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Food allergy in Sri Lanka – A comparative study

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ABSTRACT

Background: The incidence of IgE mediated food allergy (FA) is increasing in the west. Cow's milk (CM), hen's egg, wheat, soy, peanut, tree nut, fish, and shellfish are responsible for 90% of food allergy in the west; however, local dietary habits may result in specific allergies. Data on food allergies in South Asia is scarce. The present study aims to evaluate the foods that cause immediate type hypersensitivity in Sri Lanka, and to compare with Asia and the developed west.

Methods: Records of patients referred to an Immunology clinic from 2010–January 2022 were reviewed. The diagnosis of food allergy was based on standard guidelines. Confirmation of the specific food implicated was based on the history and the presence of specific IgE or component resolved diagnostics by in vitro methods (Phadia ImmunoCap) or by skin prick testing with commercial extracts (Alk Abello). Prick to prick testing was performed for fruits and vegetables when commercial extracts were unavailable.

Results: Three hundred and forty-six patients were confirmed with food allergy. CM allergy (CMA) was the commonest (31.2%) followed by red meat allergy (27.7%) and food dependent exercise induced anaphylaxis (FDEIA) (17.9%). Allergy to alpha-gal crustaceans, eggs, gelatin, wheat, coconut milk, and mollusks were seen in 2–10% of patients.
The onset of CMA was mainly in childhood. However, in 23/108 patients, onset was after 5 years, including 8 patients in adulthood, and in 14 of the 23, it was preceded by red meat allergy. Onset of primary red meat allergy was predominantly in children, but in 33/96 (34.3%) of patients, it was in adults. Most patients with alpha-gal allergy (21/29, 72.4%) had initial symptoms in childhood and adolescence.
Anaphylaxis was diagnosed in 213 patients. FDEIA is the commonest cause (24.7%) followed by red meat allergy (23%), CMA (21.5%) and alpha-gal allergy (10.3%). Allergy to peanuts and fruits were rare. Patients with red meat allergy and/or CMA developed allergy, including anaphylaxis, to vaccines containing bovine/porcine products.

Conclusion: CM was the most common food allergy in children, but egg allergy was uncommon. Primary red meat allergy was the second most common, and was associated with allergy to vaccines containing bovine products, such as the measles, mumps and rubella (MMR) vaccine. Allergy to peanuts and fruits were rare. Primary red meat allergy may be responsible for late onset CMA.

Keywords: Food, Allergy, Anaphylaxis, Alpha-gal

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INTRODUCTION

Food allergy is "an adverse health effect arising from a specific immune response that occurs reproducibly on exposure to a given food".[1] In contrast, non-allergic adverse reactions to foods may be the result of food intolerances or adverse physiologic reactions.[1] IgE mediated food allergies are the best characterized of food allergies, whose incidence is increasing in the west. IgE mediated food allergy may give rise to cutaneous (urticaria, angioedema), gastro intestinal (vomiting, diarrhoea and abdominal pain), cardiovascular (hypotension), and respiratory (oral allergy syndrome, stridor, wheeze, cough) symptoms and signs. Some of these patients will have anaphylaxis. Cow's milk (CM), egg, wheat, soy, peanut, tree nut, fish, and shellfish are responsible for 90% of food allergy in the west;[2] however, local dietary habits may result in specific allergies, for example, sesame in Israel and buckwheat in Japan.[3]

In East and Central Asian countries, the food triggers for severe allergic reactions are major components of the Asian diet: fish, shellfish, bird's nest, buckwheat, and royal jelly.[4] In Singapore, Thailand, and Hong Kong, shellfish is one of the most important food triggers of anaphylaxis in adults and children. Allergy to edible bird's nest from swiftlets has also been described in Singapore and Malaysia.[4]

Data on food allergies in South Asia are scarce. In the EuroPrevall-INCO study conducted in 8 countries, the incidence of food allergy in adults in India was 1.3% with CM and apple being the commonest food allergens.[5] A meta-analysis showed the food allergens identified in India; Apple, fish, banana, cow's milk, melon, sesame, shrimp, tree nuts, chickpea, capsicum, Indian lentils, avocado, banana, beef, bulgur wheat, coconut, corn, eggplant, garlic, ginger, green peas, jalapeño peppers, kiwi, melon, rice, and tomato.[6] In addition, there are a few case reports of allergy to mango, mushroom, fenugreek, and chickpea.[5]

The data from Sri Lanka is meagre. Using a questionnaire in 449 school children in the Colombo District, 30% of the respondents believed they had a food allergy, of which pineapple was thought to be the commonest allergic food. In addition, rambutan (*Nephelium lappaceum*), tomato, bread fruit (*Artocarpus altilis*), prawns, cuttle fish, tuna, and canned fish were implicated.[7] However, confirmatory tests were not performed.

Anaphylaxis is the most dangerous allergic manifestation. In a global review on food-based anaphylaxis,[8] the commonest foods implicated were peanut, sesame, eggs, CM, celery, lupin, tree nuts, wheat, crustaceans, mollusks, fish, soy, and fruits. Other animal foods were also implicated. However, in Sri Lanka, CM (26%), eggs (2%), sesame (2%), spices other than sesame (2%), wheat (3%), crustaceans (4%), mollusks (1%), and fish (2%) were responsible for anaphylaxis.[9] Anaphylaxis to red meats were seen in 40% of patients in Sri Lanka, much more than in other countries.

Two novel food allergies have been identified in the past 2 decades, both leading to anaphylaxis. Food-dependent exercise-induced anaphylaxis (FDEIA) occurs when physical exertion follows ingestion of the implicated food, generally within 4 hours. While many foods have been implicated, wheat is responsible for FDEIA in Sri Lanka.[10] Alpha gal allergy is responsible for allergy to red meats. A tick bite sensitizes a patient to a carbohydrate moiety (alpha gal), which is present in the saliva of ticks and in non-primate mammals.[11] Ingestion of red meat leads to delayed anaphylaxis (up to 7 hours after ingestion). While this condition has not been reported so far in Sri Lanka, we have identified a number of such persons.

The present study aims to evaluate the foods that cause immediate type hypersensitivity, and to compare with data from Asia and the west.

METHODS

Our immunology clinic in Sri Lanka caters to patients from the entire country. Patients with allergy are investigated and treated in the clinic. In this retrospective study, the clinic records from 2010–January 2022, a period of 12 years, were evaluated for probable allergy. Patients who had clinical features suggestive of immediate hypersensitivity, reproducibility between specific food ingestion and symptom(s) occurrence, and confirmation of the relevant food by detection of food allergen-specific

IgE, were selected. Patients who did not participate in testing, and those with food allergy leading to asthma or atopic dermatitis, and where a food allergen could not be identified, were excluded. The diagnosis of anaphylaxis was based on the clinical history and examination findings as noted in the diagnosis card or bed head ticket. The diagnostic criteria included one of 3 clinical scenarios; namely, (1) acute onset of skin manifestations associated with respiratory or cardiovascular signs or symptoms, (2) involvement of at least 2 systems (skin, respiratory, cardiovascular, or gastrointestinal) that occurred rapidly after exposure to a likely allergen for that patient, or (3) reduced blood pressure after exposure to a known allergen for that patient.[12] The diagnosis of food allergy was based on standard guidelines.[12] Patients with a history of food allergy within 2 hours of ingestion were selected. The food allergy (FA) included oral allergy syndrome, acute urticaria/angioedema, rhino-conjunctivitis/asthma, gastrointestinal symptoms, anaphylaxis, and FDEIA. Confirmation of the specific food implicated was based on the history and the presence of IgE to the implicated food, by the presence of specific IgE (by Phadia ImmunoCap, using a Phadia 100), or by skin prick testing with commercial extracts (ALK Abello). *In vitro* allergens included the following; cow's milk, beef/pork, bovine gelatin, shrimp, cuttle fish, egg white and egg yolk, wheat, peanut, coconut, lentil, sesame seed, soy bean, tuna, salmon, mackerel, yeast, and tomato. Skin prick reagents included cow's milk, beef/pork/mutton, egg (whole/white/yolk), coconut, lentils, almond, brazil, cashew and hazel nuts, shrimp, cuttle-fish, pineapple, banana, and melon. Where commercial extracts or *in vitro* diagnostics were not available, as for example, fruits and vegetables, prick to prick testing was performed. Component resolved diagnostics (CRD) were performed with reagents from Phadia ImmunoCap.[13] These include rTri a 19 omega-5 gliadin, nGal d 1 ovomucoid, nGal d 2 ovalbumin, nBos d 4 alpha-lactalbumin, nBos d 5 beta-lactoglobulin, nBos d 8 casein, nBos d 6 BSA, and nGal-alpha-1,3-Gal (alpha-Gal).

Alpha-gal allergy was diagnosed when there was a delayed onset of symptoms of up to 6 hours after ingestion of red meat with or without a history of tick bite.[11] Diagnosis was confirmed if IgE to alpha gal >0.35 kUA/L, IgE to alpha-gal > IgE to beef/pork,[14] and IgE to bovine serum albumin (Bos d 6) was negative.[11] Primary red meat allergy was diagnosed where symptoms appeared within 2 hours of ingestion, and IgE to beef/pork or skin prick testing with commercial extracts were positive. Patients with positive results were analyzed with component resolved diagnostics, including IgE to Bos d 6 (bovine serum albumin, BSA) and bovine gelatin.

FDEIA was identified when symptoms and signs of allergy, including anaphylaxis, occurred during or within an hour of exercise, preceded by ingestion of food (for up to 4 hours), or by ingestion immediately after exertion.[15] People who developed allergy to the food in the absence of exertion, or with exercise unaccompanied by ingestion of the food, were excluded. The diagnosis was confirmed by testing for IgE to the culprit food. IgE to omega 5 gliadin was done in patients where the implicated food was wheat. Due to safety issues, challenge testing was not done.[15]

RESULTS

A total of 1255 patients attending the allergy clinic were evaluated for possible food allergy (FA), of whom 346 (27.5%) patients were diagnosed with immediate FA (Table 1). Seventy-three (21.09%) had allergy to multiple foods. Cow's milk allergy (CMA) was the commonest allergen diagnosed in 31.2% of patients followed by red meat allergy (27.7%) and FDEIA in 17.9%. Galactose-alpha-1,3-galactose (alpha-gal) allergy, and allergy to crustaceans, egg, gelatin, wheat, coconut milk, and mollusks were seen in 2–10% of patients. Most other allergies were seen in <1% of patients. These include peanuts, jambu, pecan/walnut, spinach, horse purslane (sarana, *Trianthema portulacastrum*), moringa (*Moringa oleifera*), and jackfruit (*Artocarpus heterophyllus*).

The onset of CMA was mainly in childhood. However, the onset of CMA in 10/108 patients (9.2%) was at 12 years or later, 8 patients developing symptoms after 18 years. Thirty-three patients with CMA had red meat allergy (30.6%). Of the 67 patients with CMA in infancy, only 6 had red meat allergy, which developed after CMA, whereas of the 23 patients who developed CMA after 5 years, 16 had red meat allergy, of whom 14/23 (60.9%) developed CMA after read meat allergy (Table 2).

Food Allergen	Number of patients (n = 346)[a]						
	Age at onset						Total (%)
	0-6 months	6-12 months	1-5 years	5-12 years	12-18 years	>18 years	
Cow's Milk[b]	**38**	**29**	**18**	**13**	**2**	**8**	**108 (31.2)**
Red meat[b]	**0**	**5**	**16**	**33**	**9**	**33**	**96 (27.7)**
Beef	0	3	9	21	5	23	61 (17.6)
Pork	0	2	8	17	7	12	46 (13.3)
Mutton	0	2	3	3	2	4	14 (4)
Venision	0	0	2	2	0	0	4 (1.2)
Others (Camel, Rabbit, Wild boar)	0	0	0	3	0	0	3 (0.9)
FDEIA	**0**	**1**	**0**	**20**	**13**	**28**	**62 (17.9)**
Alpha- Gal	**0**	**0**	**8**	**11**	**2**	**8**	**29 (8.4)**
Crustaceans	**0**	**0**	**4**	**3**	**5**	**11**	**23 (6.6)**
Prawns	0	0	4	2	3	10	19 (5.5)
Crabs	0	0	0	1	1	4	6 (1.7)
Shrimp	0	0	0	0	1	2	3 (0.9)
Egg	**0**	**15**	**2**	**1**	**0**	**0**	**18 (5.2)**
Gelatin	**0**	**1**	**5**	**3**	**2**	**2**	**13 (3.8)**
Wheat	**0**	**1**	**1**	**1**	**1**	**6**	**10 (2.9)**
Coconut	**1**	**4**	**5**	**0**	**0**	**0**	**10 (2.9)**
Mollusks	**0**	**0**	**1**	**1**	**1**	**4**	**7 (2)**
Cuttlefish	0	0	1	1	1	4	7 (2)
Fish	**0**	**0**	**0**	**0**	**0**	**3**	**3 (0.9)**
Sesame	**0**	**0**	**2**	**0**	**0**	**1**	**3 (0.9)**
Other foods (Peanuts, jambu, soy, lentils/legumes mushroom, pecan/ walnut, banana, mango, spinach, horse purslane/ sarana (*Trianthema portulacastrum*), moringa (*Moringa oleifera*), jackfruit (*Artocarpus heterophyllus*), tomato)	**0**	**2**	**6**	**2**	**0**	**7**	**17 (4.9)**

Table 1. Patients' ages at onset of different food allergies *[a]Some patients had reacted to more than one food allergen. [b]CM allergy was also present in 9.3% of patients with beef allergy and beef allergy was present in 15% of patients with CMA*

One hundred and twenty-five patients had allergy to red meats, of whom 96 (76.8%) were considered as having primary red meat allergy. The onset in the majority of patients with primary red meat allergy was in childhood. However, in 33/96 (34.3%), it was in adulthood (>18 years) (Table 1). Thirty-three patients with primary beef allergy (33.3%) had CMA.

Patients with a delayed onset (2–6 hours) were diagnosed with alpha-gal syndrome. Most patients with alpha-gal allergy (21/29, 72.4%) had initial symptoms in childhood and adolescence. Eight of 29 (27.5%) patients gave a history of tick bite within the previous year; however, the identity of the tick is not known.

Almost half of patients (11/23, 47.8%) allergic to crustaceans had initial symptoms in adulthood.

Anaphylaxis was diagnosed in 213 patients (Table 3). FDEIA is the commonest cause detected in 24.7% of patients and wheat was the only food implicated. Menstruation, taking non-steroidal anti-inflammatory drugs and inhalation of cannabis were cofactors in one patient each. The other major causes of anaphylaxis were primary red meat allergy (23%), CMA (21.5%), and alpha-gal allergy (10.3%).

In adults the commonest cause of anaphylaxis was FDEIA (47.3%), followed by primary red meat (30.6%) and alpha–gal (31.8%) (Table 3). Anaphylaxis to crustaceans, wheat, and fish were also seen.

CM was the commonest cause of anaphylaxis in infancy (68.5%) followed by coconut milk (14.2%) and eggs (8.5%). CM was also the commonest cause (30.3%) in children aged 1–5 years followed by red meats (24.2%) and alpha-gal (15.1%) Primary red meat allergy was the commonest cause of anaphylaxis from 5 to 12 years (34.4%) along with FDEIA (31.1%). FDEIA was the commonest cause from 12 to 18 years (52.3%).

Patients with red meat allergy and/or CMA developed allergy, including anaphylaxis, to vaccines containing bovine/porcine products (Table 4).

Rare causes included anaphylaxis due to ingestion of horse purslane (*Trianthema portulacastrum*), locally known as "Sarana", identified in 1 patient. In addition, anaphylaxis was rarely seen with to sesame peanuts, lentils, soy, jambu, banana, mango, spinach, moringa, jackfruit, and tomato.

DISCUSSION

The pattern of food allergy depends on the feeding patterns of each country.[4] The pattern of food allergies in Asia are different compared to the western developed world.[16] However, the pattern of food allergy seen in our study has important differences with other Asian countries as well as with Europe and the United States (Table 5).[5,17-36]

Cow's milk allergy (CMA) was the commonest food allergy in childhood in our population. CMA is one of the commonest food allergies among

Age	Onset of CMA (n = 108)	Red meat allergy	Onset of red meat allergy before CMA	Onset of red meat allergy after CMA
0–6 months	38	2	0	2
6–12 months	29	4	0	4
1–5 years	18	10	4	6
5–12 years	13	9	7	2
12–18 years	2	1	1	0
>18 years	8	6	6	0

Table 2. Red meat allergy in patients with cow's milk allergy (CMA)

Cause of anaphylaxis	Number of patients with anaphylaxis (n = 213)[a]						
	Age at onset						Total
	0-6 months	6-12 months	1-5 years	5-12 years	12-18 years	>18 years	
FDEIA[b]	**0**	**0**	**0**	**19**	**11**	**27**	**57 (26.7)**
Red meat	**0**	**1**	**8**	**21**	**4**	**15**	**49 (23.0)**
Beef	0	0	4	14	2	10	30 (14.0)
Pork	0	0	5	8	3	7	23 (10.7)
Mutton	0	1	2	1	1	1	6 (2.8)
Venison	0	0	1	0	0	0	1 (0.4)
Others (camel, rabbit, wild boar)	0	0	0	2	0	0	2 (0.9)
Cow's Milk	**15**	**9**	**10**	**7**	**2**	**3**	**46 (21.5)**
Alpha- Gal	**0**	**0**	**5**	**9**	**1**	**7**	**22 (10.3)**
Crustaceans	**0**	**0**	**0**	**1**	**2**	**6**	**9 (3.9)**
Prawns	0	0	0	1	1	6	8 (3.7)
Crabs	0	0	0	1	1	1	3 (1.4)
Shrimp	0	0	0	0	1	2	3 (1.4)
Gelatin	**0**	**0**	**3**	**3**	**1**	**0**	**7 (3.2)**
Coconut	**1**	**4**	**2**	**0**	**0**	**0**	**7 (3.2)**
Wheat	**0**	**1**	**1**	**0**	**0**	**4**	**6 (2.8)**
Mollusks	**0**	**0**	**0**	**0**	**0**	**4**	**4 (1.7)**
Cuttlefish	0	0	0	0	0	4	4 (1.7)
Egg	**0**	**3**	**0**	**0**	**0**	**0**	**3 (1.4)**
Fish	**0**	**0**	**0**	**0**	**0**	**3**	**3 (1.4)**
Other foods	**0**	**1**	**4**	**1**	**0**	**8**	**14 (6.6)**
TOTAL	**16**	**19**	**33**	**61**	**21**	**77**	**213**

Table 3. Patients' ages at onset of anaphylaxis to different food [a]*Some patients had anaphylaxis to more than one food allergen.* [b]*Food Dependent Exercise Induced Anaphylaxis*

young children throughout Asia[16,17,19,22,28] and high levels are also seen in Europe and United States.[3,32,34] A substantial proportion of our patients had an onset after 5 years, and in adulthood. These patients had developed red meat allergy before onset of CMA (Table 2) which may have predisposed to subsequent development of CMA. BSA may be responsible for the cross-reactivity.[37] Convincing data have emerged that CMA may manifest in adult life,[38] and further studies on the underlying mechanisms are warranted.[39]

Allergy to red meats come in 3 different forms; primary red meat allergy, alpha-gal allergy, and pork cat syndrome. Only primary red meat and alpha-gal allergy were identified among our patients. Primary red meat allergy is the second most

Vaccine	Food Allergy				Total (n = 40)
	Red meat	Cow's milk	Red meat + Cow's milk	Cow's milk + Gelatin	
MMR[a]	4	9	5	1	19
MR[b]	0	0	1	0	1
Measles	1	0	2	0	3
Rubella	0	0	2	2	4
JE[c]	1	1	4	0	6
aTd[d]	0	0	1	1	2
DT[e]	0	2	1	1	4
ARV[f]	1	0	0	0	1

Table 4. Patients with allergy to both food (red meat, cow's milk, gelatin) and **vaccines** [a]*Measles, Mumps and Rubella.* [b]*Measles-Rubella.* [c]*Japanese Encephalitis.* [d]*Adult Tetanus diptheria* [e]*Diptheria Tetanus.* [f]*Anti-Rabies Vaccine*

common food allergy in our patients. This is unusual, as, due to cultural and religious reasons, consumption of red meat is low. Red meat allergy, while uncommon, is identified mainly in children in other countries,[11] whereas in 34.3% of our patients, the onset was in those over 18 years.

Twenty-nine patients were diagnosed with alpha-gal allergy. In a previous paper from our group, alpha -gal allergy was not detected.[9] To our knowledge, these are the first reported cases from the Indian subcontinent. None of the patients with immediate reactions (within 2 hours) to red meat were tested for IgE to alpha-gal due to financial constraints. Some of these patients may have had alpha-gal allergy. This is a limitation in our study.

Egg allergy was relatively uncommon in our patients, after infancy, unlike in Asia,[16] Europe, and United States.[16] For example, egg allergy predominates over CMA among children below 5 years in Korea,[20] Singapore,[26] and Japan.[28] However, the prevalence of egg allergy in Asia is lower than in the developed west.[16]

Shellfish allergy was seen in 6.6% of patients, unlike in studies from India, where crustacean allergy was not seen.[5,31,34]

Among Chinese children there is a high prevalence of crustacean allergy[22,23] and it is the leading cause of food allergy among younger children in some south East Asian countries such as Vietnam,[29] Taiwan,[25] and Hong Kong,[24] but is less common in Japan[28] and South Korea.[19] It is seen in older children and adults in Japan[28] and Vietnam[30] and is the commonest adult food allergy in Singapore.[27] Crustacean allergy is less common in Europe and United States.[16,34–36] The early introduction of shellfish and consumption of raw food have been considered as causes for this phenomenon.[40] Shellfish is not consumed raw, and is not a food that is introduced early in Sri Lanka. Another possibility is cross reactivity to house dust mites (HDM) and cockroaches, in tropical climes with high humidity.[40,41] However, data from India, with similar levels of humidity and exposure to HDM, reveal that, while sensitization to shrimp is high, there was no clinical allergy[5,31,34]

Peanut allergy was not seen in children born in Sri Lanka. The prevalence of peanut allergy is 1–2% in the west, but uncommon in Asia and other areas,[42] including India and China.[5] Two children, born in Europe but residing in Sri Lanka after infancy had peanut allergy. Asian children born in Australia had higher peanut allergy, compared to children from the same ethnic group born in their native country but who had subsequently migrated to Australia.[43] Early introduction of peanuts reduces the risk of peanut allergy.[44] Introduction of peanuts at 6–12 months is recommended in Sri Lanka, which may explain the low incidence of peanut allergy in our study population.[45]

Fish allergy is rare in Sri Lanka similar to India, where clinical allergy was not detected.[5] Fish allergies are relatively uncommon in South East

Sri Lanka	Thailand	Korea	China	Hong Kong[24]	Taiwan[25]	Singapore	Japan[28]	Vietnam		India	US	Europe
<1 year CM, Hen's egg	**<1 years**[17] Hen's egg CM, Soya	**0-2 years**[19] CM, Hen's egg	**0-2 year**[22] Seafood, Fruits CM, Hen"s egg			**1 year**[26] Hen's egg CM	**<1year** Hen's egg CM Wheat			**<15 years**[31] Banana Egg Brinjal Wheat Lady's finger CM	**0-5 years**[31] CM Peanut Hen's egg	
1-5 years CM, Red meat, Alpha gal, Gelatin, Coconut, Crustaceans		**0-6 years**[20] Hen's egg, Peanut, Soya, Fruits, Tree nuts, Crustaceans	**0-7 years**[23] Shrimp, Crabs, Mango, CM, Hen's egg			**18 months**[26] Hen's egg Shellfish **24 months**[26] Hen's egg **36 months**[26] Shellfish Hen's egg **48 months**[26] Shellfish Hen's egg	**1 year** Hen's egg Fish roe CM Peanuts Fruits					
				6-11 years Shrimp Fish/ Hen's egg/ crabs	**3 years** Shrimp Fish Crabs		**2-3 years** Fish roe Hen's egg Peanut Tree nut Fruits	**Hue 2-6 years**[29] Shrimp Fish Hen's egg Mollusks CM	**Tien Giang 2-6 years**[29] Shrimp Beef Mollusks Fish			**6-10 years**[34] Iceland, UK, Germany, Spain, Poland-CM Hen's egg Peanut The Netherlands-CM Hen's egg Greece-CM
	3-7 years[18] CM, Hen's eggs, Shrimp	**3-6 years**[19] Walnut, Hen's egg, CM	**3-5 years**[22] Fruits, Seafood		**4-18 years** Shrimp Crabs Fish Mango Mollusks CM Peanut Hen's egg		**4-6 years** Fruits Hen's egg Peanut Buckwheat/ fish roe			**6-11 years**[24] Very low prevalence of FA	**6-10 years**[32] Peanuts CM	**7-10 years**[35] Poland, The Netherlands, Spain, Iceland, Lithuania, Greece, Switzerland Hazelnut Peanut Apple Peach Kiwi Carrot Spain, Iceland Shrimp Fish Greece Fish

5–12 years Red meat FDEIA (wheat) CM Alpha gal			**6–14 years**[21] Fruits, Seafood **6 – 11**[24] years Shrimp,				**7–19 years** Crustaceans Fruits Hen's egg/ wheat Buckwheat			**11–13 years**[32] Peanuts CM Shellfish	
12–18 years Red meat FDEIA (wheat) CM Alpha gal											
>18 years Red meat FDEIA (wheat) Crustaceans		**Adults**[21] Pollen food allergy syndrome Crustaceans Wheat Buckwheat Peanut Walnut Alpha Gal			**>18years** CM/Shrimp Crabs Mollusks Mango Peanut	**Adults**[27] Shrimp Crabs Molluscs	**>20 years** Wheat Fish Crustaceans Fruits	**16–50 years**[30] Crustaceans Fish Mollusks Beef Egg CM	**15–40 years**[31] Banana Brinjal Lady's figure Tomato Wheat	**Adults**[33] Shellfish, CM Peanuts Tree nuts Finfish	
									20–54 years[5] CM Apple		
									>40 years[13] Banana Brinjal Hen's egg Tomato		**Adults**[36] Switzerland, Poland, The Netherlands Hazelnut Apple Peach Spain Peach Melon Shrimp

Table 5. Comparison of food allergy in Sri Lanka with countries in Asia, Europe and USA[a] [a]*The foods are displaced in descending order of prevalence*

Asian countries, even though there are regional differences.[16] Philippines has a relatively high rate of fish allergy[46]

Primary wheat allergy is less common in our population compared to Japan,[26] Korea,[21] and United States,[47] but commoner than in India and other Asian countries.[16] Sensitization to wheat was common in adults in the Indian study, but symptomatic wheat allergy was rare.[5]

Anaphylaxis

A majority of patients in our cohort had anaphylaxis, the probable reason being minor allergies not being referred to our unit for further investigation.

FDEIA was common in our cohort from 5 years of age, and was the commonest cause after 12 years. The reason for the high prevalence is possibly because many clinicians were unaware of the condition and referred such patients to our clinic. Wheat was the only food identified. While wheat is the commonest allergen, other foods are also implicated elsewhere.[10]

Red meat was the commonest allergen in the 5–12-year age group, and was the second most common in adults. In addition, patients with red meat allergy developed allergic reactions including anaphylaxis, to vaccines containing bovine/porcine components such as the measles, mumps, and rubella (MMR) and the live Japanese encephalitis (JE) vaccine. Allergy to bovine/porcine excipients have been implicated in allergic reactions to these vaccines.[48] Patients with CMA[48] or red meat allergy[49] may be at risk and therefore caution should be exercised when administering such vaccines. Gelatin or BSA[49] has been implicated as the culprit allergen. JE is a single dose vaccine, and most MMR reactions occurred with the second dose;[49] the need for further vaccines did not arise in a majority of these patients. Unfortunately, vaccines free of bovine excipients are not available in Sri Lanka. Patients with alpha-gal allergy were not at risk of vaccine allergy, possibly due to its onset being after the age of immunization with these vaccines.

Cow's milk was the most common cause of anaphylaxis in children below 5 years, as in other countries. Coconut was the second commonest cause of anaphylaxis in infancy. Coconut is part of the daily diet of a majority of Sri Lankans, and is a weaning food. Although data regarding coconut (*Cocos nucifera*) allergy is limited, a recent Australian paediatric case series reported 35 patients with allergy to coconut including 9 with anaphylaxis. [50] Anaphylaxis to hen's egg was uncommon, contrasting with data from Europe,[51] China, Japan, Korea, and Singapore.[52] Anaphylaxis to nuts and peanuts was uncommon similar to South Asia, but is relatively common in Hong Kong, Singapore, and in Europe and Australia.[8]

Anaphylaxis to fruits was also very rare in our population. This contrasts with the rest of the world, where it is common.[8] Anaphylaxis due to ingestion of horse purslane (*Trianthema portulacastrum*), locally known as "Sarana", was identified in 1 patient. This has not been reported previously.

Pollen food allergy syndrome

No patient had pollen food allergy syndrome (PFAS). There are case reports of PFAS from India, [53] but they are rare compared to the west. The reason for this discrepancy is unclear.

The present study was limited to patients referred from other centers for evaluation of food allergy. Some patients in whom the implicated food was easily identified may not have been referred to our unit, even though this may be a small number as our clinic is the only unit in the country offering diagnostic services, free of charge. In addition, we did not offer oral food challenges, which is the gold standard for food allergy diagnosis. However, the patients were included in the present study if they had clear evidence of allergy along with ingestion within 2 hours of onset of symptoms (except in FDEIA and alpha-gal allergy).[11]

CONCLUSIONS

The main cause of food allergy in children was CM, whereas FDEIA and red meat allergy were common causes of food allergy/anaphylaxis in older children and adults. Red meat allergy was also implicated in allergic reactions to some

childhood vaccines. Primary red meat allergy may be responsible for late onset CMA.

Abbreviations
CM; Cow's Milk, CMA; Cow's Milk Allergy, CRD; Component Resolved Diagnostics, FA; Food Allergy, FDEIA; Food Dependent Exercise Induced Anaphylaxis, HDM; House Dust Mites, IgE; Immunoglobulin E, LTP; Lipid Transfer Proteins, PFAS; Pollen Food Allergy Syndrome

Declaration of competing interests
The authors declare that they have no competing interests.

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Ethics statement
Ethics approval was provided by the Ethics Review Committee, Medical Research Institute, Colombo 08, Sri Lanka (ERC approval No: 01/2022).
The data were analyzed retrospectively and anonymized.

Authors' contributions
RDS, DD– conception, design of the work, acquisition, analysis, interpretation of data, drafted the work and substantively revised it.
CK- acquisition.
JI- acquisition, analysis.

Consent for publication
The authors have given their consent for the publication.

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All (anonymized) data are available with the corresponding author.

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REFERENCES

1. Sampson HA, Aceves S, Bock SA, et al. Food allergy: a practice parameter update - 2014. *J Allergy Clin Immunol*. 2014;134(5):1016–1025.e43.
2. Sicherer SH, Sampson HA. Food allergy: a review and update on epidemiology, pathogenesis, diagnosis, prevention, and management. *J Allergy Clin Immunol*. 2018 Jan;141(1):41–58.
3. Burks A Wesley, Holgate Stephen T, O'Hehir Robyn E, et al. *Middleton's Allergy 2-Volume Set*. 9th ed. Elsevier; 2020.
4. Loh W, Tang MLK. The epidemiology of food allergy in the global context. *Int J Environ Res Publ Health*. 2018 Sep 18;15(9):2043.
5. Mahesh PA, Wong GW, Ogorodova L, et al. Prevalence of food sensitization and probable food allergy among adults in India: the EuroPrevall INCO study. *Allergy*. 2016 Jul;71(7):1010–1019.
6. Arakali SR, Green TD, Dinakar C. Prevalence of food allergies in South Asia. *Ann Allergy Asthma Immunol*. 2017;118(1):16–20.
7. Wimalasiri YSG, Ratnayake RMU, Karunaratne TDN, Ranaweera KKDS. Food allergy and anaphylaxis - 2063. Identification of foods causing hypersensitivity/allergy among school children in two sub-urban schools in Colombo District, Sri Lanka. *World Allergy Organ J*. 2013;6(1):P146.
8. Baseggio Conrado A, Patel N, Turner PJ. Global patterns in anaphylaxis due to specific foods: a systematic review. *J Allergy Clin Immunol*. 2021;148(6):1515–1525. e3.
9. de Silva NR, Dasanayake WMDK, Karunatilake C, Wickramasingha GD, De Silva BD, Malavige GN. Aetiology of anaphylaxis in patients referred to an immunology clinic in Colombo, Sri Lanka. *Allergy Asthma Clin Immunol*. 2018;14(1):81.
10. de Silva NR, Dasanayake WMDK, Karunatilleke C, Malavige GN. Food dependant exercise induced anaphylaxis a retrospective study from 2 allergy clinics in Colombo, Sri Lanka. *Allergy Asthma Clin Immunol*. 2015;11(1):1–7.
11. Wilson JM, Platts-Mills TAE. Red meat allergy in children and adults. *Curr Opin Allergy Clin Immunol*. 2019 Jun;19(3):229–235.
12. Muraro A, Werfel T, Hoffmann-Sommergruber K, et al. EAACI food allergy and anaphylaxis guidelines: diagnosis and management of food allergy. *Allergy*. 2014;69(8):1008–1025.
13. Matricardi PM, Kleine-Tebbe J, Hoffmann HJ, et al. EAACI molecular allergology user's guide. *Pediatr Allergy Immunol*. 2016;27(Suppl 23):1–250.
14. Wilson JM, Schuyler AJ, Workman L, et al. Investigation into the α-gal syndrome: characteristics of 261 children and adults reporting red meat allergy. *J Allergy Clin Immunol Pract*. 2019 Sep-Oct;7(7):2348–2358. e4.
15. Feldweg AM. Food-dependent, exercise-induced anaphylaxis: diagnosis and management in the outpatient setting. *J Allergy Clin Immunol Pract*. 2017 Mar-Apr;5(2):283, 28.
16. Hossny E, Ebisawa M, El-Gamal Y, et al. Challenges of managing food allergy in the developing world. *World Allergy Organ J*. 2019;12(11), 100089.
17. Sripramong C, Visitsunthorn K, Srisuwatchari W, Pacharn P, Jirapongsananuruk O, Visitsunthorn N. Food sensitization and food allergy in allergic Thai patients from a tertiary care center in Thailand. *Asian Pac J Allergy Immunol*. 2022 Jun;40(2):147–154.
18. Rangkakulnuwat P, Lao-Araya M. The prevalence and temporal trends of foodallergy among preschool children in NorthernThailand between 2010 and 2019. *World Allergy Org J*. 2021;14(10), 100593. https://doi.org/10.1016/j.waojou.2021.100593.
19. Lee S. *A Study for Prevention and Control of Food allergy. Research 104 Report of Grant from Korea Ministry of Food and Drug Safety (MFDS) in 2015*. Cheongju: Ministry of Food and Drug Safety; 2015.

20. Park M, Kim D, Ahn K, Kim J, Han Y. Prevalence of immediate-type food allergy in early childhood in Seoul. *Allergy Asthma Immunol Res*. 2014;6:131–136.

21. Lee SC, Kim SR, Park KH, Lee JH, Park JW. Clinical features and culprit food allergens of Korean adult food allergy patients: a cross-sectional single-institute study. *Allergy Asthma Immunol Res*. 2019 Sep;11(5):723–735.

22. Sha L, Shao M, Liu C, Wu Y, Chen Y. A cross-sectional study of the prevalence of food allergies among children younger than ages 14 years in a Beijing urban region. *Allergy Asthma Proc*. 2019 Jan 1;40(1):e1–e7.

23. Zeng GQ, Luo JY, Huang HM, et al. Food allergy and related risk factors in 2540 preschool children: an epidemiological survey in Guangdong Province, southern China. *World J Pediatr*. 2015 Aug;11(3):219–225.

24. Li J, Ogorodova LM, Mahesh PA, et al. Comparative study of food allergies in children from China, India, and Russia: the EuroPrevall-INCO surveys. *J Allergy Clin Immunol Pract*. 2020 Apr;8(4):1349–1358. e16.

25. Wu TC, Tsai TC, Huang CF, et al. Prevalence of food allergy in Taiwan: a questionnaire-based survey. *Intern Med J*. 2012 Dec;42(12):1310–1315.

26. Tham EH, Lee BW, Chan YH, et al. Low food allergy prevalence despite delayed introduction of allergenic foods-data from the GUSTO cohort. *J Allergy Clin Immunol Pract*. 2018 Mar-Apr;6(2):466–475.

27. Thong BY, Cheng YK, Leong KP, Tang CY, Chng HH. Immediate food hypersensitivity among adults attending a clinical immunology/allergy centre in Singapore. *Singap Med J*. 2007 Mar;48(3):236–240.

28. Ebisawa M, Ito K, Fujisawa T. Committee for Japanese pediatric guideline for food allergy, the Japanese society of pediatric allergy and clinical immunology; Japanese society of allergology. Japanese guidelines for food allergy 2020. *Allergol Int*. 2020 Jul;69(3):370–386.

29. Le TTK, Nguyen DH, Vu ATL, Ruethers T, Taki AC, Lopata AL. A cross-sectional, population-based study on the prevalence of food allergies among children in two different socio-economic regions of Vietnam. *Pediatr Allergy Immunol*. 2019 May;30(3):348, 35.

30. Le TTK, Tran TTB, Ho HTM, Vu ATL, McBryde E, Lopata AL. The predominance of seafood allergy in Vietnamese adults: results from the first population-based questionnaire survey. *World Allergy Organ J*. 2020 Mar 5;13(3), 100102.

31. Dey D, Ghosh N, Pandey N, Gupta Bhattacharya S. A hospital-based survey on food allergy in the population of Kolkata, India. *Int Arch Allergy Immunol*. 2014;164(3):218–221.

32. Gupta RS, Warren CM, Smith BM, et al. The public health impact of parent-reported childhood food allergies in the United States. *Pediatrics*. 2018;142(6), e20181235.

33. Gupta RS, Warren CM, Smith BM, et al. Prevalence and severity of food allergies among US adults. *JAMA Netw Open*. 2019;2, e185630.

34. Grabenhenrich L, Trendelenburg V, Bellach J, et al. Frequency of food allergy in school-aged children in eight European countries-The EuroPrevall-iFAAM birth cohort. *Allergy*. 2020 Sep;75(9):2294–2308.

35. Lyons SA, Clausen M, Knulst AC, et al. Prevalence of food sensitization and food allergy in children across Europe. *J Allergy Clin Immunol Pract*. 2020 Sep;8(8):2736–2746. e9.

36. Lyons SA, Burney PGJ, Ballmer-Weber BK, et al. Food allergy in adults: substantial variation in prevalence and causative foods across Europe. *J Allergy Clin Immunol Pract*. 2019 Jul-Aug;7(6):1920–1928. e11.

37. Martelli A, De Chiara A, Corvo M, Restani P, Fiocchi A. Beef allergy in children with cow's milk allergy; cow's milk allergy in children with beef allergy. *Ann Allergy Asthma Immunol*. 2002;89(6 Suppl 1):38–43.

38. Warren CM, Agrawal A, Gandhi D, Gupta RS. The US population-level burden of cow's milk allergy. *World Allergy Organ J*. 2022 Apr 21;15(4), 100644.

39. Flom JD, Sicherer SH. Epidemiology of cow's milk allergy. *Nutrients*. 2019 May 10;11(5):1051.

40. Cyy Wai, Leung NYH, Leung ASY, Wong GWK, Leung TF. Seafood allergy in Asia: geographical specificity and beyond. *Front Allergy*. 2021 Jul 8;2, 676903.

41. Tham EH, Leung DYM. How different parts of the world provide new insights into food allergy. *Allergy Asthma Immunol Res*. 2018;10(4):290–299.

42. Lieberman JA, Gupta RS, Knibb RC, et al. The global burden of illness of peanut allergy: a comprehensive literature review. *Allergy*. 2021 May;76(5):1367–1384.

43. Panjari M, Koplin JJ, Dharmage SC, et al. Nut allergy prevalence and differences between Asian-born children and Australian-born children of Asian descent: a state-wide survey of children at primary school entry in Victoria, Australia. *Clin Exp Allergy*. 2016;46(4):602–609.

44. Du Toit G, Roberts G, Sayre PH, et al. Randomized trial of peanut consumption in infants at risk for peanut allergy. *N Engl J Med*. 2015;372(9):803–813.

45. Jayatissa R, Gunathilaka M, Gankanda W, Uduwaka C, Hewawitharana K. *Locally Available Improved Recipes for Complementary Feeding and Case Histories*. Department of Nutrition, Medical Research Institute Ministry of Health and UNICEF; 2012. http://www.mri.gov.lk/assets/Nutrition/2012-Complementary-Feeding-book-final.pdf. Accessed May 19, 2022. Accessed.

46. Connett GJ, Gerez I, Cabrera-Morales EA, et al. A population-based study of fish allergy in the Philippines, Singapore and Thailand. *Int Arch Allergy Immunol*. 2012;159(4):384–390.

47. Fleischer DM, Perry TT, Atkins D, et al. Allergic reactions to foods in preschool-aged children in a prospective observational food allergy study. *Pediatrics*. 2012;130:e25–e32.

48. Piñones M, Landaeta M, Bustos P, et al. Hypersensitivity reactions to measles-mumps-rubella vaccine in patients with IgE-mediated cow's milk allergy. *J Allergy Clin Immunol Pract*. 2020 Jan;8(1):349–351.

49. de Silva R, Dasanayake WMDK, Wickramasinhe GD, et al. Sensitization to bovine serum albumin as a possible cause of allergic reactions to vaccines. *Vaccine*. 2017;35(11):1494–1500.

50. Pathmanandavel K, Kaur N, Joshi P, Ford LS. Anaphylaxis and allergy to coconut: an Australian pediatric case series. *J Allergy Clin Immunol Pract*. 2020 Nov-Dec;8(10):3657–3659.

51. Grabenhenrich LB, Dölle S, Moneret-Vautrin A, et al. Anaphylaxis in children and adolescents: the European anaphylaxis registry. *J Allergy Clin Immunol*. 2016 Apr;137(4): 1128–1137.e1.

52. Tham EH, Leung ASY, Pacharn P, et al, APAPARI Anaphylaxis Study Group. Anaphylaxis - lessons learnt when East meets west. *Pediatr Allergy Immunol*. 2019 Nov;30(7):681–688.

53. Bansal AS. Aubergine and potato sensitivity with latex sensitisation and oral allergy syndrome. *Case Rep Med*. 2013;2013, 314658.