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The link between food allergy and atopic dermatitis

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Abstract

Food allergy (FA) is an abnormal or exaggerated specific immune response that occurs repeatedly when exposed to certain foods. The relationship between food allergies and AD is still much debated today. Some evidence supports that AD can play a role as a predisposing factor for food allergies and conversely, food allergens are also suspected as one of the triggers of AD exacerbations. Role of diet in the cause and treatment of AD is controversial and is not well-defined. Food elimination diets in food allergic cases may have a beneficial effect on AD morbidity, however prolonged diets can lead to loss of tolerance and potentially increase the risk of IgE-mediated food allergy. Emollient treatment, hidrolized formulas, vitamin D, early introduction of food allergens appears to be a promising strategy for minimizing the public health burden of food allergy in AD, though further studies of this approach is needed.

Keywords: Food Allergy; Food Sensitization; Food Elimination; Atopic Dermatitis.

1. Introduction

The term atopy originates from the Greek word "atopos," meaning "without place," which reflects the underlying mysterious pathogenesis of hypersensitivity allergic diseases. Atopy refers to a genetic predisposition to develop allergic-related conditions such as asthma, dermatitis, food allergies, or rhinitis. Food allergy (FA) itself is defined as an immune reaction to proteins in food, which can be mediated by IgE or non-IgE mechanisms. While any food can trigger an allergy, only a few foods overall are responsible for the majority of allergies. Based on data from a survey by the World Allergy Organization involving 89 countries, the prevalence of food allergy and food sensitivity in infants and preschool-age children is around 2.5-10%, and it ranges from 10-15% in older age groups [1,2,4,5].

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by recurrent flares of itching and eczematous skin lesions. Both AD and FA are associated with an exaggerated immune response to allergens and the production of specific immunoglobulin E (IgE). The pathogenesis of both diseases is complex and multifactorial, involving the skin barrier, microbiome, and immune system [1,6].

Global data indicates that over the past few decades, there has been an increase in the frequency of food allergies and atopic dermatitis. Atopic dermatitis ranks as the third most common dermatological condition (2.79%) compared to other common skin diseases and contributed the most to disability-adjusted life years (DALYs) for skin diseases (0.36%) in 2017. The morbidity caused by atopic dermatitis and food allergies impacts the quality of life, including physical, social, and psychological well-being. Moreover, food allergies can also lead to life-threatening conditions [4,7,8,9].

Numerous studies have been conducted to understand the relationship between these two conditions. For over a decade, the connection between atopic dermatitis, food allergies, asthma, and rhinitis has been referred to as the "atopic march." Around 60% of children who develop atopic dermatitis in their first year of life will subsequently develop food allergies. Some studies indicate that food allergies play a significant role in exacerbating or worsening atopic dermatitis,

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and dietary elimination can reduce its severity. On the other hand, some research suggests that atopic dermatitis is involved in the causal pathway leading to food allergies [9,10,11,12].

Based on these conditions, this literature will further discuss the relationship between atopic dermatitis and food allergies, their respective pathomechanisms, and whether food allergy interventions contribute to the clinical course of atopic dermatitis and vice versa.

2. Material and Methods

This is a literature review obtained from a collection of 39 references, consisting of 38 international journals searched using database search engines (Google, google scholar) and 1 textbook. The process for literature review started form finding journals by keyword food allergy, food sensitization, food elimination, atopic dermatitis, relationship between food allergy and atopic dermatitis, and how to reduce the risk of food allergy to be atopic dermatitis. Data in this study will be collected and analyzed for finding definition food sensitization, pathophysiology food allergy can lead to atopic dermatitis, risk factor that cause food allergies to be atopic dermatitis, and how to prevent it.

3. Literature Review

This literature review was organized into five subtopics. The first subtopic discussed how food allergies are initiated by food sensitization the second subtopic the relationship between food allergy and atopic dermatitis, The third subtopic explain about establish the diagnosis of AD, the fourth subtopic describe about diet elimination and the risk, and the last subtopic the strategy of prevention food allergy in patients with AD

3.1. How Food Allergies are Initiated by Food Sensitization

Food sensitization refers to the initial immune response triggered when allergens enter the body. There are two pathways for allergic sensitization: oral allergens, which sensitize through the digestive tract, and aeroallergens, which sensitize through the respiratory tract. Initial sensitization leads to memory T cells and memory IgE production, intensified by repeated allergen exposure (secondary immune response). Non-allergic individuals produce specific IgG and IgA upon allergen exposure, while atopic individuals prone to IgE-related allergies process allergens through APCs and Th2 cells, inducing cytokine production (e.g., IL-4, IL-13) and IgE class switching [13].

According to the National Institute of Allergy and Infectious Diseases, food allergy, as defined as involves adverse health effects from abnormal immune responses upon repeated exposure to specific foods. It can affect the skin, digestion, respiration, cardiovascular system, and more. The World Allergy Organization notes an increasing prevalence of food allergies in developed countries, affecting 10% of preschool-age children [14].

Barriers such as skin, nasal mucosa, respiratory tract, and gastrointestinal mucosa separate the environment from internal tissues. Barrier damage, immature immune systems, and T cell dysfunction can lead to ineffective oral and immunological tolerance, resulting in IgE-mediated allergic reactions or non-IgE-mediated disorders. Oral tolerance, a physiological response to ingested antigens, develops in the digestive tract, where gut-associated lymphoid tissue helps limit inflammation caused by bacteria and food proteins [17].

Gastrointestinal cells (microfold cells, intestinal epithelium, dendritic cells) play key roles in antigen presentation, inducing and maintaining food antigen tolerance, and processing food proteins. Dendritic cells migrate to mesenteric lymph nodes, presenting antigens via MHC class II, activating effector T cells. Antigen-specific regulatory T cells (Treg) are influenced by the local microbiome, activating immune response regulation through cytokine production. Disruption of food tolerance arises from epithelial barrier damage due to factors like pathogen-associated molecular patterns (PAMPs), leading to inflammation and the differentiation of naive T cells into Th2 cells. This process induces class switching of food antigen-specific B cells and IgE production [17].

Food allergen sensitization can occur via the digestive tract, skin, and rarely, the respiratory tract, often involving inflammation and barrier dysfunction. After sensitization, re-exposure to the food antigen can cause local or systemic manifestations. Specific IgE binds to high-affinity receptors (FcεRI) on mast cells and basophils upon re-contact, leading to degranulation and the release of chemical mediators causing local and systemic symptoms [16,17].

3.2. The Food Allergy and Atopic Dermatitis.

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by recurring flares of itching and eczematous skin lesions. The term "eczema" refers to the cutaneous manifestations of this condition. Acute eczematous lesions are characterized by erythematous papulovesicles, often with crusting or oozing, while subacute to chronic lesions show scaling, excoriation, and lichenification. The disease affects up to 2.4% of the global population, with prevalence varying widely between countries. The Global Burden of Disease Study 2019 (GBD 2019) estimated that in 2019, there were 171.17 million individuals worldwide affected by AD, resulting in an estimated 7.48 million Years Lived with Disability (YLDs) [14].

Atopic dermatitis is a complex and multifactorial disease. It appears to result from a complex interplay between defects in skin barrier function, immune dysregulation, environmental agents, and infections. Various triggers for atopic dermatitis have been identified in recent decades, including inhaled respiratory allergens, food allergens, irritants, and infectious microorganisms such as Staphylococcus aureus and Malassezia furfur. T cells mediate a significant portion of hypersensitivity reactions in atopic dermatitis [19].

Skin barrier abnormalities are associated with mutations or disruptions in the expression of the filaggrin gene, which encodes a structural protein crucial for skin barrier formation. Individuals with atopic dermatitic have been shown to lack ceramides (lipid molecules) and antimicrobial peptides like cathelicidins, which act as the first line of defense against infection. These barrier defects lead to increased transepidermal water loss and enhanced penetration of allergens and microbes into the skin. The most common infectious agent involved in atopic dermatitis is Staphylococcus aureus (S. aureus), which colonizes about 90% of atopic dermatitis patients. Impaired innate immune responses also contribute to increased bacterial and viral infections in atopic dermatitis patients. These factors interact to induce a T-cell response in the skin (initially a dominant Th2 response, later shifting to a dominant Th1 response), releasing pro-inflammatory chemokines and cytokines (such as IL-4, IL-5, IL-13, and tumor necrosis factor), leading to B-cell production of immunoglobulin E (IgE) and systemic inflammation causing skin inflammation and pruritus [20].

Atopic dermatitis has been considered an early stage in the "atopic march," where there is a chronological development of allergic conditions progressing to food allergies, allergic rhinitis, and asthma. Thus, atopic dermatitis is often associated with sensitization to environmental and food allergens, as well as IgE-mediated food allergies, as demonstrated by food challenge tests in about a third of moderate to severe atopic dermatitis patients [21].

3.2.1. The Role of Food Allergy in Atopic Dermatitis Exacerbation.

Food allergies commonly occur in children with atopic dermatitis (AD), ranging from 20% to 80%. Approximately 40% to 80% of AD patients have elevated specific IgE levels to foods. The presence of specific IgE and aeroallergens is associated with early onset and more severe atopic dermatitis. Higher IgE levels and early increases are linked to the likelihood of developing more severe and persistent atopic dermatitis [22].

The first documented report of food allergy as a trigger factor for AD was by Schloss in 1915, describing eczema eruptions as a response to food, with improvement upon elimination. Burks et al (1988), in two studies involving severe AD patients referred to an allergy clinic, found that 33-38.7% of children undergoing DBPCFC (double-blind placebo-controlled food challenge) reacted to food. Sampson and Scanlon (1989), in a 4-year prospective study investigating the follow-up of 34 children using elimination diets guided by DBPCFC, discovered that 17 out of 34 children improved on the diet. As confirmed through multiple studies, cow's milk, chicken eggs, wheat, soy, and peanuts are responsible for 75% of food-related AD cases [17].

In atopic dermatitis, food factors are more likely to cause exacerbations in infants or children with moderate to severe AD compared to other populations. Food can trigger hypersensitivity reactions mediated by IgE or lead to advanced eczematous reactions. Food-triggered AD exacerbations occur in about one-third of infants, 5% of toddlers, and 10% of older children, but are rare in adults. When the clinical history indicates that the recurrence of AD occurs several hours to a few days after eating, reintroduction of the food can be carried out at home to confirm whether it indeed triggers a worsening of AD [23].

Atopic dermatitis exacerbation due to food occurs through increased binding of antigens to immature intestinal microvilli, heightened gut permeability initiating an immune response by altering antigen transfer. Pathogenic bacteria in the gut can also act as infectious agents and superantigens, thereby worsening AD through food. The immunologically relevant food antigens can enter circulation and distribute throughout the body, including the skin. Subsequently, they can directly interact with specific IgE, which binds to Fc receptors on Langerhans cells, mast cells, monocytes, and basophilic granulocytes, as well as on infiltrating T lymphocytes in the skin. Li et al.'s study (2001) in mice induced with

food-induced AD confirmed the crucial role of specific food-reactive T cells in AD. In this study, female C3H/HeJ mice were orally sensitized to cow's milk or peanuts and then exposed to low-level allergen exposure. An AD eruption developed in about one-third of the mice after low-level exposure to milk or peanut proteins. Histological examination of skin lesions revealed spongiosis and cellular infiltrates consisting of CD4+ lymphocytes, eosinophils, and mast cells. Expression of IL-5 and IL-13 mRNA only increased in the skin of mice with AD eruptions [4,19].

There are three patterns of skin reactions to food allergy in AD patients. First, immediate-type reactions occur minutes to 2 hours after exposure and can involve various systems such as skin, respiration, cardiovascular, and gastrointestinal system. Skin reaction of food allergy can include urticarial, angioedema, pruritus, eritema, morbiliform eruption, and contact urticarial. Second, pruritus occurs immediately after ingesting food, leading to scratching and AD exacerbation. Third, delayed hypersensitivity reactions mediated by T cells manifest symptoms 6 to 48 hours after exposure and exacerbate AD [5,19,22,24].

Clinical studies have documented food allergy prevalence in AD ranging from 20% to 80%. Common food allergens triggering AD include cow's milk, peanuts, eggs, soy, wheat, seafood, and shellfish. Raw food consumption and the effects of inherent food microbes on gut flora can influence food allergy development in AD. Exacerbation of AD by food involves increased antigen binding to immature microvilli, increased gut permeability, and immune responses altering antigen transfer [4].

3.2.2. The Role of Atopic Dermatitis in the Onset of Food Allergy.

Atopic dermatitis (AD) is proposed as a major risk factor for food sensitization and both IgE-mediated and non-IgE-mediated food allergies. Preventing or treating AD during infancy or childhood is hypothesized to potentially prevent the development of food allergies. This idea is reinforced by evidence suggesting that skin plays a role in sensitization pathways for both AD and food allergies. The progression from AD to other atopic diseases, including food allergies, is known as the "atopic march." [25].

The prevalence of food allergies is significantly higher in children with AD compared to healthy children. National Health Interview Survey data from the US indicates that food allergy prevalence in children with and without AD is 15.1% and 3.6% respectively. Population-based studies have shown that infants with AD have a 6-fold higher likelihood of food sensitization compared to healthy controls. Prevalence of food sensitization in AD reaches 66%, with confirmed food allergies through Oral Food Challenge (OFC) testing at 81% [21].

Several studies support the association of more severe AD phenotypes with a higher frequency of food allergy diagnosis, ranging from 33% to 39%. Some studies have reported the highest prevalence of food allergies in AD to be 80%, while its prevalence in the general population is estimated to be around 0.1-6%. Therefore, atopic dermatitis is proposed as a primary risk factor for food sensitization and IgE-mediated food allergies. The Danish Allergy Research Cohort (DARC) study indicated that there is up to a 53% occurrence of food sensitization in children with AD aged 6 months to 6 years, with 15% of them having food allergies. In the Health Nut study, research based on a large population in Australia involving 4,453 infants with AD showed that infants with AD are six times more likely to have egg allergies and eleven times more likely to have peanut allergies at 12 months of age compared to infants without AD at the same age [26].

A recent systematic review supports the association between early-onset atopic dermatitis (AD) and the development of food allergies. In another international multisite study involving a large cohort of children, Hill et al. (2008) demonstrated that the earlier the onset of AD, the higher the frequency of elevated IgE levels associated with food allergies, particularly milk, eggs, and peanuts. In fact, high levels of specific IgE for foods were found in infants whose eczema developed in the first three months (64%), and the lowest levels were observed in infants whose eczema developed after 12 months. A similar relationship was found between the severity of eczema and the results of specific IgE tests for food allergens [37].

In the dual-allergen hypothesis, exposure of food antigens to the skin is more likely to lead to allergy compared to early oral consumption, which tends to promote tolerance. Conceptually, oral exposure to peanut allergens leads to oral tolerance, while skin exposure without oral contact leads to allergy. Skin barrier disruption, often caused by atopic dermatitis, has long been associated with peanut allergy development. A study indicated a correlation between the severity of atopic dermatitis and specific IgE to peanuts. Two epithelial cytokines, TSLP and IL-33, are elevated in the skin of patients with atopic dermatitis and play a significant role in inflammation after allergen exposure. Food allergy is believed to result from a combination of skin and intestinal exposure to food antigens, with a higher tendency for sensitization if initial exposure occurs through the skin. There is no direct evidence that applying peanut protein to human skin, whether damaged or intact, directly leads to peanut allergy. However, research using a mouse model of

food allergy directly demonstrated that sensitization can occur through the skin. In this model, the stratum corneum was removed from the mice, and peanut protein was applied to the exposed area, resulting in the production of Th2 cytokines and serum IgE. Another study on mice with atopic dermatitis induced by skin stripping revealed a mechanism involving the expansion and activation of mast cells dependent on IL-33 in the gastrointestinal tract, indicating an interactive role between the skin barrier and the gut. Factors that disrupt immune tolerance through the skin, including skin barrier damage due to filaggrin mutations and microbes like Staphylococcus enterotoxin B, induce innate inflammatory responses on the skin that lead to sensitization. Further research on non-human primates, specifically African green monkeys, showed an increase in specific IgG to peanuts in serum, but not IgE levels, suggesting that peanut application to the skin triggers an immune response. Collectively, these studies also support the presence of sensitization through the transcutaneous pathway involving the key role of IL-33 [17].

Epidermal barrier dysfunction and transepidermal water loss (TEWL) serve as the foundation in the pathophysiology of atopic dermatitis preceding food allergy development. In a study using the Isle of Wight cohort (2014), loss-of-function mutations in filaggrin were linked to food sensitization in early years and later food allergies during childhood, underscoring the crucial role of skin barrier function in the development and persistence of food allergies. Skin barrier defects contribute to dehydration, persistent inflammation, and other clinical symptoms of atopic dermatitis. Environmental allergens, including food allergens, can breach the compromised skin barrier, potentially increasing food sensitization. Following penetration of food allergens, antigen-presenting cells (dendritic cells and Langerhans cells) expressing high-affinity IgE receptors bind invasive antigens that migrate to lymph nodes. Specific peptide epitopes (sometimes carbohydrate epitopes from allergen molecules) are further processed and presented to naïve CD4+ T cells. Within the lymph nodes, the presence of IL-4 and type 2 cytokines derived from endothelial cells or "alarmins" (mainly IL-33 and TSLP) leads to Th2 polarization and the development of specific CD4+ T cells producing substantial amounts of IL-4 and IL-13. Subsequently, class switching of IgE occurs, driving the production of specific IgE allergen (sIgEs) by mature plasma cells. Specific IgE binds high-affinity FcεRI receptors on the surfaces of mast cells and basophils, leading to food allergy upon subsequent allergen contact [26].
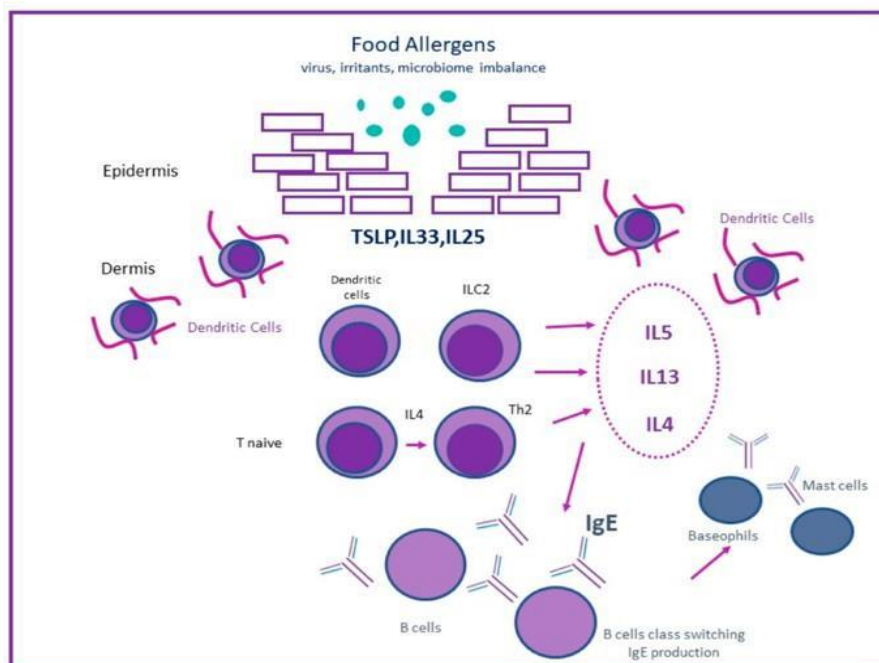

Figure 1 Penetration of food allergens through compromised skin barrier [26]. A damaged skin barrier can cause food allergens to easily penetrate into the skin, resulting in sensitization and triggering food allergies.

Skin microbiome dysbiosis plays a role in predisposing to impaired skin barrier function, epicutaneous sensitization, and food allergies. Up to 90% of patients with Atopic Dermatitis (AD) have colonization of Staphylococcus aureus on their skin, and pathogenic S. aureus is more common on AD skin compared to healthy controls. Abnormalities in the stratum corneum, including S. aureus colonization and microbiome dysbiosis, are believed to differentiate children with AD and food allergies from those with AD only, even on non-lesional skin. A study by Leung et al. (2020) showed that children with AD and food allergies (AD FA+) represent a unique endotype distinguishing them from AD without food allergies (AD FA−) and non-atopic controls (NA). There is a positive correlation between transepidermal water loss and

Staphylococcus aureus colonization on non-lesional skin in AD FA+ but not in AD FA− or NA. Filaggrin breakdown products on non-lesional skin of AD FA+ children are significantly lower compared to AD FA− and NA, indicating unique properties of the non-lesional stratum corneum in AD FA+ children. Furthermore, S. aureus superantigens can induce a strong immune response, activating non-specific T cells and downstream IgE-mediated inflammatory responses [19,26].

Several studies support the association between transepidermal water loss (TEWL) and early onset of atopic manifestations (FA) and dermatitis atopic. Research indicates that an increase in TEWL two days after birth serves as a predictor for allergy development by the age of two. Dysfunctional of neonatal skin barrier predicts FA at age 2, supporting the concept of transcutaneous allergen sensitization, even in infants without dermatitis. A study investigated the relationship between skin barrier function and FA in children. TEWL was measured during the neonatal period, at 2 months, and 6 months of life. Two-year-old children with food sensitivities (SPT+) underwent Oral Food Challenge (OFC). A total of 1,355 children were evaluated at the age of 2, with 1,260 undergoing skin prick tests and OFC screening. The results showed a prevalence of 6.27% for food sensitization and 4.45% for FA.[28]

Early oral exposure to food allergens leads to antigen recognition by antigen-presenting cells (APC) in the intestinal mucosa, inducing differentiation of naïve CD4+ T cells within the mesenteric lymph nodes into gut-associated 4β7+ T cells. These cells stimulate the production of Foxp3+ regulatory T cells (Treg) and cytokines IL10 and TGF-b, which exert immunoregulatory effects by promoting IgG4 antibody production and inhibiting Th2-dependent allergic responses. Consequently, early epicutaneous sensitization due to compromised skin integrity and concurrent loss of oral tolerance can lead to clinical food sensitization and allergies [26].

3.3. Diagnosis of Food Allergy in Atopic Dermatitis

Establishing diagnosis of atopic dermatitis can be made from history from patien then confirmed by clinical manifestation and diagnostic test. At history taken, examiner should ask about history of food and drug that patient consume and any symptoms after consume it, or history of patient family [24].

Recent paper on food allergy by the International Collaboration in Asthma, Allergy and Immunology, allergy testing should be considered in children: (1) AD with a history of an immediate allergic reaction to one or several foods; (2) moderate to severe AD under five years of age unresponsive to topical and other skin care treatments; (3) There are foods indicated by the patient or parents as persistent AD triggers (even without a history of direct allergic reactions) [27].
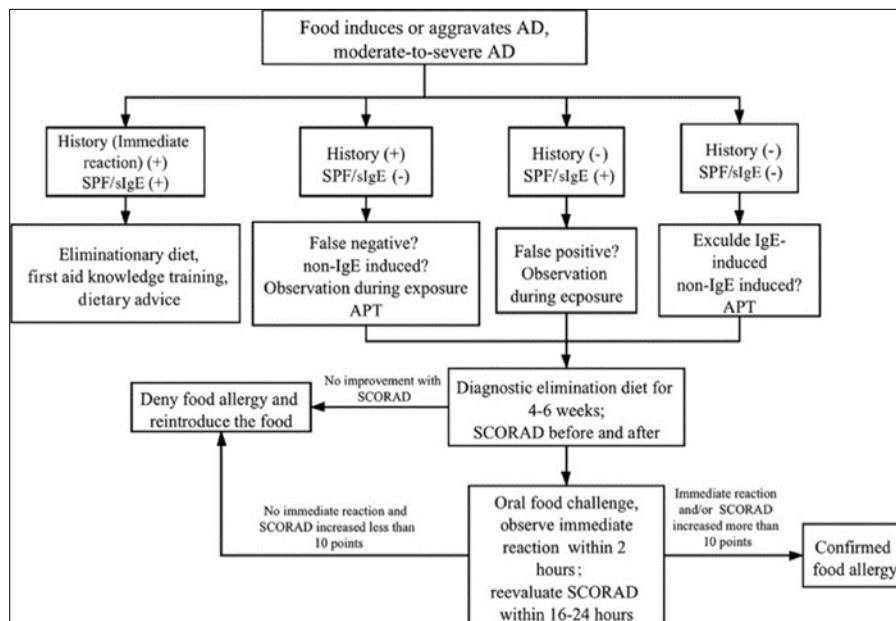

Figure 2 Flowchart of the Food Allergy Diagnosis Process in Atopic Dermatitis [24].

3.3.1. Skin Prick Test (SPT)

Allergy test that should be done is Skin Prick Test (in vivo) and measurement of specific IgE levels (in vitro). Skin Prick Test generally use for first line diagnostic instrument because it's cheaper, minimaly invasive, results are available within 15 minutes, and allow detection of the presence of specific IgE in various foods. This test uses a drop of the allergen extract to be placed on the skin, then the skin is pricked with a standard lancet. When an allergen injected to the epidermis of the skin, sIgE bound to mast cells will cross-link resulting in mast cell degranulation and histamine release. This histamine produces urticarial responses and flares [29].

3.3.2. Specific IgE Level

Measurement of total IgE level cannot be considered as a reliable marker of allergic status because elevated IgE levels can be found in atopic conditions such as eczema as well as in non-allergic conditions. This led to the introduction of specific IgE (sIgE) antibody testing. The patient's serum is incubated with the relevant allergen and the sIgE from the patient will bind to the allergen. Then it will be identified with fluorescently labeled anti-IgE antibodies, so that sIgE antibodies to allergens can be measured [25].

3.3.3. Atopic Patch Test (APT)

Atopic patch test (APT) in the diagnosis of FA in patients with AD may be an additional test in certain cases where the SPT or specific IgE fail to identify the suspected food.[31] The APT aids in the diagnosis of non-IgE-mediated food allergy, example is wheat allergy. APT have high specificity (>90%) but low in sensitivity [30].

3.3.4. Elimination Diet

Diagnostics by elimination diet is performed over 4 to 6 weeks and can be a practical approach to evaluate clinical relevance when a suspected food is tested positive for allergy testing. However, successful elimination diets alone are not completely reliable because increased AD may be due to other factors or may reflect a placebo effect, especially in older children and adults [5].

3.3.5. Oral Food Challenge (OFC)

The Oral Food Challenge (OFC) is the gold standard for the diagnosis of IgE and non-IgE-mediated food allergies. The OFC is useful to confirm or rule out a diagnosis of food allergy (both for IgE and non-IgE mediated reactions), to assess food tolerability in a child with a prior food allergy, or to identify threshold responsiveness. Other indications for an oral food challenge are to test certain foods in sensitive patients who have never ingested those foods or to test cross-reactive foods that have never been included in a diet [32].

OFC can be done in 3 ways: open OFC, single-blind OFC, and the double-blind placebo-controlled food challenge (DBPCFC). Open OFC is the most frequently used examination because it is simple, inexpensive in terms of time and cost. On the other hand, this examination has a weakness because there is a risk of failure due to psychogenic disorders that cause symptoms. In some cases, open OFC must be confirmed with blind OFC. In single-blind OFC, only the doctor knows the composition of the food being given. Food or placebo is given in a vehicle which causes the shape and taste of the food given to be unknown to the patient. This eliminates the psychogenic disturbance of the patient in producing the symptoms, but does not eliminate the possibility of bias in the physician's interpretation of the symptoms. In the DBPCFC test, neither the doctor nor the patient knew when the suspected food or placebo was given. This minimizes physician interpretation bias and patient psychogenic disturbances. For this reason, the DBPCFC is considered the gold standard for the diagnosis of food allergies. Due to its difficult implementation, this test is only used for research purposes. This test is performed for clinical purposes when an open or single blind test is unclear or in certain cases where psychogenic disorders must be ruled out [17]

The interpretation of the OFC test: (1) Positive, when clear objective signs of an allergic reaction occur or recur (at least three times) or multiple subjective symptoms in multiple organ systems occur; (2) Negative, if no symptoms occur; or (3) Inconclusive (or conclusive only to partial tolerance) if the test is discontinued before the total food dose is ingested [17].

3.3.6. Another Test

In another test, the basophil activation test is an in vitro assessment that uses flow cytometry to detect upregulation of cell surface markers (eg, CD63) following antigen stimulation. Only a few studies exploring its validity in the clinical setting have been reported. Food-specific IgG and IgG4 assays do not show any validity in the diagnosis of FA and should not be measured, as they are likely to be positive in patients with FA as well as in healthy individuals, reflecting a normal immune response to foods the person has been exposed [30].

3.4. Diet Elimination and The Risk

Diet elimination have advantages in reducing the severity of AD and disadvantages in increasing the risk of food allergy in patients with AD

3.4.1. Beneficial Effects of Diet Elimination on AD Severity

In patients with a positive OFC test an elimination diet is recommended to reduce the severity of symptoms of severe atopic dermatitis that does not improve with standard treatment. This strategy can be applied in cases where a particular food is a chronic trigger or in cases of confirmed IgE-mediated food allergies [5].

A study using 55 children diagnosed with AD with egg allergy (as evidenced by the OFC test) experienced improvement after eliminating eggs from the diet.[33] This is also supported by an open pilot study in India on elimination diets in 100 children which showed a significant improvement. in AD.[33] Subsequent studies using a sample of 113 children with severe AD, children who were diagnosed with food allergies from a positive DBPCFC test were carried out by diet elimination, most of them showed significant improvement in AD complaints within 1 to 2 months [34].

3.4.2. Diet Elimination Increase the Risk of Food Allergy in Patients with AD

Food elimination is beneficial in one subset of AD, but carries risks. The effects of the elimination diet include: nutritional deficiencies, affecting the growth and development of children, causing social isolation, can cause anaphylaxis after the reintroduction of restricted foods, and low quality of health. There is several evidence that elimination of previously consumed foods in patients with AD can result in IgE-mediated food allergy upon re-exposure, because sensitized subjects may lose immune tolerance [5,33].

3.5. Strategy of Prevention Food Allergy in Patients with AD

In AD patients, strategies are needed to prevent food allergy, example is daily emollient care, breastfeeding and hydrolyzed formula milk, then supplementation of prebiotics, probiotics, and vitamin D, and parent/caregiver can give early recognition of allergenic foods.

3.5.1. Daily Emollient Care

Daily emollient therapy can prevent atopic dermatitis in high-risk newborns, based on 2 randomized trials with 124 healthy newborns [27,28]. They concluded that daily emollient use in high-risk newborns prevents the development of AD [35, 36].

3.5.2. Breast Milk and Hydrolyzed Formula Milk

Studies show that there is no significant effect between maternal elimination diets during pregnancy and breastfeeding and prevention of AD and AM in newborns. To date, there is insufficient evidence to draw conclusions about recommending dietary changes or supplements in pregnant and/or lactating women with normal or high risk. Several national and international Pediatrician Organizations have included the use of hydrolyzed formulas to prevent AM in their recommendations for at-risk children who cannot exclusively breastfeed in the first 4-6 months of life [12, 21].

3.5.3. Prebiotics, Probiotics, Vitamin D

Prebiotic and probiotic supplementation for the prevention of food allergy in children (with or without atopic dermatitis) is not currently recommended due to inconsistent evidence. One of recent study evaluated the effects of combining an emollient and a synbiotic (probiotic and prebiotic mixture) either alone or in combination in infants from birth to 6 months of age. Unfortunately, this strategy had no effect on preventing food allergies at one year of age. In conclusion, the Food Allergy and Anaphylaxis Guidelines (EAACI) do not provide sufficient evidence to recommend probiotics for preventing food allergies. Deficiency of vitamin D at certain times of life can increase susceptibility to colonization by abnormal intestinal microbial flora, where it contributes to increased intestinal permeability, leading to inappropriate and excessive exposure of the immune system to food allergens. Causes of food allergen sensitization can

also be triggered by sensitization through the skin, which may be important especially in children with vitamin D deficiency. Thus, in AD patients, supplementation with vitamin D may be recommended if levels are low. [37, 38].

3.5.4. Early Recognition of Allergenic Foods

Recent studies have shown that exposure to skin or inhalation allergens can increase IgE sensitization, consumption of food allergens can lead to oral tolerance. As a result, many health organizations have updated their guidelines on allergen avoidance in early infancy. Early recognition of food allergens appears to be an effective strategy for minimizing the burden on the food allergy population. Recognition of potential food allergens in high-risk infants should be performed after allergy testing, including food-specific IgE measurement and/or skin prick testing, because of the risk of IgE-mediated reactions in already sensitized infants. infants with severe AD. Exposing infants to food allergens earlier via the gut immune system than inflamed skin may reduce the risk of food allergy [20,39].

4. Conclusion

Food allergy is an abnormal or exaggerated specific immune response that occurs repeatedly when exposed to certain foods. Careful anamnesis, clinical manifestations, and confirmation with allergy tests are needed in detecting food allergies. There is a reciprocal relationship between FA and AD, where AD plays a role in the causality pathway of food allergy and AM is associated with the cause of exacerbations, early onset, and severity of AD.

Several preventive interventions such as the use of emollients, early introduction of allergenic foods, and hydrolyzed formulas have benefited AD and FA in several studies. Elimination diets bring improvement and benefit when certain foods are chronic triggers or in the case of confirmed IgE-mediated food allergies. Although recommended in cases of certain food allergies, this diet has several adverse effects, so careful consideration is required in applying it to patients.

Compliance with ethical standards

Disclosure of conflict of interest

The authors assure that there is no conflict of interest with the publication of the manuscript or an institution or product mentioned in the manuscript and/or important for the result of the presented study.

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