



The role of elimination diet in reducing allergy symptoms and improving cow's milk protein tolerance in children



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ABSTRACT

Cow's milk allergy (CMA) is an adverse immunological response to cow's milk proteins, primarily involving immunoglobulin E (IgE)-mediated type I hypersensitivity reactions, although non-IgE-mediated and mixed responses may also occur. In Indonesia, CMA represents the second most common food allergy, with a prevalence of 2–7.5%, and allergic responses have been reported in up to 0.5% of exclusively breastfed infants. This condition poses significant health concerns in children, with symptoms affecting the gastrointestinal tract (50–70%), skin (50–60%), and respiratory system (20–30%), and may lead to growth failure due to inadequate nutritional intake if not properly managed. This literature review aims to examine the role of an elimination diet in reducing allergy symptoms and improving tolerance to cow's milk protein in children. Literature was retrieved from international databases, including PubMed, Google Scholar, and ScienceDirect, restricted to articles published between 2013 and 2023 in English and Indonesian. The review found that an elimination diet—defined as the strict avoidance of all cow's milk and its derivatives—is the primary management strategy for CMA. Its effectiveness is influenced by diagnostic accuracy, parental adherence, and appropriate nutritional substitution. Gradual reintroduction of cow's milk protein under medical supervision may promote immune tolerance over time. However, an elimination diet carries potential contraindications and nutritional risks that must be carefully monitored. In conclusion, an elimination diet, when properly implemented with adequate nutritional support, can effectively reduce CMA symptoms and facilitate tolerance development in affected children.

Keywords: cow's milk allergy, elimination diet, hypersensitivity, pediatrics.

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INTRODUCTION

Cow's milk allergy (CMA) is an undesirable immunological reaction to cow's milk proteins.¹ In general, CMA involves a type I hypersensitivity reaction mediated by immunoglobulin E (IgE), although it may also be triggered by non-IgE-mediated immunological responses or a combination of both.^{2,7} In Indonesia, cow's milk allergy is the second most prevalent food allergy, with a prevalence of approximately 2–7.5%, and allergic responses have been reported in up to 0.5% of exclusively breastfed infants.^{1,3,21}

Cow's milk allergy poses a serious concern, particularly in children, necessitating appropriate and timely interventions to manage this condition effectively. Male children carry approximately twice the risk of

developing CMA compared to their female counterparts, while in adults, approximately 80% of CMA cases occur in women. Individuals with a family history of atopic conditions—including atopic dermatitis, asthma, and allergic rhinitis—also face an elevated risk of developing CMA.^{2,7}

Clinical manifestations of CMA typically emerge within the first month of life and within one week of cow's milk protein ingestion, generally involving symptoms across two or more organ systems.^{1,6} Common manifestations include gastrointestinal symptoms (50–70%), cutaneous symptoms (50–60%), and respiratory symptoms (20–30%).⁶ Based on the onset of reaction, symptoms may appear within one hour (immediate reaction) or after one hour (delayed reaction) following the ingestion of cow's

milk protein.^{1,3}

Given the broad spectrum of symptoms associated with CMA, prompt and comprehensive management is critical. Treatment should be initiated as soon as a diagnosis is established, to prevent potential growth failure resulting from inadequate nutritional intake in children.^{4,5} The fundamental principle of CMA management is elimination diet—the avoidance of all cow's milk products and their derivatives while maintaining a balanced diet sufficient to support the growth and development of the child and, where applicable, the breastfeeding mother.^{4,10,11} In addition to dietary management, acute CMA cases may require pharmacological intervention, including H1-receptor antagonists (antihistamines) or epinephrine injections in severe cases.^{8,9}

Prior research has demonstrated that elimination diet is an effective strategy for reducing allergy symptoms and improving cow's milk protein tolerance in children by protecting the body from allergen exposure that triggers immunological responses.¹² Elimination diet is thought to target the adaptive immune system by suppressing antigen-driven T-cell responses.^{13,15} The effectiveness of elimination diet is closely linked to the provision of adequate caloric and nutritional intake, which is essential to the success of CMA management. Accordingly, this study aims to examine the role of elimination diet in reducing allergy symptoms and improving cow's milk protein tolerance in children.

METHODS

This study employed a literature review methodology. Keywords used in the literature search included cow's milk allergy, elimination diet, IgE, and type I hypersensitivity reaction, combined using Boolean operators ("AND" and "OR") to retrieve relevant literature from international journal databases including PubMed, Google Scholar, and ScienceDirect. Retrieved data were subsequently organized according to predefined inclusion and exclusion criteria. Inclusion criteria were as follows: (1) articles or journals published between 2013 and 2023; (2) written in English or Indonesian; (3) available in full text; and (4) addressing cow's milk protein allergy and elimination diet. Exclusion criteria included articles or journals published more than ten years prior to the review period and articles accessible only through paid access.

RESULTS

Pathogenesis of Cow's Milk Allergy **Role of Immunoglobulin E (IgE)**

The failure to develop tolerance to a particular food antigen stimulates the production of immunoglobulin E (IgE). IgE binds to receptors present on mast cells, basophils, macrophages, monocytes, lymphocytes, eosinophils, and platelets, albeit with relatively low affinity. Binding of IgE to food allergens leads to the release of mediators including histamine, prostaglandins, and leukotrienes. This

release induces vasodilation, smooth muscle contraction, and mucus secretion, culminating in a type I hypersensitivity reaction. Concurrently, activated mast cells release cytokines that further amplify this reaction. Upon repeated allergen exposure, mononuclear cells are stimulated to release histamine, a process that is particularly prominent in individuals with atopic dermatitis.^{24,25}

Role of Non-IgE-Mediated Mechanisms

Unlike IgE-mediated food allergies, symptoms of non-IgE-mediated food hypersensitivity are typically delayed by several hours to several weeks following ingestion of the causative food.²⁶ Moreover, compared to IgE-mediated food allergy, the diagnosis of non-IgE-mediated food hypersensitivity syndromes can be challenging due to the absence of non-invasive confirmatory tests for most of these disorders.²⁷

Several immune mechanisms beyond type I hypersensitivity have been proposed as potential contributors to food allergy. However, the available scientific evidence remains limited. Some studies suggest that type III hypersensitivity reactions may play a role, yet supporting evidence for food-antigen immune complex disease is sparse. Similarly, type IV hypersensitivity reactions—occurring several hours after

exposure—have been implicated, though definitive evidence remains insufficient.²⁵

Diagnosis and Management of Cow's Milk Allergy

IgE-mediated CMA can be diagnosed by evaluating clinical symptoms and performing specific IgE tests, such as the skin prick test or radioallergosorbent test (RAST).²³ A positive result on specific IgE testing indicates elevated IgE levels against cow's milk proteins. Avoidance of cow's milk protein-containing foods is the subsequent step upon a positive specific IgE test result. To establish a definitive diagnosis, elimination and provocation challenges may be performed.²³

The diagnostic approach for non-IgE-mediated CMA involves a comprehensive evaluation of the patient's allergy history in relation to cow's milk protein ingestion, followed by an elimination diet, an oral food challenge, and, if necessary, additional investigations such as endoscopy and biopsy.²³

For breastfed infants, a diagnostic approach may be initiated through maternal elimination of cow's milk protein from the diet for a period of two to four weeks.⁵ If symptoms resolve, the mother may resume cow's milk protein intake; however, if symptoms recur upon reintroduction, an allergic diagnosis is

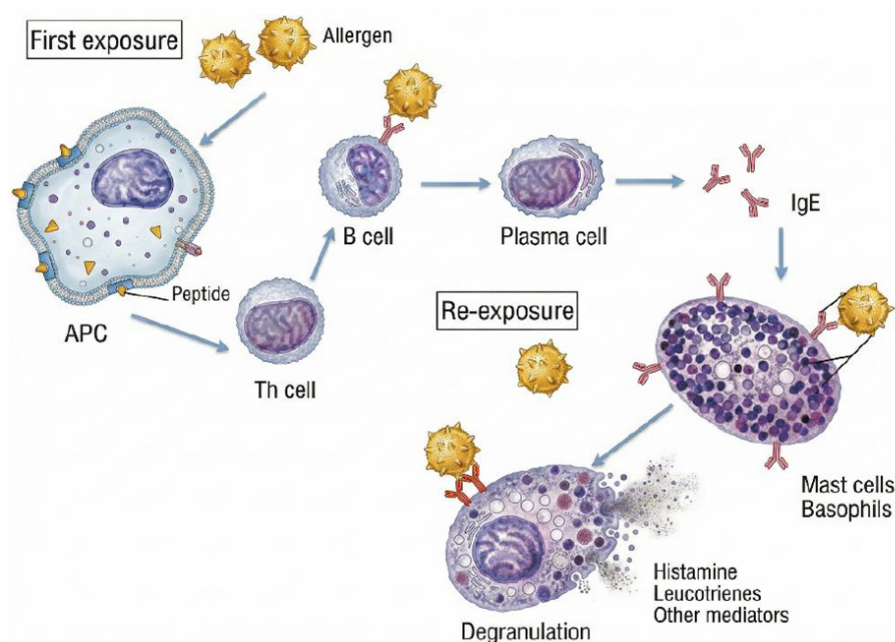


Figure 1. Schematic diagram illustrating the type I hypersensitivity reaction

Table 1. Classification of hypersensitivity reactions by immunological mechanism

Reaction Type	Mechanism	Clinical Manifestations	Time of Reaction
Type I	IgE-mediated immunological reaction. IgE complexes bind to mast cells and trigger histamine release	Urticaria, angioedema, bronchospasm, anaphylaxis	Minutes to hours after exposure
Type II	Cytotoxic reaction mediated by IgG or IgM	Hemolytic anemia, neutropenia, thrombocytopenia	Variable
Type III	Immune complex reaction. Tissue deposition of antibody complexes with complement activation	Vasculitis, lymphadenopathy, fever, arthropathy, rash, serum sickness	1–3 weeks after exposure
Type IV	Delayed-type reaction. Cell-mediated (T-cell) with cytokine release	Allergic contact dermatitis	2–7 days after exposure

considered confirmed. If the elimination period yields no clinical improvement, alternative diagnoses should be considered.⁵

For formula-fed infants, the diagnostic process involves substituting standard infant formula with a cow's milk protein-free alternative. Options include extensively hydrolyzed formula for infants with mild to moderate clinical symptoms, or amino acid-based formula for those with severe manifestations.⁵

Clinical Manifestations of Cow's Milk Allergy

Cow's milk allergy does not present with a single pathognomonic symptom. CMA can produce a range of systemic symptoms affecting the gastrointestinal tract, including pruritus and swelling of the lips, nausea, vomiting, and more severe digestive complications such as hematochezia.⁵ The most prominent manifestations involve gastrointestinal problems (50–60%), cutaneous problems (50–60%), and respiratory problems (20–30%).²³ The severity of these symptoms varies considerably depending on the degree of allergy and the individual's immune response to cow's milk protein exposure.

Atopic dermatitis is the most frequently encountered cutaneous manifestation of CMA, second only to gastrointestinal symptoms.⁵ Acute urticaria and angioedema may also be triggered by an allergic reaction to cow's milk proteins. Urticaria is characterized by pruritic wheals and skin swelling, while angioedema results in swelling of the deeper skin layers, particularly in areas such as the hands, lips, or eyelids.⁵

Food allergy-associated asthma is a notable health concern among young

children and is often closely associated with atopic dermatitis.⁵ In these patients, symptoms affect not only the skin but also the respiratory tract. Respiratory manifestations may include stridor or wheezing, persistent cough, rhinitis, and dyspnea. These symptoms can vary considerably in severity, ranging from mild to severe.⁵

Classification of Cow's Milk Allergy

Cow's milk allergy is classified into two main categories: IgE-mediated and non-IgE-mediated.²³ IgE-mediated CMA involves an immune response regulated by IgE antibodies, with clinical symptoms typically appearing within 30 minutes to one hour following ingestion of cow's milk protein. Clinical manifestations may include skin rash, cutaneous swelling, atopic dermatitis, vomiting, abdominal pain, and diarrhea.²³

Non-IgE-mediated CMA is mediated primarily by IgG rather than IgE and is characterized by a delayed onset of clinical symptoms, typically occurring more than one hour after cow's milk protein ingestion. Clinical manifestations of non-IgE-mediated CMA may include infantile colic, enterocolitis, anemia, and growth failure.²³

Role of Elimination Diet in Reducing Allergy Risk

The primary therapeutic approach for food allergy is the strict avoidance of allergenic foods. Dietary restrictions must be tailored to meet each patient's nutritional requirements. Patients should be educated on safely avoiding allergens, including familiarity with common ingredient terminology and the ability to interpret food labels. Information regarding safe, cost-effective, and widely available food

substitutes should be provided for foods that are eliminated. Patients should be periodically reassessed to determine whether they have developed tolerance.²⁸

Breastfeeding mothers of infants with CMA should be supported and encouraged to continue breastfeeding. Partially hydrolyzed infant formula, which is not hypoallergenic, is not recommended for the treatment of CMA, although it may have a role in preventing eczema in high-risk individuals. Certain extensively hydrolyzed formulas and amino acid-based formulas are considered truly hypoallergenic.²⁸

For infants who are not breastfed and present with mild to moderate CMA, extensively hydrolyzed cow's milk formula is the preferred dietary management option. For non-breastfed infants and children with severe CMA, amino acid-based formula is recommended. Soy-based formula may be appropriate for IgE-mediated CMA with confirmed soy tolerance, and for some mild to moderate non-IgE-mediated CMA cases, given the increased risk of co-reactivity between CMA and soy allergy in non-IgE-mediated conditions. Other mammalian milks and plant-based alternatives—including rice and oat milk—are not suitable as sole nutritional sources for infants with CMA.²⁹

Elimination Diet Can Improve Cow's Milk Protein Tolerance

Elimination diet is the cornerstone of CMA management, involving the strict avoidance of all cow's milk products from the daily diet.⁴ Through this approach, exposure to cow's milk proteins is reduced, thereby decreasing the immune response to milk protein and facilitating the gradual development of tolerance.¹⁶

Over time, gradual reintroduction of cow's milk protein can reduce immune system reactivity and enable better-controlled immune responses.^{17,18} Therefore, elimination diet not only reduces CMA symptoms but also contributes to improving the body's tolerance to cow's milk protein. The development of tolerance is influenced by the type of CMA, with tolerance developing more slowly in IgE-mediated compared to non-IgE-mediated CMA.¹⁷

Factors Affecting the Effectiveness of Elimination Diet

Several factors may influence the effectiveness of elimination diet in managing CMA. Accurate diagnosis is the critical first step in ensuring that the elimination diet is genuinely indicated and appropriate for the health condition of the child or breastfeeding mother.¹⁹ Furthermore, adherence to the elimination diet is important; parental understanding, social support, and psychological well-being are significant determinants of consistent dietary implementation in both children and breastfeeding mothers.²¹

Selection of appropriate dietary substitutes is also an important consideration in supporting the success of the elimination diet. Adequate nutritional intake must be ensured, and consultation with a registered dietitian or nutritionist can assist in designing an elimination diet that meets the nutritional needs of both the child and the breastfeeding mother.²⁰ Involving both parents in elimination diet planning and providing consistent support can enhance the overall effectiveness of the intervention.²¹

Contraindications and Side Effects of Elimination Diet

Elimination diet is one of the primary management strategies for cow's milk protein allergy (CMA). Its aim is to eliminate exposure to cow's milk protein so that allergic symptoms may improve or resolve. Elimination diet is contraindicated in patients with malnutrition, growth disorders, metabolic disorders, hepatic or renal disease, cardiac disease, or diabetes, as it may precipitate adverse effects in these conditions.⁵

The most common adverse effect of elimination diet is nutritional deficiency.

This is because cow's milk is a primary source of protein, calcium, vitamins, and minerals. Therefore, patients undergoing elimination diet must obtain these nutrients from alternative food sources. Other potential side effects include gastrointestinal disturbances (such as diarrhea, constipation, and nausea), impaired growth and development, and psychological disturbances, including depression and anxiety.²⁹

CONCLUSION

Cow's milk allergy (CMA) is an adverse immunological response to cow's milk proteins that may manifest as symptoms affecting the gastrointestinal, cutaneous, and respiratory systems, and may ultimately lead to growth failure due to inadequate nutritional intake if not properly addressed. The primary management approach for CMA is elimination diet—the strict avoidance of all cow's milk products from the daily diet—which aims to reduce the body's immune response to milk proteins and thereby alleviate allergic symptoms, improve quality of life, and support the gradual development of immune tolerance. Dietary restrictions must be individualized to ensure that adequate nutritional needs are met throughout the management period. In practice, elimination diet should be guided by a physician or registered dietitian with expertise in pediatric nutrition and food allergy. Prior to initiating an elimination diet, children with CMA are recommended to undergo an oral food challenge to determine their degree of tolerance to cow's milk protein. Further research is warranted to establish the optimal duration of elimination diet, evaluate its long-term impact on quality of life, and develop more precise clinical guidelines for its implementation in the pediatric population.

CONFLICT OF INTEREST

All authors declared that there is no conflict of interest regarding this article.

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AUTHOR'S CONTRIBUTION

All authors contributed equally in the writing process of this article.

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