Section A -Research paper

ATOPIC DERMATITIS (AD) INSIDE-OUT

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ABSTRACT

With a lifetime prevalence of 15-20%, AD, is one of the most prevalent inflammatory skin disorder in developed nations. Now, it is mainly concerned for factors like epidermal barrier disruption, T cell subset activation, and skin microbiome dysbiosis. Its relationship pathology with asthma, allergic rhinitis, and food allergies is yet unknown. As of October 1, 2017, the Global Health Data Exchange reported that the non-fatal disease burden of skin diseases is the leading cause of AD. Previous studies have also showed linked between environmental, and genetic factors. Thus, disease needs further research in this area .

Keywords: Atopic Dermatitis, Atopic Eczema, Epidermal Barrier Disruption, Environmental & Genetic Factors.

INTRODUCTION

AD or atopic eczema, is the most common hereditary inflammatory skin disorder in across whole world.[1] In this symptoms like recurrent eczematous lesions i.e., poorly defined, erythematous (red) patches with exudation, blistering, and crusting in the early stages and scaling, fissuring (cracking), and lichenification (thickening) in the later stages, as well as extreme itching and pain occurs . Its clinical manifestations ranges from minimal flexural eczema to erythroderma affecting >90% of the body surface that can lead to skin cracking to eczema limited to the hands, suggesting that it encompasses a variety of subtypes with distinct and overlapping pathological mechanisms.[2]

Since the early 2000s, focus has shifted from models that held type 1 hypersensitivity-mediated (IgE) allergies & atopy to epidermal barrier disruption, activation of different T cell subsets, and dysbiosis in the skin's microbiome. Even though it is strongly connected to atopic comorbidities such as asthma, allergic rhinitis & food allergies, the processes behind this relationship are still poorly understood.[2] Therefore, studies conclude that, AD results in psychological difficulties.[3] It treatment is costsly worldwide.

Henceforth, a confused vocabulary has developed as a result of the disease's variability and uncertainties surrounding its etiology, with terms like (atopic) eczema, AD and infantile eczema being used interchangeably in the medical literature. Although many other sets of diagnostic criteria, outcomes, and measurement tools have been proposed, only a subset of these sets has been shown to be valid, reliable, and practically usable.[2]

PREVALENCE

AD varies greatly throughout the world[4], although it affects around one-fifth of all individuals at some point in their lives. In several countries, there is an increased between 1950 and 2000, seen which was referred to it as an "allergic epidemic." [5] Evidences showed that it is also quite prevalent in adults, with 7–10%. On the other hand, in many past studies, it said that , it is the disease of early childhood with 25%.[2] Global Health Data Exchange in October 1, 2017 concluded that, the primary cause is non-fatal illness burden of skin disorders.[6] In many developed nations, especially in urban areas, the lifetime prevalence is more than 15%.[1] It has been suggested by studies that the problem will raise further, when unfavorable environmental conditions, likely industrialization & western lifestyle increases & leads to skin disease in predisposed individuals.[7]

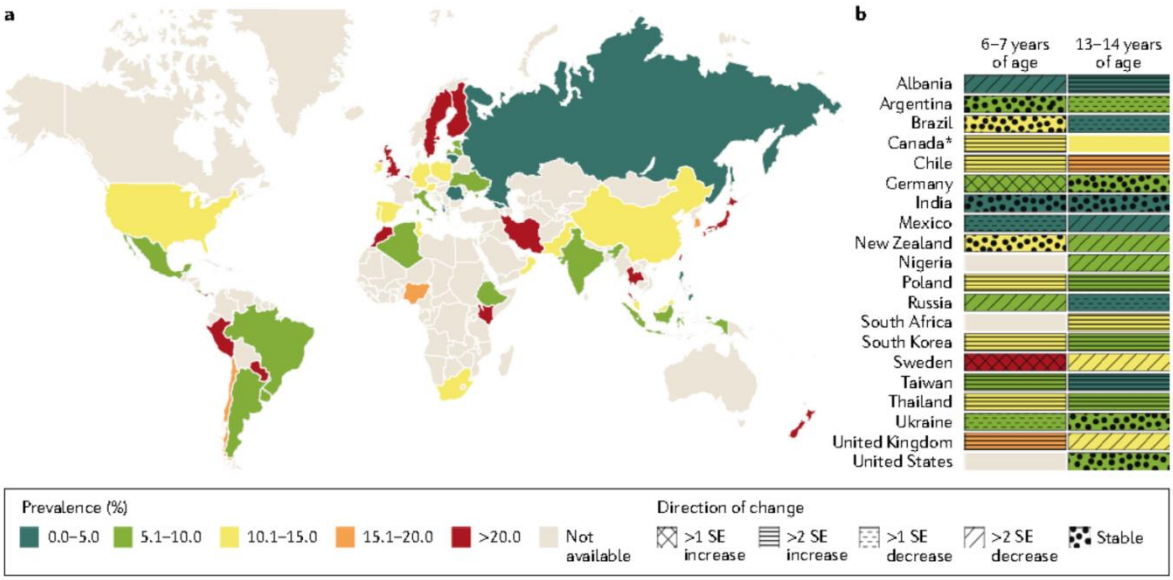

FIGURE 1 : GLOBAL PREVALENCE OF AD.[2]

RISK FACTOR

Studies have proved that ,family history of AD or other atopic illnesses is considered as strongest risk factor. (For example - Any atopic condition of 1 parent is projected to child risk by1.5 times, whereas this risk is increased by 3-5 times, if both parents have AD.[8,9] Those with affected family members are at a substantially increased risk of having AD.[10]

GENETICS

There are various genes listed , according to various studies that have been associated with AD that encode epidermal structural proein & immune system.The strongest known risk factor gene is filaggrin gene (FG) as mentioned by various past studies. F gene mutations (FGM) are present in around 10% of people from western nations and in about 50% of all patients with AD. The skin barrier is disrupted by FGM, which result in dysfunctional F proteins. Dry skin with fissures & increased risk of eczema are some of the clinical manifestations of such deficits.[5] Other genetic variants have also been implicated,[11] and these mutations are not present in all patients with AD. All of these genetic variants, in addition to environmental and developmental risk factors, work together to bring about AD.[5]

ENVIRONMENT

According to studies, only few environmental factors have been accepted for causative factor for AD. For example, according to various studies western lifestyle contributes to part of rise in eczema. Furthermore, when asked to explain the huge increase in eczema prevalence, many people point to inadequate hygiene.[13] In support of above theory studies have also concluded , the decrease in exposure to archetypal diseases in early childhood such as hepatitis A & tuberculosis.[14] Some studies have also shown correlation between breastfeeding & AD.[15]

PATHOPHYSIOLOGY

Various studies have concluded that , there are basically 2 main hypothesis related to AD that are as follows:-

1. Hypothesis of Imbalance of adaptive immune system.
2. Hpothesis of Defective skin barrier.

Hypothesis of Imbalance of adaptive immune system

According to many studies this theory involves T helper cell of 1, 2, 17& 22, as well as regulatory T cells for the development of AD.[16] Wherein ,Th2 differentiationnis mostly

involved in allergic state for acute eczema. Which in turn results in increased synthesis of IL-4,5,13, level of IgE & decrease Th1 differentiation.[5]

Hypothesis of Defective skin barrier .

This type of hypothesis , was more recent discovered type according to various studies.Furthermore, in this type of hypothesis 'FGM' leads to AD.[5] Here, FGM helps to hold keratinocytes together by encoding "structural proteins".This helps the stratum corneum stay moist and the skin's protective barrier be maintained. Reduced production of F due to genetic flaws promotes transepidermal water loss and barrier malfunction in the skin, which in turn leads to eczema.[17]

PATHOGENESIS & MECHANISM OF AD

Various studies have shown that ,FLG mutations or secondary mechanisms, showed itch-scratch cycle , reduced expression of epidermal structural proteins & lipids in response to type 2 hypersensitivity and cytokines like IL-4, IL-13, and IL-33[18,19] ,contributes to form epidermal

barrier dysfunction in AD patients. Furthermore, epidermal changes have also observed in

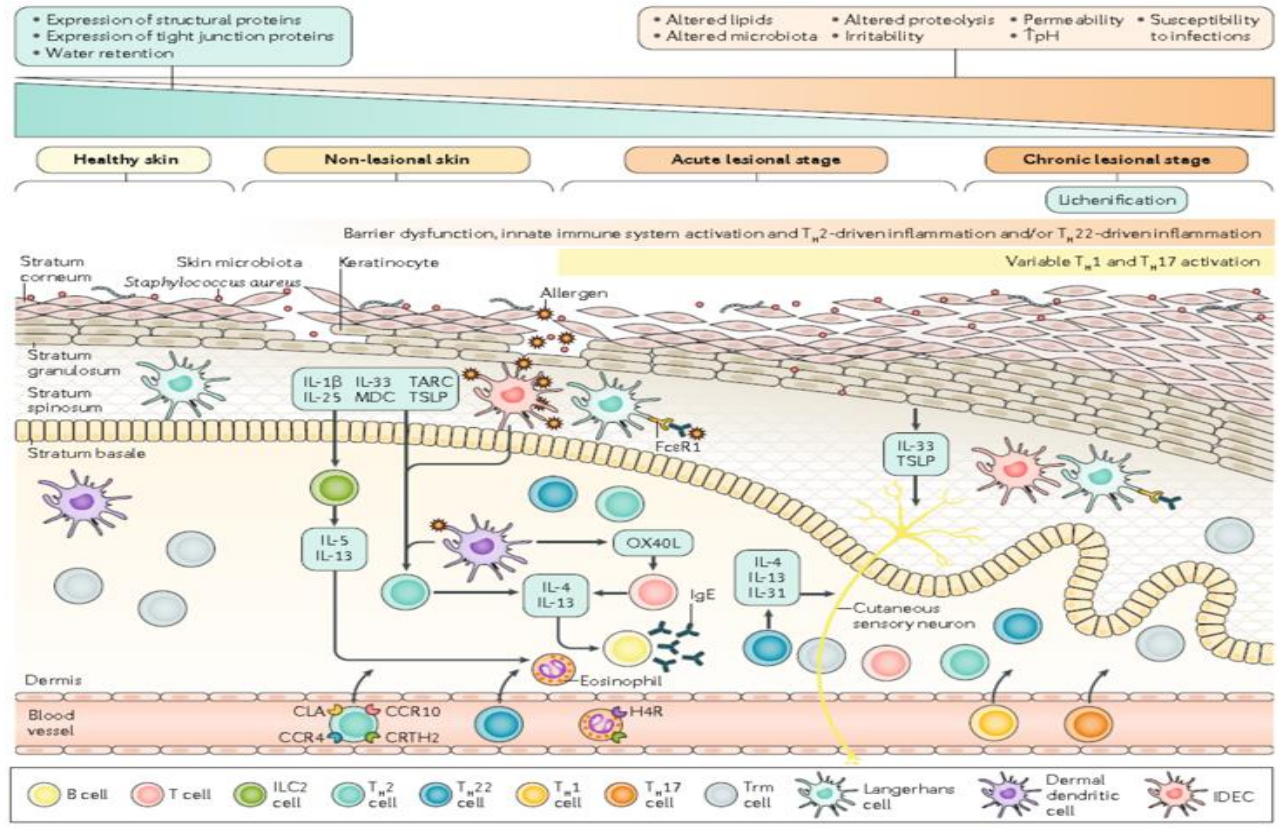

FIGURE 2 : PATHOGENESIS & MECHANISM OF AD.[2]

both affected and non-affected patients with increased pH[20] , water retention[20,21], easy irritability,[22] permeability to low molecular mass chemicals & susceptibility to infection. These changes in the composition & lamellar organization of epidermal lipids, reduced expression of tight junction proteins & altered surface microbiota colonization patterns, with a higher abundance of staphylococcus aureus as shown in figure 2.[2]

DIAGNOSTIC CRITERIA FOR AD[5]

1. Essential features
    a) Itch
    b) Eczema with typical morphology & age –specific pattern.
2. Important Feature
    a) Early age of onset
    b) Atopy (personal or family history)
    c) Dry skin
3. Associated Feature
    a) Atypical vascular respoinse (i.e. facial pallor, white dermographism).
    b) Keratosis pilaris, palmar hyperlinearity, ichthyosis Ocular & periobaital changes
    c) Other regional findings (eg – perioral & periauricular lesions).
4. Perifollicular accentuation
5. Lichenification
6. Excoriation

TREATMENT

AD is not a curable disease according to many studies as many patients will experience chronic course of disease. The goal of treatment is to minimize the number of exacerbation of disease so called flares & reduce the duration & degree of flare.[5]

It includes as follows :-

1. **Mainitainig intact skin**- (eg- emollient). It should be used several times a day to reduce the need of corticosteroid cream.[23,24,5]
2. **Use of tropical corticosteroid** (on basis of different classes)[5]
    a) Mild (CLASS I)
        Hydrocortisone
    b) Moderate (CLASS II)
        Hydrocortison -17- butyrate

Clobetason -17-butyrate

c) Strong (CLASS III)

Betamethason -17-valerate

Fluticasone propionate

Betamethasone

Mometasonfuroate

Desoximethasone

Fluocinonide

Fluocinolonacetonide

d) Very strong (CLASS IV)

Clobetasol Propionate

3. **Use of calcineurin inhibitors**- [eg- Pimecrolimus cream (mild corticosteroid) & Tacrolimus ointment(moderate to strong corticosteroid)].[5]
4. **Use of Phototherapy for treatment** - In this , studies have concluded that , narror band UV –B light is suitable for treatment of recalcitrant eczema.[5]
5. **Use of systemic Immunosuppresent-** It is recommended to use for short term in combination with corticosteroid. Further , if staphylococcus infection is present then oral antibiotics can be prescribed along with this. In addition, studies have also shown , several risk factors for oral corticosteroid so its continue use is not recommended. Instead , tapering dose is adviced by many studies. (eg – Azathioprine, Methotrexate or Cyclosporine A for very severe, chronic or relapsing type of AD).[25]
6. **Other Medications[5]-**
   a. Specific immunotherapy , it will effect upper airway symptoms.
   b. Oral antihistamine use in case of itching but it will not reduced activity of eczema.
   c. Nonsedating antihistamine use , but when in night time itching starts & hamper sleep cycle then sedating antihistamines are recommended by many studies in past.

CLINICAL MANIFESTATION OF AD [2]

Below are some of the examples of AD symptoms visible in different picture which is as follows:-

a. Extensive erythema visible on trunk with excoriation.

b. Acute vesicular AD of face

c. Child showed more localized & chronic AD which was affecting flexor structure.

d. Skin is lichenified (thick) from repetitive stracting.

e. According to many studies & photograph of patient also showed chronic hand or head – neck AD only.

Histological view of AD

f. **Acute exudative lesion**- epidermal acanthosis , spongiosis , dermal oedema & perivascular or periappendageal lymphocytic & eosinophilic infiltrate was seen with the help of haematoxylin & eosin staining.

g. Chronic lichenified skin - acanthosis, hyperkeratosis , parakeratosis , dense monomuclear cells & increased mast cells together with fibrosis was seen with the help of haematoxylin & eosin staining.

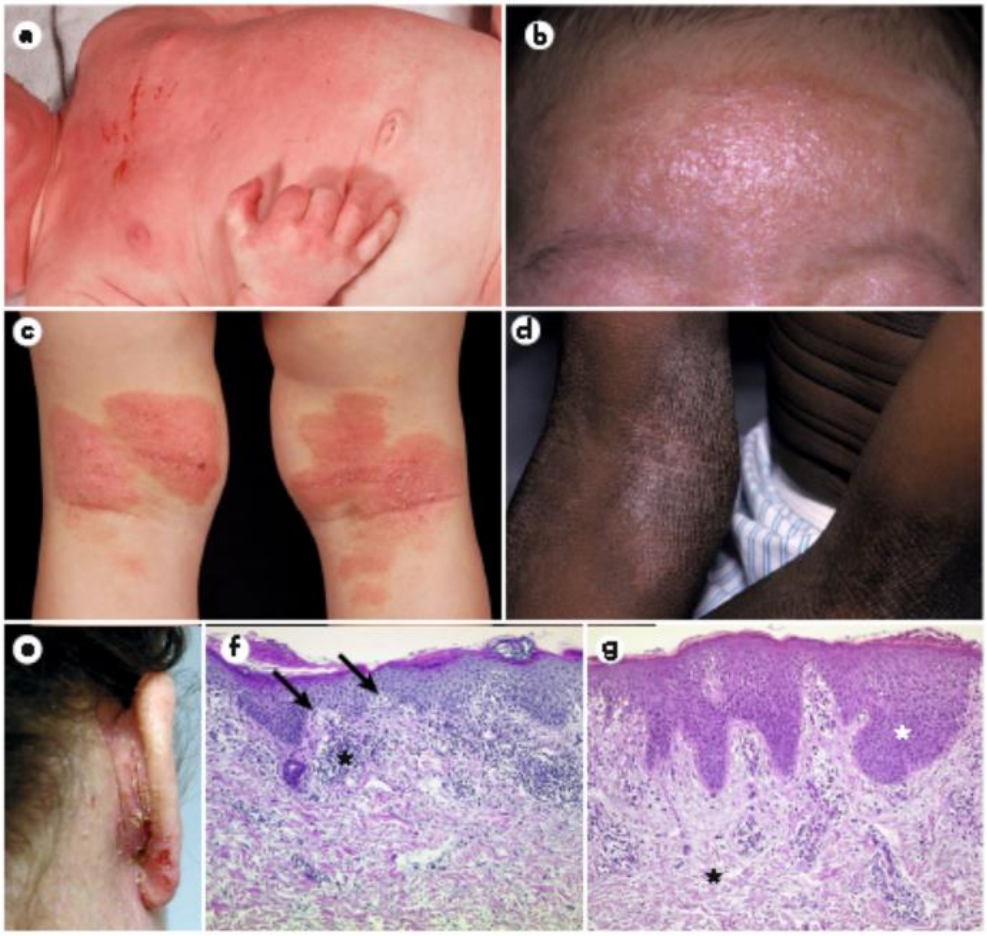

FIGURE 3 : CLINICAL MANIFESTATION[2]

CONCLUSION

We come to conclusion that the non-fatal illness burden of skin disorders is the main cause of AD. Risk factors, environmental factors, and genetic factors have all been concluded in past research. More studies are thus required since treating this condition is essential.

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