

## The management of food allergy in Indonesia

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Prevalence of allergic diseases is increasing worldwide, including food allergy. It is different between countries because food allergy can vary by culture and population. Prevalence of food allergy in Indonesia is unknown; therefore it is not known yet the burden and impact of food allergy in our population. However, we already start to formulate guidelines for diagnosis and management of food allergy, especially cow's milk allergy.

**Key words:** Food allergy; Cow's milk allergy; Indonesia

### INTRODUCTION

Food allergy is an immunological adverse clinical reaction to food. Food can cause different clinical manifestations of type I hypersensitivity reactions according to Gell and Coomb [1]. Food allergy is one of important issues in children because food is needed for children's growth and development. When children have food allergy, the disease itself and unnecessary diet avoidance may influence their growth process, and it may disturb their growth and development in the future.

The prevalence of food allergies in the last decade appears to be increasing. There is marked heterogeneity in the prevalence of food allergy due to differences in study design or differences between populations. The spectrum of food allergy in the last

decade was relatively unchanged, although the individual food allergy can vary by culture and population. Cow's milk, eggs, soy, wheat, tree nuts, peanuts, fish and shellfish are major allergens in childhood [2-4].

Indonesia does not have a great number of studies on food allergy, because allergy does not our country's priority at this time. Therefore, we adapted some of recommendations from other countries that could be suitable in our settings to diagnose and manage food allergy in our country. This review was intended to give illustration of management of food allergy in Indonesia.

### Prevalence of food allergy

Prevalence of food allergies varied among studies, particularly

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due to methodology on how to diagnose food allergies. Studies that used self-report food allergy had higher prevalence of food allergies compared to studies that used skin prick test (SPT) of food specific immunoglobulin E (sIgE) examination or food challenge [2-4].

The result of meta-analysis on prevalence food allergy showed that prevalence of self-reported food allergy was very high compared to objective measures. There were heterogeneity between studies regardless of type of assessment or food item considered, and in most analyses this persisted after age stratification. Self-reported prevalence of food allergy varied from 1.2% to 17% for milk, 0.2% to 7% for egg, 0% to 2% for peanuts and fish, 0% to 10% for shellfish, and 3% to 35% for any food. However, confirmed prevalence of food allergy varied only from nearly 0% for fish and shellfish, 0% to 3% for milk, 0% to 1.7% for egg, and 1% to 10.8% for any food [2].

Food allergy can affect skin (urticaria, angioedema, atopic dermatitis), gastrointestinal tract (oral allergy syndrome, vomiting, allergic eosinophilic esophagitis, diarrhea, proctocolitis), and respiratory tract (nasal congestion, rhinorrhea, sneezing, itching of the nose and throat, wheezing). Anaphylaxis is severe manifestation of food allergy and it is increasing in prevalence, especially for peanuts allergy [1, 4].

The prevalence of food allergy in individuals with moderate to severe atopic dermatitis was reported around 30% to 40%, and these patients have clinically significant IgE-mediated food allergy as assessed by combination of convincing symptoms, SPTs, sIgE levels, or oral food challenges [5] or a definite history of immediate reactions to food [6].

Indonesia does not have data on national prevalence of food allergy. However, in our clinic we found that from 42 atopic dermatitis patients in 2012, most of them were sensitized by white egg (31%), cow's milk (23.8%), chicken (23.8%), yolk egg (21.4%), nuts (21.4%), and wheat (21.4%) [7]. A different pattern was found in our clinic back in 2011, which found that most of our atopic dermatitis patient was sensitized with maize, followed by white egg, tuna, chicken, cow's milk, and peanuts [8]. Meanwhile, we also found 3% of our diarrhea patients were cow's milk allergy (CMA) [9].

### Diagnosis of food allergy

Diagnosis of food allergy in children is very difficult, especially in Indonesia where a lot of food with different kinds of spices added. Therefore, a careful history taking and daily record are important before further investigation.

The wrong perception or unawareness of mother on food allergy also can make difficulty in food allergy diagnosis. Prawirohartono [10] in Yogyakarta, Indonesia found that among 114 of medium to highly educated mothers, there were still wrong perceptions about food allergy. From 114 mothers, 48.2% of them believed that food allergy cannot be inherited, egg causes furuncle (54.3%), breast milk causes atopic eczema (46.5%), and food allergy does not related to respiratory symptoms. There was a relationship between these perceptions and mothers' educational level. According to these mothers, most common allergic manifestation was skin manifestation. Egg, shrimp, fish, and shellfish were types of animal foods which were recognized as major food allergen, while peanut, soy, banana, rice and vegetables were recognized as the major causes of food allergy among non animal products [10]. The variety of food composition, combined with other food additive, food color, preservative and spices in Indonesian food also make difficulty in food allergy diagnosis.

Consensus on the diagnosis and management of food allergy and allergy to cow's milk is made by Allergy Immunology, Nutrition and Metabolic Diseases, and Gastrohepatology Working Group of Indonesian Pediatrics Society (Ikatan Dokter Anak Indonesia) to prevent misdiagnosis and mismanagement of food allergy [11]. Before we made this consensus, many food allergy diagnoses was based only on history taking and excessive dietary restrictions by doctors that will surely disrupt child growth and development.

The diagnosis of food allergy in Indonesia based on careful history taking, physical examination, daily diet records, and SPT or sIgE as a guide to conduct elimination and provocation test (Fig. 1). Interpretation of SPT or sIgE should be done carefully, because positive results of SPT or sIgE only indicate sensitization and it does not always related to clinical symptoms. Provocation test is conducted in an open challenge methods because it is difficult technically to perform provocation test with double-blind



**Fig. 1.** Diagnosis of food allergy. sIgE, specific immunoglobulin E; SPT, skin prick test.

placebo-control for children in our settings [11]. Safri et al. [12] found that only 67% subjects with positive results on cow's milk SPT had positive cow's milk challenge, while only 64% subjects with positive cow's milk IgE had positive cow's milk challenge. However, in this study definition of positive specific IgE for cow's milk was more than 0.4 kUA/L, which was lower than suggested predictive value for cow's milk IgE that correlate to cow's milk challenge in other review (Table 1) [13].

**Management of food allergy**

Management of food allergy is strict avoidance of food allergen. Substitute the allergen with other food, which is comparable for its nutrition value in order to prevent malnutrition. In breastfed babies, they can continue breastfeeding with food allergen elimination in maternal diet. Many studies tried to evaluate whether immunotherapy and pharmacotherapy, such as anti-IgE or anti-cytokine, will be effective for food allergy. Education about the diseases, natural history of food allergy, treatment including prevention of accidental ingestion or exposure, how to read label should be given to the parents or patients [1, 3, 13].

**Management of CMA in Indonesia**

Diagnosis of CMA based on history taking and confirmed by elimination-provocation test. sIgE or SPT for cow's milk protein can be used to support the diagnosis. There are some differences in the management of CMA among different countries reflecting general and local needs and vision (Table 2).

In Indonesia, management of CMA in exclusively breast-fed infants is continuing breastfeeding and mother should avoid cow's milk formula and its products. Management of CMA in formula fed infants is based on severity of the disease. Extensively hydrolyzed formula should be given for infants with mild to moderate symptoms, while amino acid should be given for infants with severe symptoms. These special formulas should be given for

minimum 6 months (Fig. 2). Re-challenge should be done every 6 months to evaluate tolerance. If symptoms still appear after re-challenge, infants should be back on free cow's milk protein diet for another 6 months [11].

Soy is recommended for infants above 6 months old who cannot tolerate extensively hydrolyzed formula in term of palatability or cannot get this formula due to cost or availability issues. Parents should be informed that some of CMA patients are also allergy to soy, therefore careful follow up should be done [11].

Soy formula consider to be safe for CMA patients in Indonesia, as Muktiarti et al. [18] found that only 17.5% patient with CMA sensitized to soy and Santi et al. [19] also found none of CMA patients were sensitized to soy. In addition, a lot of Indonesian traditional foods use soy as its ingredients.

**Prognosis**

Most of food allergy can be grow out in certain time. Routine assessment for tolerance is needed to avoid unnecessary extended avoidance of food allergen. We should observe for multiple food allergies and other allergic diseases in the future especially respiratory tract allergic disease [1].

**Prevention of food allergy**

Preventive measures are needed to prevent allergic diseases especially in children with atopic family. Studies on breastfeeding for preventing allergy showed conflicting results [3]. Indonesia national survey found that only 25.2% infant who had exclusive breastfeeding for 4 months, and 15.3% infants who had exclusive breastfeeding for 6 months [20]. Munasir et al. [21] found that breastfeeding has no impact on occurrence of atopic dermatitis. Nevertheless, we still encourage breastfeeding as allergy preventive measure. Partially hydrolyzed can be used for infants from atopic family who cannot get breastfeeding [11].

**Table 1. Suggested predictive values of sIgE and SPT for selected food allergen**

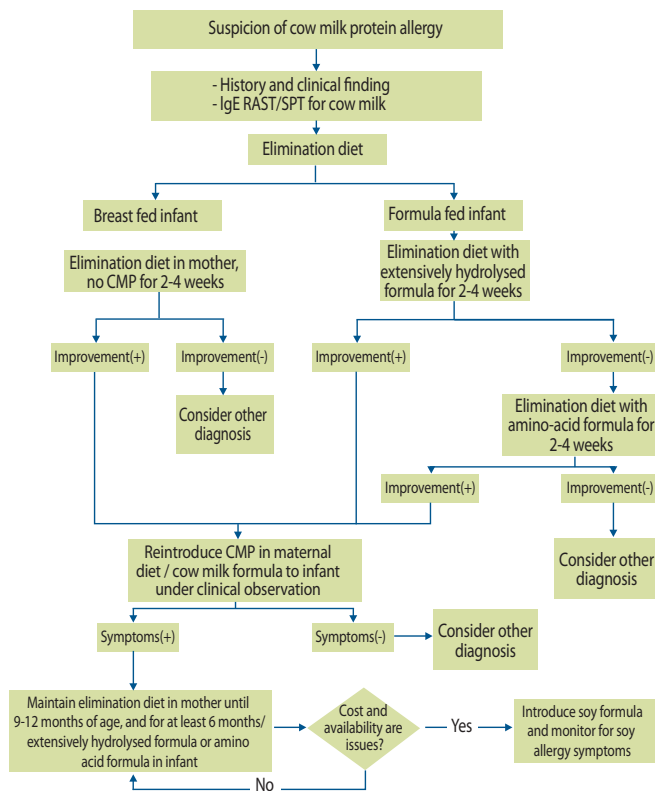
	~ 50% react	~95% react (> 2 years of age)	~95% react (< 2 years of age)
Milk	sIgE = 2 kUA/L	sIgE = 15 kUA/L SPT = 8 mm wheal	sIgE = 5 kUA/L SPT = 6 mm wheal
Egg	sIgE = 2 kUA/L	sIgE = 7 kUA/L SPT = 7 mm wheal	sIgE = 2 kUA/L SPT = 5 mm wheal
Peanut	sIgE = 2 kUA/L (convincing history) sIgE = 5 kUA/L (unconvincing history)	sIgE = 14 kUA/L SPT = 8 mm wheal	- SPT = 4 mm wheal

sIgE, specific immunoglobulin E; SPT, skin prick test. Adapted from reference [13].

**Table 2.** Treatment of CMA according to the current recommendations in different countries

	Europe (ESPACI/ESPGHAN, 1999) [14]	America (AAP, 2000) [15]	Australia (2008) [16]	Singapore (2010) [17]	Indonesia (2010) [11]
Breastfed	In exclusively breast infants, a strict elimination of the causal protein from the diet of the lactating mother should be tried.	Elimination of cow's milk from maternal diet may lead to resolution of allergic symptoms in the nursing infants. If symptoms do not improve or mother are unable to participate in a very restricted diet regimen, alternative formulas can be used to relieve the symptoms.	Breastfeeding may be continued, and recommendations are provided for eliminating maternal intake of CM protein.	Continue BF and eliminate cow's milk from the mother's diet.	Continue BF, avoid cow's milk and its product in maternal diet.
Formula-fed	Allergen elimination is relatively easy in exclusive formula fed infants.	Formula replacement with eHF or AAF. Soy formula is recommended for IgE mediated CMA.	Soy, extensively hydrolysed and amino acid may be appropriate for treating cows milk protein allergy.	IgE-mediated CMA: Formula replacement with a soy-based formula and if not tolerated, an eHF or AAF. Non IgE mediated CMA: Formula replacement with eHF or AAF.	Replace cow's milk with: -eHF -AAF for patients with severe -Symptom -Soy infant formula (above 6 months of age)
Partially hydrolyzed formula (pHF)	Not to be used for treatment of CMA.	Not intended to be used to treat CMA.	pHF is not used for formula replacement in CMA.	Not for CMA treatment.	Not for CMA treatment.
Extensively hydrolyzed formula (eHF)	Extensively hydrolyzed protein are recommended for the treatment of infants with cow's milk protein allergy.	At least 90% of CMA infants extensively hydrolyzed formulas.	Appropriate for treating CMA.	eHF is recommended treatment for IgE and non IgE mediated CMA.	eHF is used for CMA treatment.
Soy formula	Formula based on intact soy protein isolates are not recommended for the initial treatment of food allergy in infants.	Although soy formulas are not hypoallergenic, they can be fed to infants with IgE-associated symptoms of milk allergy, particularly after the age of 6 months.	Appropriate for treating CMA.	Soy based formula is recommended for IgE mediated CMA.	Unmodified soy formula cannot be used for CMA treatment.
Other milks	CMA children should not be fed preparations based on unmodified milk of other species (such as goats' or sheep's milk) because of a high rate of cross reactivity.	Milk from goats and other animals or formulas containing large amounts of intact animal protein are inappropriate substitutes for breast milk or cow's milk-based infant formula.	There is no place for other mammalian milks (such as goats milk) in treating CMA.	Goat or sheep milk should not be prescribed to CMA. Patients as these milks cross-react with cow's milk.	CMA patients should not consume other mammalian milk (such as goat or sheep milk).
Soy hydrolyzed formula (HSF)	Extensively hydrolyzed protein are recommended for the treatment for infants with cow's milk protein allergy (non specified if also HSF).	Although soy formulas are not hypoallergenic, they can be fed to infants with IgE-associated symptoms of milk allergy, particularly after the age of 6 months.	Appropriate for treating CMA.	Soy based formula is recommended for IgE mediated CMA.	Soy hydrolyzed formula can be used for CMA treatment in infants above 6 months of age.
Amino acid formula (AAF)	Highly extensive patients (ie, patients reacting to eHF) may require an amino acid based dietary product.	Tolerated.	Appropriate for treating CMA.	AAF can be used for formula replacement in IgE and non IgE mediated CMA.	It is recommended for CMA treatment especially for patients with severe symptoms.

CMA, cow's milk allergy; IgE, immunoglobulin E; AAF, amino acid formula; AAP, American Academy of Pediatrics; ESPACI, European Society of Paediatric Allergy and Clinical Immunology; ESPGHAN, European Society of Paediatric Gastroenterology, Hepatology and Nutrition.



**Fig. 2.** The management of cow's milk protein allergy (modification from reference [11]. IgE, immunoglobulin E; RAST, radioallergosorbent; SPT, skin prick test; CMP, cow's milk protein.

## CONCLUSION

Food allergy is one of important problem in children and its prevalence is increasing. Accurate diagnosis is needed to prevent mismanagement of food allergy especially extensive food elimination that can be influenced the children's growth. We still need national data and more research to evaluate the burden of food allergy in Indonesia and its impact to Indonesian population.

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