

Soy Formula as An Alternative for Infants with Cow's Milk Allergy: Perspective from Pediatricians and Midwives in Indonesia

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ABSTRACT: The prevalence of food allergy in children is increasing globally, with cow's milk allergy being the most common in infants and increasing from 2% to 3% in developed countries. However, data on cow's milk allergy in infants is limited in Indonesia. This study used a mixed methods approach using an online survey and in-depth interviews. The survey was conducted from September 2021 to March 2022. Qualitative analysis, all interviews were recorded and transcribed. Data were analyzed using simple thematic analysis. The results showed that a total of 93 pediatricians and 104 midwives participated in the survey. However, among the 93 pediatricians, only 56 (60.2%) completed the survey. Meanwhile, 11 midwives (10.6%) were excluded because they had no experience in handling CMA cases. The majority of CMA cases occurred in children under two years old, and most were treated by pediatricians. In terms of diagnostic tests, 51.8% of pediatricians recommended all specific IgE tests, prick tests, and provocation tests to diagnose allergies. More than 80% (46/56) of pediatricians chose to avoid all types of cow's milk products in the mother and child's diet as the main treatment. Meanwhile, only 22.1% of midwives did the same. Milk choice will differ depending on the severity of CMA. Soy milk formula is preferred by midwives for patients with low-level and moderate to severe allergies. Meanwhile, pediatricians recommend extensive hydrolysate formula for low severity patients and amino acid-based formula for moderate to severe.

Keywords- food allergy, soy formula, infants, pediatrician, child health

INTRODUCTION

Food allergy (FA) is a significant public health concern among children. Globally, the prevalence of FA is reported to range from 1% to more than 10% in under-five children (Prescott et al, 2013). Determining the prevalence of FA is difficult because it is associated with geographic region, food

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availability, race, age, eating habits, and different standards applied to establish the diagnosis (self-perception versus food challenge rate) (Prescott et al, 2013; Feng et al, 2021). Self-reported FA often leads to overestimating the prevalence of FA. Oral food challenges (OFC) are the gold standard for FA diagnosis. Nevertheless, there is the possibility of OFC failures and it is assumed that patients might have risks to develop mild to severe systemic reactions due to the procedure (Kowalski et al, 2016).

Cow’s milk and egg allergy are the most common FA among infants and children in the world. The incidence of cow’s milk allergy (CMA) is estimated from 2% to 3% in developed countries (Hossny et al, 2019). Currently, there is no data available to reflect the prevalence of CMA among infants in Indonesia. However, a study performed in Jakarta, the capital city of Indonesia, surveyed about 286 children under-3-year-old from 2011 to 2013 and found that the prevalence of FA was 10.5% in these children. The main culprit of the FA was cow’s milk, contributing to more than 75% (Tanukusumah & Kurniati, 2016).

The British Society for Allergy and Clinical Immunology (BSACI) recommends the avoidance of cow’s milk and its products as the main treatment for CMA. Breast milk is undoubtedly the first choice for infants. Nonetheless, children with CMPA generally begin because they were unable to consume breast milk. Therefore, the choice of substitute milk will be limited to hypoallergenic formulas and soya-based milk. Extensively hydrolysed formulas (eHF) and amino-acid formulas (AAF) are included as hypoallergenic formulas, these would be the first choice for infants with severe CMPA (Luyt et al, 2014). The World Allergy Organization emphasizes the need for substitute formulas for children under two-year-old. The substitutes include eHF, AAF, and soy-based milk (Fipcchi et al, 2022). Indonesian Pediatric Society (IDAI) also recommends the use of eHF for mild to moderate allergy or AAF for severe conditions (Avianti et al, 2020). Nevertheless, many parents complain about the high cost of these hypoallergenic formulas and the lack of access to the marketplace. Where this situation takes place, soy-based milk can be used as an alternative. However, parents should be educated about the possibility of allergy to soy formula before giving soy milk to their children (Strzalkowski et al, 2022)

Pros and cons exist regarding the use of soy-based formula as an alternative for children with CMA. The soy formula components, i.e., phytoestrogens/ isoflavones, are suspected to inhibit the cell growth pathway and affect human reproductive health. Babies fed with soy formula have high concentrations of phytoestrogen, about 13,000-22,000 times higher than their endogenous estrogen levels. Nevertheless, some studies also revealed no significant differences in terms of growth patterns, metabolic, endocrine, and reproductive functions between children fed with soy-based milk and cow’s milk (Strzalkowski et al, 2022).

Soy-based formulas have been developed since 1909, using soy flour as a protein source. Nevertheless, in the 1960s, soy protein isolates began to replace soy flour. About 90% of the nutritional

content of soy protein isolate is protein, and the rest consists of fat (maximum 1%), fibre (0.2%), and carbohydrates (usually around 4%). The soy protein isolates are easier to be digested, compared to soy flour. The heating and extraction process to produce the soy protein isolates could also reduce the levels of other unwanted ingredients, such as isoflavones, trypsin inhibitors, and phytic acid (Vandenplas et al, 2021).

Pediatricians and midwives are at the front line in diagnosing and treating children with CMA. Their recommendations would become an important consideration for parents. However, suggesting soy-based formula as an alternative is still under debate, even among health professionals. Despite the existence of several guidelines for CMA, the practices of health professionals are not fully in line with these recommendations. Thus, this study aimed to evaluate the knowledge and practice of health professionals regarding the use of soy-based formula as an alternative for infants with CMA.

RESEARCH METHODS

Study design and respondents

This study applied a mixed-method approach, using online surveys and in-depth interviews. Online surveys were disseminated from September 2021 to January 2022, while interviews were performed in February to March 2022. The survey was hosted on the Google form survey platform and distributed through email and WhatsApp to all respondents. The eligibility criteria were pediatricians and midwives who have been actively working in health facilities in Indonesia, at least 6 months, and had experiences in managing CMA cases among under-one-year-old children. Respondents were obtained from third-party health professionals’ database (Alomedika). Using the proportion of 14.8% doctors who recommended soy-based milk, we calculated the minimum sample size of 49 respondents. In the survey for pediatricians, we also asked their participation for in-depth interview following the survey. The interviews were conducted using Zoom platform. Those agreed to participate in the interviews were then invited to join the interviews. The invitations were sent via email, text message, and WhatsApp message.

Questionnaire development

The questionnaire used in the online survey was modified and adapted from previous cross-sectional studies. It contains four different parts, i.e., 1) respondents’ characteristics; 2) diagnosis; 3) treatment; and 4) prognosis. Modifications were applied for the questionnaire to midwives, since they were usually not involved with establishing a diagnosis, and related merely to the management of the children. In terms of the interview questions, we explored factors that influence the pediatrician’s choice

in giving recommendations to the patients and challenges in using the hypoallergenic formulas and soy-based formulas.

Data analysis

Demographic characteristics of the pediatricians and midwives were analyzed descriptively and presented in tables. Knowledge and perception regarding diagnosis, treatment and prognosis were measured on a Likert Scale from 1 (disagree) to 6 (agree). Respondents were asked to provide the scale according to each statement. The knowledge and behavior of respondents were assessed using χ^2 or Fisher’s exact tests, with $p < .05$ considered a significant result. The analyses were done using SPSS version 20. Regarding the qualitative analysis, all interviews were recorded and transcribed. Data were analyzed using simple thematic analysis. Data were classified and coded accordingly. These were done using Microsoft Excel. This study was approved by institutional review board for conduct study in Indonesia (No: 28/07/KEP-FKIKUAI/2021).

RESULTS AND DISCUSSION

Demographic characteristics

A total of 93 pediatricians and 104 midwives participated in the survey. The respondents were from various regions in Indonesia, representing from Sumatra Island to Eastern Indonesia. However, among 93 pediatricians, only 56 (60.2%) completed the survey. While for the midwives, 11 (10.6%) were excluded because they had no experience in managing CMA cases.

Table 1.

Demographic characteristics of the respondents

Variable	Pediatrician	Midwives
	n (%)	n (%)
Age (median, min-max)	37, 29-70	43, 23-58
Length of work in years (median, min-max)	5, 1-35	18, 3-34
Gender		
• Female	33 (58.9)	103 (99.0)
• Male		

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Variable	Pediatrician	Midwives
	n (%)	n (%)
	23 (41.1)	1 (1.0)
Workplace		
• Public health facilities	25 (44.6)	103 (99.0)
• Private health facilities	31 (55.4)	1 (1.0)
Domicile		
• Java Island	42 (79.2)	41 (39.4)
• Outside Java Island	11 (20.8)	63 (60.6)
Number of cases monthly		
• < 5	28 (50.0)	88 (84.6)
• 5-10	23 (41.1)	2 (1.9)
• > 10	5 (8.9)	3 (2.9)

The majority of CMA cases occurred among those under-two years, and most were handled by pediatricians. In terms of a diagnostic test, about 51.8% of pediatricians suggested all specific IgE tests, prick tests, and provocation tests are necessary, followed by 23.2% suggested merely specific IgE test, 23.2% with only provocation test, and 1.8% for prick test alone. CMA diagnosis was established by pediatricians, whilst midwives usually did not establish the diagnosis, and merely followed up the treatment after the patient was treated by pediatricians.

Table 2.
Knowledge about diagnosis of CMA by pediatricians

Statement	Agree (%)	Disagree (%)
The diagnosis of CMA is based primarily on a positive result on any IgE-specific test	27 (48.3)	29 (51.7)
If the specific determinant of IgE in the blood is negative, any type of CMA can be ruled out.	5 (8.9)	51 (91.1)

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Statement	Agree (%)	Disagree (%)
The Oral Food Challenge is mandatory in the diagnosis of CMA.	38 (69.1)	17 (30.9)
Improvement of symptoms after elimination of cow’s milk on most occasions is sufficient to establish the diagnosis of CMA	50 (89.3)	6 (10.7)
The diagnosis of non-IgE-mediated CMA is based primarily on a positive patch test result.	26 (46.4)	30 (53.6)

More than 80% (46/56) of pediatricians chose to eliminate all kinds of cow’s milk products in the mother and child’s diet as the main treatment. This was in contrast with midwives, whom merely 22.1% of them did a similar thing. About 48.1% (50/104) of the midwives chose to treat the allergic reactions and still recommend milk consumption. The choice of milk would differ depending on the severity level of CMA. Figure 1 showed the different recommendations for milk based on the level of severity by pediatricians and midwives.

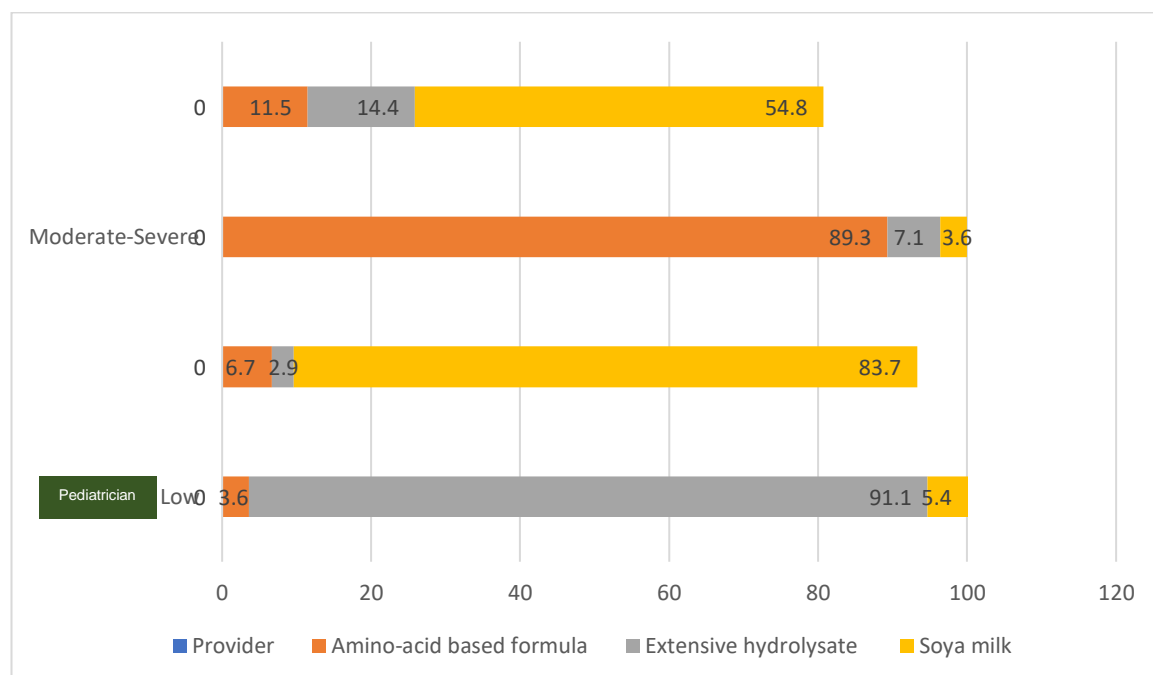


Figure 1. Milk recommendation based on the severity level by pediatricians and midwives

Source: Data processed by researchers, 2023

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Soya milk was preferred by the midwives for patients in the low and moderate to severe levels. Meanwhile, pediatricians recommended extensive hydrolysate formula for patients in the low severity level and amino acid-based formula for moderate to severe levels. Differences in the treatment given between pediatricians and midwives can also be influenced by differences in knowledge. About 59.6% (62/104) of midwives did not understand the practice guideline for CMA management, while all pediatricians (100%) understood the guideline. Regarding the treatment and perception of the use of soya milk for patients with CMA, we summarized the answers from pediatricians and midwives in table 3.

Table 3.

Level of agreement on the recommendation of soya milk for children with CMA

Statement	Pediatricians (%)	Midwives (%)
I recommend soy milk if the price of AAF or eHF or pHF milk is not affordable for the patient	48 (85.7)	78 (75.0)
I recommend soy milk if AAF or eHF or pHF milk is not available	51 (91.1)	88 (84.6)
I recommend soy milk as the first priority in children with cow's milk allergy.	6 (10.7)	89 (85.6)
Children who consume soy milk have growth that is comparable to children who consume cow's milk	40 (71.4)	80 (76.9)
Children who consume soy milk have a comparable development with children who consume cow's milk.	42 (75.0)	88 (84.6)
Soy milk is safe to give in the long term (> 6 months)	46 (82.1)	90 (86.5)

Note: AAF = amino acid-based formula; eHF = extensive hydrolysate formula; pHF = partial hydrolysate formula : The survey was in line with the result of the interviews. The pediatrician preferred to give extensive hydrolysate for those in low severity levels and an amino acid-based formula for moderate to severe levels.

"If it leads to low or moderate severity level, I usually recommend extensive hydrolysate, but if it was severe, (I choose) amino acids" (Pediatrician)

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Breast milk is undoubtedly the first choice for the child. Nevertheless, extensive hydrolysate would be the next preferable milk, and soya formula would be the last option.

"Usually we emphasize breast milk....if we couldn't, we should use extensive hydrolysate...if the patient can't, we replace with soya formula" (Pediatrician)

Discussions

Our results showed that the majority of midwives recommended soya formula for children with CMA, both for low and moderate to severe levels. However, the pediatricians had different opinions. Soya formula was not preferred as the first choice, and only recommend when amino acid-based formula and extensive hydrolysate were not affordable nor available in the market. BSACI recommends breast milk as the first choice to replace cow’s milk in the diet, followed by hypoallergenic formulas, such as extensively hydrolyzed formulas and amino acid-based formulas (Luyt et al, 2014). IDAI also recommends hypoallergenic formula as the substitute and offers soya formula only if the patients had problems with affordability and availability. This study highlights the gap in knowledge between pediatricians and midwives, as many of the midwives did not know the practice guideline for CMA.

Previously, many people concern about the use of soya formula due to the similarity of soya proteins with cow’s milk proteins. Nonetheless, this statement is debatable. An in-vivo study revealed that soybean protein P34 had a similarity with bovine casein, cow’s milk protein that induced allergic reactions in mice (Reynaldo et al, 2014). A cross-sectional among children under 3.5 years old with CMA found about 14% (13/93) of the children had been diagnosed with soy allergy (Vandenplas et al, 2014). Nevertheless, the production of soya formulas has been improved by adding amino acids and other nutrients. One of the pediatricians interviewed in this study also agreed that currently the soya formulas have been fortified and therefore, the risk for cross-reaction is reduced (Dai et al, 2017).

In terms of growth and development, the survey showed that over 70% of both pediatricians and midwives agreed that soya formula has a comparable outcome with cow’s milk (Setiabudiawan et al, 2021) observed that the weight, height, and head circumference of children with CMA for six months and found that those who consumed soya formulas also had a normal pattern of growth. Though there are concerns concerning sexual development. No evidence had been proven that soy formula could induce sexual development disorders (Vandenplas et al, 2014) did a review on the safety of soya formula and found no significant difference in terms of reproductive function in children who consumed soya-based compared with cow’s milk formula. In our study, both pediatricians and midwives had no concern about the children's growth and development if they consumed soya formula for the long term.

There are some concerns related to the composition of the soy formula. Phytoestrogens are present in large amounts in the soya formula and are suspected to have a role in the development of

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reproductive health (Verduci et al, 2020). Up until now, there is not enough evidence to prove the above statement. At present, soy formulas have been supplemented with amino acids, such as methionine, taurine, and carnitine. Previously, there was concern with phytate, one of the components in the soy formula, as it might prevent the absorption of micronutrients. However, phytate, nowadays, has been eliminated in the soy formula (Fiocchi et al, 2022).

One of the flaws in our work was that the data collection was performed via online in which it might be difficult to reduce the respondent’s subjectivity. In addition, the interviews were performed merely on the pediatricians. The response rate for in-depth interviews was very low due to schedule clash with the prospective respondents.

CONCLUSION

We conclude that gaps still exist in the knowledge and practices of pediatricians and midwives about the management of CMA. Education to improve awareness on the use of practice guidelines to treat CMA for midwives should be proposed. Whilst evidence to use soya formula as an alternative to hypoallergenic formulas should be shared among health professionals to understand the safety and potential side effects of soya formula. Further research to obtain evidence on the long-term effects should be encouraged.

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