

## Cow's milk allergy in patients with diarrhea

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### ABSTRACT

**Background** Cow's milk allergy (CMA) might be one of the causes of diarrhea in children. Previous prospective studies found the prevalence of CMA in children aged 0-3 years between 1.1-5.2%, but data about the prevalence of CMA in children with diarrhea was very limited.

**Objective** This study intended to estimate the prevalence of CMA in children with diarrhea.

**Methods** Children aged 0-3 years, who came with diarrhea and consumed milk formula were selected for further evaluation. A diagnostic procedure was developed i.e., elimination diet with partially hydrolyzed formula (pHF) for 2 weeks, and then open milk challenge. If diarrhea was not resolved with pHF, the children were given extensively hydrolyzed formula, or soy-based formula.

**Results** Ninety-nine children participated in this study, 87 came with acute diarrhea and 12 with chronic diarrhea. There were 3 children (2 children with acute diarrhea and one with chronic diarrhea) who reacted to the milk challenge.

**Conclusion** The estimated prevalence of CMA in children with diarrhea in our study was 3% [Paediatr Indones 2004;44:239-242].

**Keywords:** cow's milk allergy, diarrhea, partially hydrolyzed formula, extensively hydrolyzed formula.

Diarrhea is still a major health problem in Indonesia, especially in children below 5 years. One of the causes might be adverse reactions to food.<sup>1,2</sup> Food allergy and intolerance are common among them, and cow's milk allergy (CMA) is the most prevalent food allergy as a result of an abnormal immunologic reaction to cow's milk protein.<sup>3-5</sup> Based on several prospective-population based study, the prevalence of CMA in children aged 0-3 years varies between 1.1-5.2%.<sup>6-9</sup> The gastrointestinal symptoms, including diarrhea, occur in 50-60% of children with CMA,<sup>6,10</sup> but there was no data on the prevalence of CMA in children

with diarrhea. The purpose of this study was to estimate the prevalence and the possible risk factors of CMA in children with diarrhea.

### Methods

This was a descriptive cross sectional study conducted at the Department of Child Health Cipto Mangunkusumo General Hospital. The sample size was calculated with 95% confidence interval and a proportion of 50% since there was no data on the prevalence of CMA in patients with diarrhea. Patients aged 0-3-years, who came with complaint of diarrhea and consumed standard or soy-based formula, were included in the study. Patients with major congenital anomaly or malignancy of the gastrointestinal tract were excluded. After informed consent was obtained, the parents were interviewed with a questionnaire concerning the onset, frequency of diarrhea, other symptoms, other atopic diseases, diet, and family history of atopic diseases.

Patients' previous formula was changed to partially hydrolyzed formula (pHF: Nan HA<sup>®</sup>, Nestlé) for 2 weeks. If the diarrhea did not subside, pHF was replaced with either extensively hydrolyzed for-

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mula (eHF: Pepti-Junior®, Nutricia), soy-based formula, or exclusive breastfeeding for another 2 weeks. If the patient was still breastfed, the mother was advised to avoid CM in her diet.

By then if diarrhea resolved, an open challenge was performed. The challenge was started with one drop of standard formula (SF). After that SF was given in incremental quantities of 5, 10, 20, 30, 60, and 90 ml at intervals 10 to 30 minutes. The parents were asked to record all adverse symptoms occurring within 24 hours after challenge. If no adverse reaction occurred in 24 hours, the challenge was considered negative (Figure 1). The challenge was considered positive if 1 or more of the following symptoms appeared i.e., urticaria, exanthema, angioedema, diarrhea, vomiting, abdominal pain/ colic, wheezing or allergic rhinitis. This study was approved by the Medical Ethics Committee of Cipto Mangunkusumo General Hospital, Jakarta.

## Results

A hundred infants and children with mean age of 13.2 months (1-34 months), were enrolled in this study. Eighty-eight patients came with acute diarrhea and 12 with chronic diarrhea (Table 1). The challenge was performed in only 99 patients. One patient developed urticaria, followed by severe vomiting in 15 minutes after ingesting 30 ml of pHF, and 30 minutes later she had diarrhea. We considered her to have gastrointestinal anaphylaxis, and the cow's milk challenge was omitted. Though the patient clinically had CMA, we excluded her from this study for not fulfilling our diagnostic procedure.

Two of 87 patients with acute diarrhea and one of 12 patients with chronic diarrhea (Table 1 and 2) showed positive reaction to milk challenge. The prevalence of CMA in patients with diarrhea found in this study was 3%.

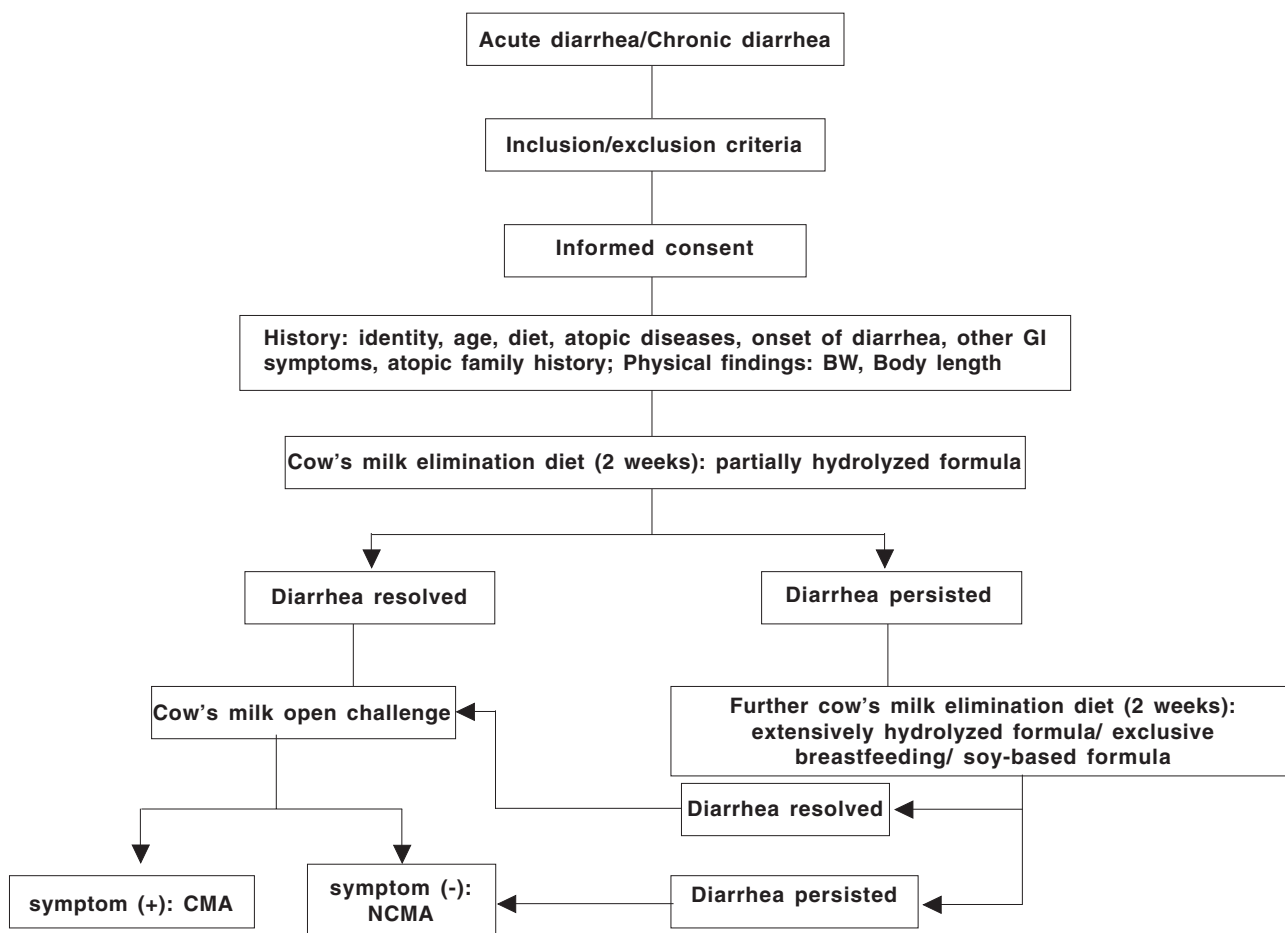


FIGURE 1. STEPWISE DIAGNOSTIC PROCEDURE OF CMA (CMA: COW'S MILK ALLERGY; NCMA: NO COW'S MILK ALLERGY)

**TABLE 1.** CHARACTERISTICS OF PATIENTS WITH DIARRHEA

Characteristics	CMA	NCMA	Total
▪ Acute diarrhea	2	85	87
▪ Chronic diarrhea	1	11	12
Mean age (range: months)	20.3 (10-30)	13.0(1-34)	13.6 (1-34)
▪ <4 months	0	7	7
▪ 4-12 months	1	51	52
▪ >12 months	2	38	40
Sex			
▪ Male	2	65	67
▪ Female	1	31	32

After elimination diet with pHF, diarrhea did not subside in six patients (Table 2). The cow's milk elimination was continued by giving eHF in 4 patients, soy-based formula in 1 patient and breast milk in 1 patient for 2 weeks. All of them showed improvement on the elimination diet and one patient developed reaction after milk challenge. In 93 patients, diarrhea improved with pHF and 2 of them reacted to the milk challenge (Table 2). The only clinical reaction was diarrhea, which developed in 45 minutes to 20 hours after challenge. No other type of reaction occurred.

Nineteen parents suggested that their children's diarrhea was due to adverse reaction to milk. Only one parental-perceived reaction was confirmed by the milk challenge.

All of the affected patients had family history of atopic diseases. None of them had other clinical manifestations of atopic diseases.

## Discussion

Formulas based on partially hydrolyzed cow's milk proteins have 1,000-100,000 times higher concentration of intact cow's milk proteins compared with eHF. About 50% patients with CMA may show reaction to pHF, while at least 90% of these children tolerate eHF.<sup>11,12</sup> The limitation of this study was that we used pHF in the first step of elimination diet. One patient reacted severely to this formula, and diarrhea of one CMA patient did not resolved.

Until now, as far as we know, there was no data on the prevalence of CMA in patients with diarrhea. The estimated prevalence of CMA in patients with diarrhea in our study was 3%.

**TABLE 2.** RESULTS OF ELIMINATION AND CHALLENGE TEST IN PATIENTS WITH DIARRHEA

Elimination	Acute diarrhea		Chronic diarrhea	
	Challenge +	Challenge -	Challenge +	Challenge -
Diarrhea resolved	1	80	1	11
Diarrhea not resolved*	1	5	0	0
<b>Total</b>	<b>2</b>	<b>85</b>	<b>1</b>	<b>11</b>

\*Diarrhea did not resolved with pHF, but after having eHF/ soy formula or breast milk as elimination diet, diarrhea resolved

Diagnosis of CMA could be established in two patients whose diarrhea resolved with pHF. But in one patient, whose diarrhea did not disappear with this formula and got eHF instead as CM elimination diet, diagnosis of CM intolerance could not be excluded. So the diagnosis of this patient was cow's milk allergy/intolerance.

Symptoms suggestive of CMA may be encountered in approximately 5-15% of infants, while the incidence of CMA in infancy seemed only to be approximately 2-3%.<sup>13</sup> Our study demonstrated that only one of 19 parentally reported reactions to milk was confirmed by elimination-milk challenge procedure. This emphasized the importance of elimination-milk challenge so that an unnecessary diet restriction can be avoided.

We concluded that the prevalence of CMA in patients with diarrhea was 3%. Unfortunately, we could not make any conclusion about risk factors of CMA in patients with diarrhea, because the number of affected patients was too small.

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