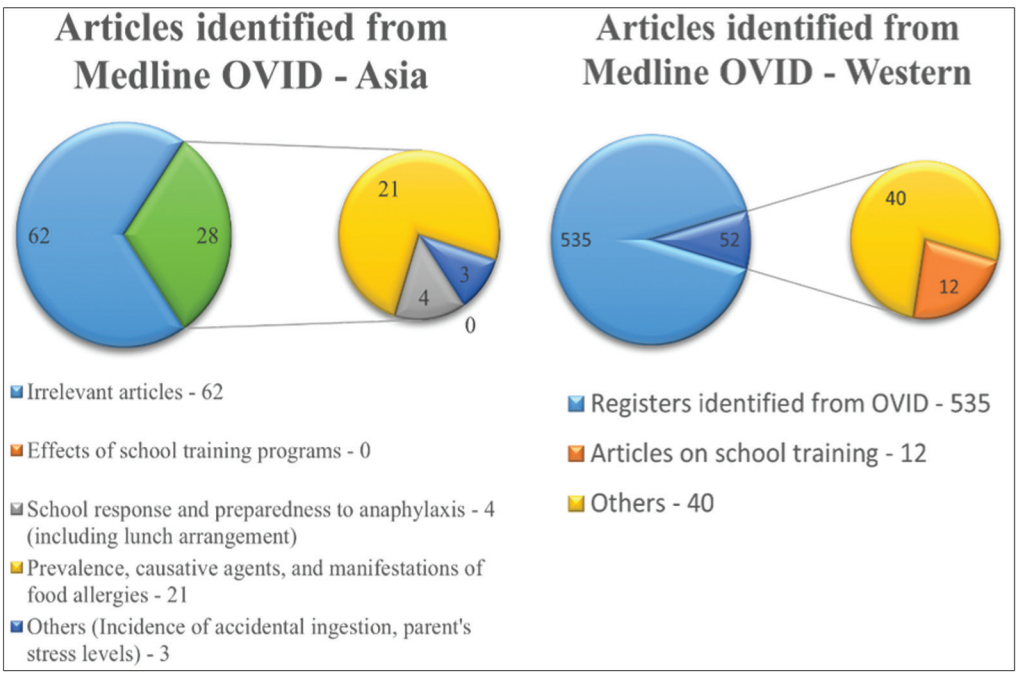

Figure 2: Two charts summarizing the distribution of articles identified from the scoping search. Left: Articles restricted to Asian countries; Right: Articles restricted to Western countries

Table 1: Summary of articles' country of origin, research design, aims, and findings, presented in chronological order[2,8-34]

First author, year	Country	Research design	Type of school	Aim	Findings
Korematsu S, 2022[8]	Japan	Survey	Nurseries to secondary	School responses to anaphylaxis onset	Most children who developed symptoms which an adrenaline autoinjector was recommended had no prescription for an adrenaline autoinjector.
Nantanee R, 2022[9]	Thailand	Review	Preschool	Causes of food induced anaphylaxis	Identified common causes of food allergies—The common causes of FIA in our study in Asian children were egg in infants, wheat and peanut in preschool children, and shrimp/shellfish in school-age children and adolescents.
Dai H, 2020[10]	China	Survey	Preschool	Prevalence of food allergy	Parent-reported rate of FA in preschool children in urban Wenzhou was 12.86%. The prevalence of FA was at least 0.84%. Among all cases, the most common allergic food was eggs, and the most common allergic manifestation was skin symptoms.
Li J, 2020[11]	Mainland China, Hong Kong, Russia, India	Study	Primary	Prevalence of food allergy	Prevalence of food allergy was highest in Hong Kong (1.50%), intermediate in Russia (0.87%), and lowest in Guangzhou (0.21%), Shaoguan (0.69%), and India (0.14%)
Yu QQ, 2019[12]	China	Survey	Primary and junior secondary	Prevalence of allergies, causative agents	7.28% in grade one had food allergies, 6.97 in grade seven. Prevalence higher in boys than girls. most common allergenic food were shrimp and crabs, followed by milk and milk products, eggs, and shellfish. Cutaneous symptoms and oral allergy symptoms were predominant clinical manifestations in all students with food allergy.
Yanagida N, 2019[13]	Japan	Survey	Preschool	Incidence of accidental ingestion in children with food allergies	Egg allergy was the most common FA (74.8%). A person accountable for FA was identified in 65.6% of nursery schools. Adrenaline autoinjectors (AAIs) were prescribed to 5123 (11.2%) children, 1154 (2.5%) of whom brought them to their nursery school. Of 4853 children with a history of anaphylaxis, 1450 (29.9%) had been prescribed AAIs, 784 (16.2%) of whom brought them to their nursery school. Overall, 3497 (7.6%) children had experienced accidental ingestion with symptoms in the current fiscal year, 44 (0.1%) of whom required hospitalization. Only, 11 children (0.02%) had used an AAI in their nursery school.
Mori H, 2019[14]	Japan	Survey	Care home, preschool	Prevalence of food allergy	The prevalence of food allergies at the 392 institutions was found to be 3.31%.
Yanagida N, 2018[15]	Japan	Survey	Preschool	Prevalence of food allergy	The overall prevalence of FA was 4.0%, with 6.4% at age less than 1 year, 7.1% at age 1, 5.1% at age 2, 3.6% at age 3, 2.8% at age 4, 2.3% at age 5, and 0.8% at age 6.
Kiyota K, 2015[16]	Japan	Study	Primary	Current status of lunch provision for students with food allergy	The egg elimination diet was provided in five of the seven cities.
Zeng GQ, 2015[17]	China	Survey	Preschool	Prevalence, clinical manifestations, spectrum of allergens, and related risk factors of food allergy	Adverse food reactions (AFRs) were due to the consumption of shrimp (4.4%), crab (3.2%), mango (2.3%), cow's milk and dairy products (1.9%), and eggs (1.4%).
Manabe T, 2015[18]	Japan	Survey	Secondary	Prevalence of food-dependent exercise-induced anaphylaxis FEIAn; school's response and management	Approximately 90% of school nurses had at least heard of FEIAn compared with 32% in the previous study. However, their level of understanding of FEIAn was insufficient and they had not collected precise information from students. Only 30% of schools that had students with FEIAn had previously implemented some measures to prevent recurrence, and approximately 35% of schools did not know how to implement these safeguards.
Zhang Y, 2015[19]	China	Study	Preschool & primary	Prevalence and associated factors of food allergy	The prevalence of self-reported food allergy and food intolerance were 8.4% and 7.7%, respectively. The common foods led to food allergy reported by children's parents were seafood, fish, egg, fruit and milk.
Yang Z, 2015[20]	China	Survey	Primary	Effect of the environment on allergy	Prevalence of food allergy did not differ significantly between urban and rural areas unlike asthma and eczema
Ahn K, 2012[21]	Korea	Study	Primary and secondary	Prevalence of food allergy	Eggs, crustaceans, fruit were the main causative agents of food allergy. In children aged 6–7 years, the prevalence of confirmed immediate-type FA was 0.3%; 0.6% in 12–13 years old

Table 1: Continued

First author, year	Country	Research design	Type of school	Aim	Findings
Kim S, 2012[22]	Korea	Survey	Primary and Secondary	Current status of managing food allergies in schools	Over 80% of the schools relied on self-care only without any school-wide measures for food allergies in place. Among the 890 menu items most frequently served in school lunch programs, a total of 664 (75%) were found to contain more than one food allergen. The causative foods of the anaphylactic reactions were mainly fruits (including peaches and kiwis), shellfish, fish, and nuts.
Connett GJ, 2012[23]	Philippines, Singapore, and Thailand	Survey	Secondary	Prevalence of food allergy	Prevalence of food allergy was 2.29%, 0.26%, 0.29% for Philippines, Singapore, and Thailand respectively
Lin YT, 2012[24]	Taiwan	Study	Preschool	Distributions of sensitivity to peanut allergen components among children sensitized to peanuts	Ara h 1, Ara h 2, and Ara h 3 were major components contributing to peanut sensitization in Taiwanese children
Lao-araya M, 2012[25]	Thailand	Study	Preschool	Prevalence of food allergy	The prevalence of IgE-mediated FA confirmed on OFC was ≥ 1.11%. The most common causative food was shrimp. Ant eggs were a unique food allergen causing severe reactions in preschool children in northern Thailand.
Sivaraj H, 2010[26]	Singapore	Survey	No restriction	Determine how parents of expatriate children coped with food allergy in Singapore	Most common allergenic foods were peanuts (72.7%), egg (63.6%), tree nuts (57.6%), and milk (45.6%). Stressors included concern about their child's teacher's lack of awareness about handling the allergic condition (84.5%), poor food labeling (85.7%), and poor food preparation in eateries (85.7%). Food preparation (71.4%) and food labeling (52.4%) caused the greatest rise in stress levels. Almost 35% of parents were concerned that epinephrine autoinjectors were not available in Singapore
Wan KS, 2010[27]	Taiwan	Study	Primary	Causative agents of food allergy	Most common allergens that induced sensitization were (in order of prevalence) crab, milk, egg white, and shrimp (88.08%, 22.45%, 24.23%, and 21.44%, respectively).
Wong GW, 2010[28]	China, Hong Kong, India, Russia	Study	Primary	Prevalence of food allergy	First comparative study of the epidemiology of food allergies in China, India, and Russia using the same standardized methodology
Ebisawa M, 2009[29]	Japan	Review	No restriction	Review guidelines for food allergy management in Japan	
Kusunoki T, 2009[30]	Japan	Survey	Primary, Secondary	Prevalence of food allergy	The rate of 7-year-old children who were food avoiders in infancy was 5.4%. This rate decreased as the current age of the children increased, down to 3% in 15-year-old children, indicating that food allergy in infancy tended to become more prevalent over the past 8 years.
Leung TF, 2009[2]	Hong Kong	Survey	Preschool	Prevalence of food allergy	AFR is a common atopic disorder in Hong Kong preschool children, and prevalence rates are comparable to the Caucasians. The prevalence rates of parent-reported AFR and parent-reported, doctor-diagnosed AFR were 8.1% and 4.6%, respectively
Imamura T, 2008[31]	Japan	Survey	No restriction	Average age of anaphylaxis, common places, causative agents	The average age of the first anaphylactic attack was 3.20 ± 6.327 years. The most common allergens causing anaphylaxis were in order milk, eggs, wheat, peanuts, and soybeans, followed by sesame and buckwheat. The most common place where anaphylaxis developed was the patient's own home, followed by fast food restaurants, places visited, restaurants, and schools
Lee SI, 2001[32]	Korea	Study	primary and secondary	Prevalence of food allergy	For allergic conjunctivitis, food allergy, and drug allergy, the prevalences in 6–12 year olds were 11.2%, 6.5%, and 1.5%, respectively
Takahashi Y, 1998[33]	Japan	Survey	Primary	Prevalence of buckwheat food allergy	The incidence of anaphylactic shock due to buckwheat was higher than those due to egg and milk allergy. incidence of buckwheat allergy was determined 0.22%
Tanaka S, 1994[34]	Japan	Survey	No restriction	Prevalence and characteristics of food-dependent exercise-induced anaphylaxis	The incidence of FEA was 0% in the kindergartens. 0.06% in the elementary schools and 0.21% in the junior high schools.

AFR = adverse food reaction, IgE= Immunoglobulin E, OFC= oral food challenge

FA= food allergy, FEIAn= food-dependent exercise-induced anaphylaxis, FIA= food induced allergy

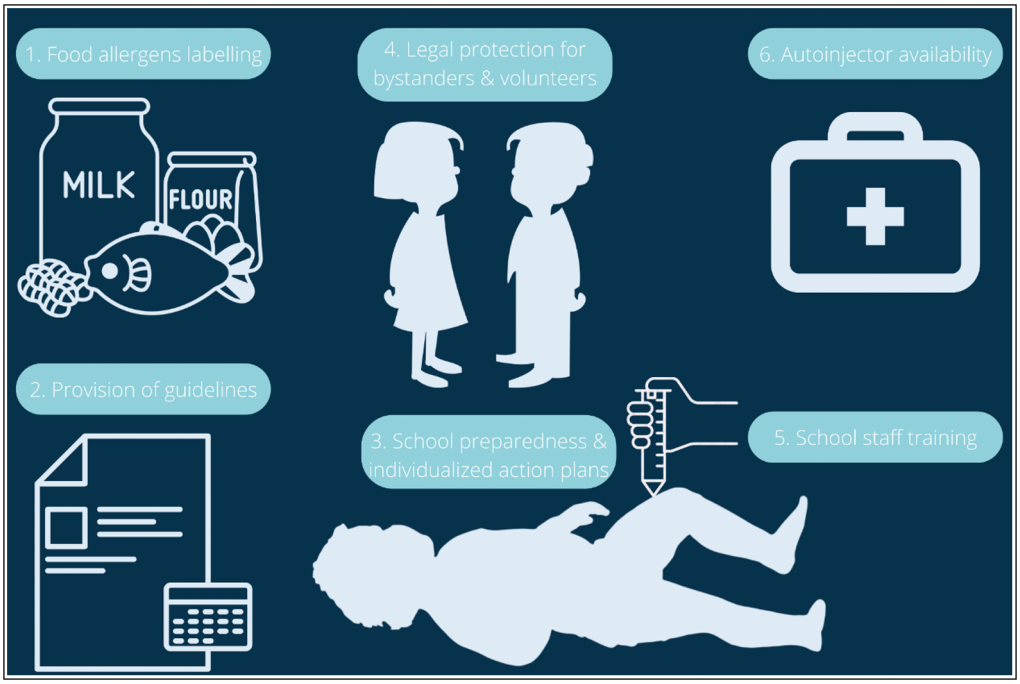

Figure 3: A schematic diagram of potential interventions to improve schools' anaphylaxis management

Table 2: Recommendations for governmental intervention improvements – A comparison of Hong Kong and other developed countries

Intervention	Hong Kong	Other developed countries
Food allergens labeling	Prepackaged foods are required by the Food and Drugs Regulations (Cap. 132W) to declare presence of 8 common allergens, including dairy & nuts.	Singapore Food Agency: mandatory requirements that foods and ingredients known to cause hypersensitivity must be declared on labels (list of food same as that of Hong Kong)
School preparedness for anaphylaxis	No legal requirement for schools to develop individualized action plans	Australia and European countries: Legal requirement for schools to develop individualized action plans for students with known food allergies, after receiving the physician-issued anaphylaxis action plan from carers. These include risk assessment of the school environment, proposed actions to minimize such risks, and is reviewed annually with the parents.
Provision of guidelines for schools	None issued by the Hong Kong government	The CDC, in consultation with the US Department of Education, have developed national voluntary guidelines for food allergy management in schools. These provide practical information and strategies for reducing allergic reactions for school administrators and staff.
Legal protection for volunteers	No Good Samaritan Law to reduce bystanders' fear of legal consequences after assisting in epinephrine autoinjector administration	California's version of the Good Samaritan law (Health and Safety Code 1799.102 HS) was first passed in 2009 and was designed to protect both medical and nonmedical personnel trying to help others in times of crisis.
School staff training	No legal requirement; no requirement for schools to station nurses either.	School staff are required by law in Australia to undertake regular training in anaphylaxis management as part of the school anaphylaxis management policy. Free online training courses are available, developed by the government specifically for school staff and carers.
School EpiPen availability	Autoinjector costs: $100 in Public Hospitals, up to $1000 in private sectors No legal requirement for schools to have a stock of epinephrine autoinjectors in case of anaphylaxis.	USA: the School Access to Emergency Epinephrine Act gives financial incentives to states that require elementary and secondary schools to maintain a supply of epinephrine in an easily accessible and secure location. UK: the Human Medicines Regulations was amended in 2017, allowing schools to purchase epinephrine autoinjector devices without prescription.

CDC = Centers for Disease Control and Prevention

of and the appropriate actions to be taken in event of anaphylaxis; these greatly help in the prevention of allergic reactions.[35] Standardized, easily understandable action plan templates are now being promoted and distributed freely by organizations such as the CUHK Allergy Team at Prince of Wales Hospital.

In Hong Kong, where the main carers at home may not be the parents who accompanied the children to the doctor's office, but instead domestic helpers and grandparents, the emergency action plans and leaflets help convey and provide clear guidance, thus minimizing the risk of miscommunication and inadequate relay of information. However, more could still be done in the school setting. The Hong Kong government could refer to practices in Australia and European countries, where it is required by the law that schools develop individualized action plans for students with known food allergies, after receiving the physician-issued anaphylaxis action plan from the child and carer.[36] These include risk assessment of the school environment, actions to be taken to minimize such risks, and such action plans are reviewed annually between the school and the parents. School staff could thus pay more attention to students with known allergies and be better prepared on how to react to anaphylaxis.

Legal protection of volunteers and bystanders

Apart from improving prevention of food allergy, governmental support is crucial in enhancing the response to anaphylaxis. In the event of anaphylaxis, administration of injectable adrenaline, such as Epipen, Anapen, or JEXT, is lifesaving. However, the patient may not be capable of self-administration during the life-threatening event, particularly in the pediatric age group.

Legal protection of "good Samaritans" is necessary as the fear of being sued for negligence following administration of Epipen to a student may deter teachers or volunteers at school from offering assistance. Hong Kong currently does not have any measure of statutory protection offered to volunteer rescuers that can protect bystanders from civil liability after providing emergency assistance to a victim.[37] Although teachers may be considered to be in a special relationship with students, thus having a duty of care, the lack of legal protection and reassurance is still a barrier that may deter bystanders. Instead of proceeding with assisting in administration of Epipen, volunteers may cease to help after calling the emergency hotline.

Training of school staff

Even if bystanders and school staff are willing to intervene, adequate training is necessary to ensure prompt identification of anaphylaxis and proper administration of intramuscular adrenaline. There are currently no standardized training programs in Hong Kong, nor is it a legal requirement for schools to host education programs for staff on anaphylaxis management. Skin signs, such as generalized urticaria and flushing, may be absent in 10%–20% of anaphylactic reactions, and the lack of knowledge and other signs and symptoms may lead to delay in the administration of epinephrine.[38] Administration of Epipen also requires some baseline knowledge—apart from differentiating between the safety cap and needle cap of the autoinjector, it needs to be injected at a 90° angle against the outer thigh, pressed down for 10 s, and afterward, the patient should be laid flat with legs elevated to prevent empty vena cava syndrome, in a position similar to that in Figure 3.[35] Much could be learnt from countries like Australia, where school staff are required by law to undertake regular training in anaphylaxis management as part of the school anaphylaxis management policy.[39] Free online training courses are available and are developed by the government specifically for school staff and carers. Studies have shown participants to have better knowledge and increased confidence in managing food allergy and anaphylaxis after training.[1] As most schools in Hong Kong do not employ full-time nurses, the government could work hand in hand with healthcare professional outreach teams to educate school staff on anaphylaxis management. Apart from training programs for teachers, many other countries, such as the Centers for Disease Control and Prevention, in consultation with the US Department of Education, have developed national voluntary guidelines for food allergy management in schools.[40] These could help support the implementation of food allergy management and prevention plans and practices in schools by providing practical information and strategies for reducing allergic reactions for school administrators and staff.

Epinephrine autoinjector availability

The availability of injectable epinephrine could also be further improved in Hong Kong. Although children with known food allergies are often given an Epipen to carry around, there is always a risk of not having the prescription medication by their side in the event of anaphylaxis, or other possibilities such as malfunction and expired devices. Combined with the schools' lack of individualized action plans for students with allergies, access to the child's prescribed epinephrine may thus be hampered. Although Epipens prescribed to patients by the Hospital Authority cost around $100 apiece, commercial epinephrine autoinjectors could cost up to $1000.[41] Together with the short shelf-life of 1–2 years, schools may lack incentive to purchase back-up stocks of unassigned epinephrine autoinjectors.

Governmental regulations and subsidization could assist in ensuring community availability of these life-saving medication. In the United Kingdom, the Human Medicines Regulations was amended in 2017, allowing schools to purchase epinephrine autoinjector devices without prescription. In US, the School Access to

Emergency Epinephrine Act gives financial incentives to states that require elementary and secondary schools to maintain a supply of epinephrine in an easily accessible and secure location.[42]

Limitations

This article is liable to evidence selection bias. While efforts have been made to follow the PRISMA extension for Scoping Reviews (PRISMA-ScR) 2020 Checklist as closely as possible, the screening and selection of registers in this scoping search was completed by only one individual researcher.

Furthermore, while the search terms have been kept intentionally identical to the PRISMA scoping review by Santos *et al*.[1] for comparison, the number and size of the databases utilized differ significantly, and the search for registers limited to the Asian geographic location could be expanded to include more registers.

Conclusion

In conclusion, raising awareness of anaphylaxis, as well as improving guidelines and policies in schools are integral in the management of food-induced allergic reactions and anaphylaxis. Governmental support through policymaking and legislation in Hong Kong can significantly enhance and hasten the process. With cooperation by stakeholders including the patient, carers, physicians, schools, and the government, the impact that AFRs bring to the pediatric population can be minimized.

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Conflicts of interest

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Interventional Pulmonology: The New Horizon in Pediatric Pulmonology

Pediatric interventional pulmonology science is considered a new field in children's lung science and has progressed significantly in recent years. This progress has been not only in new methods but also in the invention of tools and necessities needed for the special age of children. Many interventional methods in children have been copied from their use in adults, but due to the special conditions of children and the significant difference in the anatomy and physiology of the airways, many subtle changes have been made in them. Now it seems that the speed of manufacturing and the availability of the required equipment have exceeded the number of trained pediatric lung specialists to perform such interventions, which indicates the necessity of training experienced pediatric interventional bronchoscopists. Interventional methods are now used by pediatric pulmonologists, pediatric surgeons, otolaryngologists, anesthesiologists, and sometimes intensivists. However, it seems that pediatric pulmonologists have a smaller proportion of the mentioned doctors. A bronchoscope is the main tool for performing such interventional techniques. In general, there are two types of bronchoscopes: rigid and flexible. Rigid types require deep anesthesia and should be performed only in the operating room, but flexible bronchoscopes, in addition to being more maneuverable, can be performed in bronchoscopy suits outside the operating room and even at the patient's bedside, with minimal need to use sedation drugs and anesthesia. Although rigid bronchoscopes can only be inserted orally, there are several ways to enter the flexible bronchoscopes into the airways, including the nostrils, oral, and through artificial tubes such as endotracheal tube and tracheostomy tubes, which also can prevent in some circumstances, the more complicated and invasive procedures. Although rigid bronchoscopy is still used as the gold standard, such as when airways need to be kept open or to maintain hemostasis, flexible types are now considered a good alternative in some situations. Bronchoscopic interventions are used for both diagnostic and therapeutic purposes. Diagnostic indications can include visual anatomical and dynamic examinations of airways, as well as taking pathobiology samples from respiratory tracts and even lung tissue. Bronchoscopy indications for diagnostic proposes can include: the presence of any acute, chronic, or recurring symptoms such as coughing, choking, gagging, apnea, stridor, wheezing, shortness of breath, infections, and inflammations, persistent and recurrent atelectasis, difficult extubation, and pulmonary hemorrhage. These methods are now more specific to clarify important clinical conditions that have received little attention in infants in recent years, such as pharyngomalacia, aspiration syndrome, airway malformations, and children's interstitial lung diseases.

Diagnostic bronchoscopy will not only prevent the imposition of high diagnostic expenditures but also lessen the occurrence of complications caused by the disease itself or the use of undesirable methods in patients. Moreover, they are more convenient, effective, and reliable strategies in this age. Pathobiological samples can be obtained with a wide spectrum of techniques such as bronchoalveolar lavage, airway brushing, tracheobronchial, and even lung and lymph node tissue biopsies. Samples can be taken with a special biopsy device through the working channel of the flexible bronchoscope. In recent years, newer techniques that are currently used in adults, such as cryobiopsy, have been successfully used in the pediatric age groups. Concerning therapeutic procedures, bronchoscopes have high capabilities with low side effects and can be used in different conditions. Among their most common proven effectiveness, the removal of foreign objects from children's airways can be mentioned. Flexible bronchoscopes also have a high ability to open blocked airways due to various congenital stenoses (webs) or acquired strictures (tumors, mucosal plugging, and endobronchial blockages causing persistent and recurrent atelectasis due to the inflammatory process or infections such as tuberculosis) and even bronchoscopy-assisted airway intubation in difficult intubation situations. Such treatments can be performed by using various types of equipment such as balloons, lasers, electrocautery knives, cryotherapy, argon plasma coagulation, and silicone, metal, and biodegradable stents.

Fortunately, most of the published articles indicate a low complication rate for pulmonary interventions which are usually minor and transient. The most common type of these complications are physiological complications (such as transient hypoxia during bronchoscopy and, fever and cough after the procedure). Mechanical complications (such as laryngospasm, tracheo-bronchospasm, vocal cord injury, pulmonary derecruitment and atelectasis, pneumothorax, and bleeding) can also occur. Anesthetic and bacteriological complications are also reported. It is clear that with sufficient experience, modern equipment, and an experienced treatment team, all these complications can be minimized.

The undersupply of well-designed randomized clinical trials in pediatrics renders interventional pulmonary procedures without many globally accepted standard

guidelines. One way to overcome this problem and standardize such practices is to publish more reports on most multicenter studies at the national and international levels. Also, the centers that have significant activity in this regard should be identified to train more interested doctors. Of course, these pieces of training should be based on well-designed guidelines. Developing a communication infrastructure between pediatric pulmonologists from different centers in the form of designing social networks and organizing national and regional workshops could be a pathway to the medical training needed to carry out such measures. Meanwhile, regional associations can play a very important role in creating educational convergence.

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The **FIRST AND ONLY** asthma biologic to inhibit IL-4 and IL-13 signaling

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Convenient subcutaneous injection[1]

LIBERTY ASTHMA VENTURE Study Design[2]: 210 patients were randomly assigned with oral glucocorticoid-treated asthma to receive add-on DUPIXENT (at a dose of 300 mg) or placebo every 2 weeks for 24 weeks. After a glucocorticoid dose-adjustment period before randomization, glucocorticoid doses were adjusted in a downward trend from week 4 to week 20 and then maintained at a stable dose for 4 weeks. The primary end point was the percentage reduction in the glucocorticoid dose at week 24. Key secondary end points were the proportion of patients at week 24 with a reduction of at least 50% in the glucocorticoid dose and the proportion of patients with a reduction to a glucocorticoid dose of less than 5 mg per day. Severe exacerbation rates and the forced expiratory volume in 1 second (FEV_1) before bronchodilator use were also assessed.

LIBERTY ASTHMA QUEST Study Design[3]: 1902 patients who were 12 years of age or older with uncontrolled asthma were randomly assigned in a 2:2:1:1 ratio to receive add-on subcutaneous DUPIXENT at a dose of 200 or 300 mg every 2 weeks or matched-volume placebos for 52 weeks. The primary end points were the annualized rate of severe asthma exacerbations and the absolute change from baseline to week 12 in the forced expiratory volume in 1 second (FEV_1) before bronchodilator use in the overall trial population. Secondary end points included the exacerbation rate and FEV_1 in patients with a blood eosinophil count of 300 or more per cubic millimetre. Asthma control and DUPIXENT safety were also assessed.

EOS, eosinophils; FeNO, fractional exhaled nitric oxide; ICS, inhaled corticosteroid ; OCS, oral corticosteroid; Q2W, once every 2 weeks; SOC, standard of care.

References: 1. DUPIXENT Summary of Product Characteristics. May 2020. **2.** Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. N Engl J Med. 2018;378(26):2475-2485. **3.** Castro M, Corren J, Pavord ID, et al. Dupilumab Efficacy and Safety in Moderate-to-Severe Uncontrolled Asthma. N Engl J Med. 2018;378(26):2486-2496.

Presentation: Dupilumab solution for injection in a pre-filled syringe with needle shield. **Indications:** Atopic Dermatitis (AD): Moderate-to-severe AD in adults and adolescents ≥12 years who are candidates for systemic therapy; severe atopic dermatitis in children 6 to 11 years old who are candidates for systemic therapy. Asthma: In adults and adolescents ≥12 years as add-on maintenance treatment for severe asthma with type 2 inflammation characterised by raised blood eosinophils and/or raised FeNO, who are inadequately controlled with high dose ICS plus another medicinal product for maintenance treatment. Chronic rhinosinusitis with nasal polyposis (CRSwNP): As an add-on therapy with intranasal corticosteroids for the treatment of adults with severe CRSwNP for whom therapy with systemic corticosteroids and/or surgery do not provide adequate disease control(for 300mg) **Dosage & Administration:** Subcutaneous injection. AD adults: Initial dose of 600 mg (two 300 mg injections), followed by 300 mg every other week. AD adolescents(12-17y/o): Body weight <60 kg- initial dose of 400 mg (two 200mg injections), followed by 200 mg every other week. Body weight ≥60 kg- same dosage as adults. Dupilumab can be used with or without topical corticosteroids. Topical calcineurin inhibitors may be used, but should be reserved for problem areas only, e.g. face, neck, intertriginous and genital areas. Consider discontinuing treatment in patients who have shown no response after 16 weeks. AD Children(6-11y/o): Body weight 15Kg~<60 kg- initial dose of 300mg on Day 1 follow by 300mg on Day 15, then 300mg every 4 weeks. Body weight ≥60 kg- same dosage as adults. * The dose may be increased to 200 mg Q2W in patients with body weight of 15 kg ~ < 60 kg based on physician's assessment. Asthma: Initial dose of 400 mg, followed by 200 mg every other week. For patients with severe asthma and on oral corticosteroids or with severe asthma and co-morbid moderate-to-severe AD or adults with co-morbid severe CRSwNP- initial dose of 600 mg, followed by 300 mg every other week. Patients receiving concomitant oral corticosteroids may reduce steroid dose gradually once clinical improvement with dupilumab has occurred. The need for continued dupilumab therapy should be considered at least annually as determined by a physician. CRSwNP: for adult patients initial dose of 300 mg followed by 300 mg given every other week. Consideration should be given to discontinuing treatment in patients who have shown no response after 24 weeks of treatment for CRSwNP. Some patients with initial partial response may subsequently improve with continued treatment beyond 24 weeks. If a dose is missed, administer it asap and thereafter, resume dosing at the regular scheduled time. **Contraindications:** Hypersensitivity to dupilumab or any of the excipients. **Precautions:** Safety and efficacy in children <6 years or <15kg not been established. Not be used to treat acute asthma symptoms, acute exacerbations, acute bronchospasm or status asthmaticus. Do not discontinue corticosteroids abruptly upon start of dupilumab. Reduction should be gradual and performed under supervision of a physician; it may be associated with systemic withdrawal symptoms and/or unmask conditions previously suppressed by systemic corticosteroid therapy. Biomarkers of type 2 inflammation may be suppressed by systemic corticosteroid use. If systemic hypersensitivity reaction occurs, discontinue dupilumab and initiate appropriate therapy. Be alert to vasculitic rash, worsening pulmonary symptoms, cardiac complications, and/or neuropathy presenting in patients with eosinophilia. Treat pre-existing helminth infections before initiating dupilumab. If patients become infected while receiving dupilumab and do not respond to anti-helminth treatment, discontinue dupilumab until infection resolves. Patients who develop conjunctivitis and keratitis that does not resolve following standard treatment should undergo ophthalmological examination. AD patients with comorbid asthma should not adjust or stop asthma treatments without consultation with physicians. Carefully monitor patients after discontinuation of dupilumab. Do not give live and live attenuated vaccines concurrently with dupilumab. Patients should be brought up to date with immunisations before starting dupilumab. **Drug Interactions:** Immune responses to TdaP vaccine and meningococcal polysaccharide vaccine were assessed. Patients receiving dupilumab may receive concurrent inactivated or non-live vaccinations. **Pregnancy and lactation:** Should be used during pregnancy only if potential benefit justifies potential risk to foetus. Unknown whether dupilumab is excreted in human milk or absorbed systemically after ingestion. Decision must be made whether to discontinue breast-feeding or dupilumab taking into account benefit of breast feeding for the child and benefit of therapy for the woman. **Undesirable effects:** Most common adverse reactions reported- injection site reactions, conjunctivitis, oral herpes and eosinophilia. Safety profile observed in adolescents consistent with that seen in adults. For other undesirable effects, please refer to the full prescribing information. **Preparation:** 2 x 300mg/2ml in pre-filled syringe with needle shield, 2 x 200mg/1.14ml in pre-filled syringe with needle shield. **Legal Classification:** Part 1, First & Third Schedules Poison **Full prescribing information is available upon request.** API-HK-DUP-22.06

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