A HOSPITAL-BASED CROSS-SECTIONAL STUDY TO CORRELATE THE LEVELS OF NLR, PLR AND MPV WITH DISEASE DURATION AND SEVERITY IN PEDIATRIC ATOPIC DERMATITIS

By

Dr. MOHANISH SHEKAR

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Dr.ARUN.C.INAMDAR

PROFESSOR

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"A HOSPITAL-BASED CROSS-SECTIONAL STUDY TO CORRELATE THE LEVELS OF NLR, PLR AND MPV WITH DISEASE DURATION AND SEVERITY IN PAEDIATRIC ATOPIC DERMATITIS"

In

DERMATOLOGY, VENEREOLOGY AND LEPROSY

List Of Abbreviations

AD - Atopic dermatitis

UKC – United kingdom Working Party Criteria

SCORAD- Scoring Atopic Dermatitis

IL – Interleukin

NLR- Neutrophil Lymphocyte Ratio

PLR – Platelet lymphocyte ratio

MPV – Mean Platelet Volume

ISAAC – International Study of Asthma and allergies in childhood

IgE – Immunoglobulin E

FLG – Fillagrin Gene

TEWL – Transepidermal water loss

KLK – Kallikrein

LEKT – Lymphoepithelial Kazal Type 5 Serine protease inhibitor

SPINK5 – Serine Protease Inhibitor Kazal Type 5

DCs – Dendritic cells

Th 1& 2 – T- helper 1 & 2

TSLP – Thymic Stromal Lympho protein

UV – Ultraviolet

P.alba – Pityriasis Alba

HSV – Herpes Simplex Virus

QOI – Quality of life

APT – Atopy patch test

SPT – Skin prick test

RAST – Radioallergen Sorbent test

HdM – House dust mite

TCS – Topical corticosteroids

TCI – Topical calcineurin inhibitor

ABSTRACT

Introduction:

Atopic dermatitis (AD) is a prevalent, persistent, recurring, inflammatory skin condition that primarily affects children, with few cases progressing into adulthood. Many theories show the relationship between AD and systemic inflammation. Neutrophil-lymphocyte ratio (NLR), Platelet-lymphocyte ratio (PLR), and mean platelet volume (MPV) are markers of systemic inflammation that were shown to be associated with Atopic dermatitis.

Objectives:

To calculate NLR, PLR and MPV ratio and correlate their levels with the disease duration and severity of AD in pediatric atopic dermatitis.

Materials and methods:

A cross-sectional study of Hundred and sixty-five (165) patients with atopic dermatitis belonging to the paediatric age group confirmed clinically were included, but patients with co-existing conditions such as molluscum contagiosum and eczema herpeticum were excluded. Mean/SD values of NLR, PLR, and MPV were compared among severity groups classified according to SCORing Atopic Dermatitis (SCORAD). Correlation of disease duration and SCORAD with NLR, PLR, and MPV values was examined.

Results:

There were significant differences between the severity groups among NLR, PLR and MPV values. NLR had a positive correlation with SCORAD score and duration. PLR had a positive correlation with the SCORAD index, whereas MPV had an inverse correlation with the SCORAD score. PLR had better diagnostic accuracy in predicting high SCORAD with 100% sensitivity and specificity with a cut-off value > 172.

Conclusion:

NLR, PLR and MPV are cost-effective, feasible and readily available alternative tests to detect systemic inflammation in AD with good sensitivity and specificity.

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INTRODUCTION

Atopic dermatitis (AD) is a prevalent, persistent, recurring, inflammatory skin condition that primarily affects children, with few cases progressing into adulthood.[1] It is characterised by intense itching, dryness and eczematous regions with crusting manifesting in an age-dependent pattern, with face, scalp, and extensor involvement in infants and flexural predominance in the older age group.[2,3] Familial and Personal history of "atopic diathesis" is present in most affected patients. Mere existence like allergic rhinitis, bronchial asthma, or atopic dermatitis is referred to as "atopic diathesis."[4] Clinical characteristics differ depending on age, population, and race.[5]

There is no gold standard diagnostic laboratory marker or diagnostic criteria.[6] The United Kingdom Working Party criteria (UKC) was created in 1994 to modify the original Hanifin-Rajka criteria to make them easier to apply and more suitable for population-based investigations.[7,8] They are the sole diagnostic criteria that have undergone many validation trials in hospital and population-based settings.[7,9,10,11]

The severity of Atopic dermatitis must be analysed to assess the process of disease and quantify intervention by treatment or eradication. As a result, it must be objective as possible. This is critical in research and clinical practice.[12] SCORAD system was created with the help of the European Task Force Group on Atopic Dermatitis (ETFAD). The word SCORAD was coined by Arnold Oranje, which stands for 'scoring atopic dermatitis.'[13] The SCORAD Index analyses the disorder's area of involvement, the severity of six components, and subjective symptoms.[12]

There is a link between serum thymus, activation-regulated chemokine, the severity of atopic dermatitis and serum interleukin (IL) 10, 17 and 23.[14,15.] These substances, however, cannot be tested regularly. Neutrophil-lymphocyte ratio (NLR), Platelet lymphocytic ratio (PLR),

and Mean platelet volume (MPV) have been linked to several chronic inflammatory illnesses.[16-27]

This study aims to calculate NLR, PLR and MPV ratios and correlate their association with duration and severity in pediatric atopic dermatitis.

OBJECTIVE OF THE STUDY

To calculate NLR, PLR and MPV ratios and correlate their association with duration and severity in pediatric atopic dermatitis.

REVIEW OF LITERATURE

DEFINITION:

The term “atopy” is derived from the Greek word “atopos,” meaning strange or unusual.[28] Atopic dermatitis (AD) is a prolonged inflammatory process characterized by pruritus and a cyclical pattern of flare-ups and remissions. Asthma, allergic rhinoconjunctivitis and other allergic diseases are all related to it.[29]

Clinical features are categorized into Acute, subacute, or chronic eczematous dermatitis with distinctive morphology and age-specific patterns with pruritus, facial and extensor involvement in infancy, and flexural lichenification in children and adults.[30]

EPIDEMIOLOGY:

The prevalence of AD is roughly 20% worldwide.[2,29] Adult prevalence is 1-3%, while children range from 0.7 to 26%.[31] The estimated frequency of AD in India is around 0.98%.[32] Many studies have found a slight male predominance.[33,34,35] In both winter and summer, the symptoms are seen to worsen.[32,34,35] In the ISAAC phase 3 study, it was found that a diet predominantly consisting of fish, fruits, and vegetables reduces the risk of contracting atopic dermatitis, but consuming fast food raises that risk.[36]

ETIOPATHOGENESIS:

Differentiation between Extrinsic AD and Intrinsic AD :

Intrinsic AD or Non-allergic AD → Total immunoglobulin E (IgE) within normal range and absence of allergen-specific IgE.[37]

Extrinsic AD or Allergic AD → Rise in total IgE with the presence of allergen-specific IgE.[37]

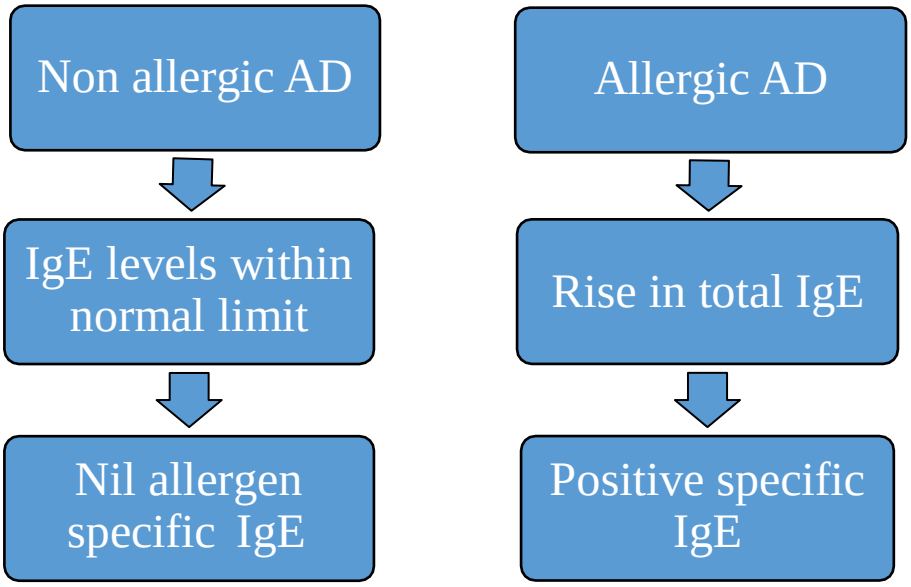

Figure 1: Comparison between Intrinsic and Extrinsic AD

Atopic March→ corresponds to "the evolution of AD to other atopic illnesses like allergic rhinitis and asthma" in a diseased individual.[2]

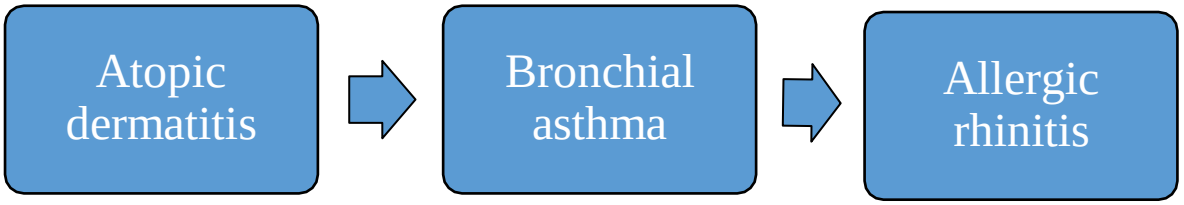

Figure 2: Atopic March

AD occurs as a result of the exquisite interactions between genetic, environmental, immunological, and skin barrier abnormalities.[30]

The following factors can lead to impairments in the skin's barrier function:[38]

- **Filaggrin (FLG) gene defect:** An significant risk factor for AD is a loss-of-function mutation in the FLG gene encoding epidermal barrier protein filaggrin. Filaggrin maintains the skin's barrier function by cross-linking keratin intermediate filaments to form compact bundles. Consequently, greater significant transepidermal water loss (TEWL) results from loss of function mutation.

  Natural moisturising factors that hydrate the stratum corneum to retain the skin's pH are produced due to the compounds created during filaggrin degradation.[38] Mutations in the filaggrin gene are present in only around 50% of all children with moderate to severe AD.[39]

  Those with mild AD are far less likely to experience this relationship.[38] Atopic individuals with the filaggrin gene mutation are more prone to develop allergic rhinitis, palmar hyperlinearity, allergic contact sensitisation, early initiation of the disease, food allergies (IgE stimulated), and asthma. Ichthyosis Vulgaris is caused by a null mutation of this gene.[40]

- **Ceramide Deficiency:**

  Ceramide, a type of lipid, is vital for the stratum corneum to retain water. Ceramide levels are vital for maintaining the epidermal permeability barrier, as evidenced by the correlation between low ceramide levels and increased TEWL in AD patients.[38] Ceramide synthesis is reduced as a result of a combined reduction in the essential lipids that make up the skin barrier and increased

sphingomyelin deacylase activity.[41] Ceramide levels have significantly decreased in lesional as well as non-lesional skin regions of AD individuals. Furthermore, in infants with AD, a decrease is only evident in the lesional skin, suggesting that perhaps ceramide reduction happens as a post-inflammatory event. Contrary to filaggrin, no null mutation in ceramide-related genes has been identified in AD patients.[38]

- **Elevation in activation of endogenous skin proteases:**

  Peptidase KLK14, KLK7, and KLK5, which are linked to human kallikrein (KLK), are essential proteolytic enzymes that cause corneocytes to desquamate. The proteases mentioned above depend on the skin's pH to function; thus, as the pH is raised, their activity is increased. The action of these peptidases is also controlled by enzymes that inhibit proteases, such as Lymphoepithelial Kazal-type 5 Serine Protease Inhibitor (LEKTI). The Serine Protease Inhibitor Kazal-type 5 (SPINK5) gene encodes LEKTI. Netherton syndrome, caused by a mutation in the SPINK5 gene, manifests as food allergy, asthma, and dermatitis similar to AD. Serum IgE levels are also markedly elevated. The association of this gene with AD is well established. This evidence indicates that excessive endogenous skin protease activity and subsequent corneocyte desquamation can trigger dermatitis similar to AD.[38]

- Both innate and adaptive immune system impairments are seen in AD on the immunological front.[40] In people with AD, the development of eczema requires many skin cells, including T cells, keratinocytes, dendritic cells (DCs), mast cells, macrophages, monocytes, and granulocytes.[38]

  Immune responses mediated by T-helper-1 (Th1) and T-helper-2 (Th2) are observed as AD progresses. Th2-predominant responses are detected during the

acute stage of AD, whereas Th1-dominant cytokine profiles are seen during the chronic phase when the Th1-Th2 balance changes.[31] Interleukins (IL), viz IL-12 and IL-5, are predominant in chronic lesions, while IL-13 and IL-4 are less so. Acute conditions had a substantial Th17 cell infiltration. This results in increased production of IL-6 and IL-8 by IL-17, which in turn regulates fibroblast activity.[38] Th2, Th22, and Th17 cytokines are predominantly responsible for the acute phase of the disease, whereas Th1, Th2, and Th22 cytokines are significant during the chronic phase.[42]

Thymic stromal lymphopoietin (TSLP), a protein with DCs receptor, is essential for promoting the Th2-response that mediates the onset of AD.[38,42] Increased susceptibility to infections results from Th2 cells suppressing the expression of antimicrobial peptides like defensins, cathelicidins, calprotectin, and inducible nitric oxide synthetase.[42,43] The polymorphisms in several pattern recognition receptors, including NOD1, TLR2 and CD14 (expressed by keratinocytes), found in AD patients are connected to an increased propensity for infection, exacerbation of the disease, and allergy sensitisation.[42]

IL-5 induces eosinophil's activation and chemotaxis (mediated by eotaxin) (a Th2 cytokine). IL-5 and eotaxin blood levels rise when the disease is acute. Additionally, the lesions of AD show increased levels of two cytokines associated with eosinophils, namely eosinophil cationic protein and major essential protein, which indicate eosinophil degranulation in the skin.[38] Elevated IgE production, present in about 80% of patients, is a significant immunoglobulin defect in AD. Without hypersensitivity to environmental allergens, dermatitis is solely associated with a slight increase in blood IgE

levels. However, concurrent asthma or allergic rhinitis is associated with greater serum levels of total IgE.[31]

- Several environmental factors, including food, climate, aeroallergens, and gut flora, can affect the development of AD.[38]
  - **Role of infections:** Two significant theories are implicated in the pathogenesis of AD
  - **The 'Outside-Inside' hypothesis→** proves that a compromised skin barrier is a gateway for allergens and microorganisms.[44,45]
  - **The 'Inside-Outside' hypothesis→** proves that AD individuals have a deranged sensitive immune system, which results in a disproportionately strong response to a small number of allergens.[45]
  - **Hygiene hypothesis→** Based on this, early exposure to various microorganisms, especially those that produce lipopolysaccharide endotoxins like Escherichia coli, is essential for developing mediated immune responses.[31] Therefore, decreased early exposure to microorganisms due to overprotective parenting results in increased Th2-mediated immunity, which is responsible for atopy, and reduced activation of Th1-mediated immunity. (Th1 cells control Th2 cell downregulation, and vice versa.)[46,47,48] Probiotic supplementation in mothers during the third trimester of pregnancy and breastfeeding is thought to enhance the microbiome and reduce the risk.[49] Most AD patients have Staphylococcus aureus (S.aureus) colonisation on their skin, which increases their risk of infection and aggravates their eczematous condition.[40,43,50] Malessezia is linked to eczema flare-ups as well.[31]

- **Aeroallergens:** House dust mites (HdM), grass pollen, and animal dander are some causes of AD symptoms.[51] The development or worsening of eczema occurs

in AD patients with specific IgE antibodies against these factors.[52] The disruption of barrier function is caused by the disintegration of corneodesmosomes by cysteine proteases generated by HdM.[41]

- **Climate:** The onset of dermatitis in AD is influenced by several climatic conditions, including temperature, humidity, and ultraviolet (UV) exposure.[38] High exposure to UV Radiation and rising temperatures are protective against AD.[38,53] Patients have a flare-up due to reduced sun exposure in the winter season. Dry skin is more prone to develop in dry climates, which exaggerates the condition leading to intense itching.[53]
- **Diet:** Up to 30% of kids with AD have food allergies.[28] However, most of these kids develop this allergy within the initial phase of life.[54] Egg, peanut, wheat, soy, and crustacean and shellfish products are responsible for almost 90% of allergy reactions.[28,29] Unpasteurized milk may contain infective pathogens, which may lead to this. Additionally, an increasing fish intake is thought to be beneficial since it contains a lot of n-3 polyunsaturated fatty acids (n-3 PUFAs), which have anti-inflammatory properties.[55]
- Additional elements: The skin's acidic mantle, or pH, supports the barrier function. The pH of the skin rises when soaps and detergents are used. This results in excessive skin protease activity, which promotes hyperdesquamation and aggravates eczema.[56]
- Farm animals and pets, particularly dogs, are considered protective against the onset of AD. However, there are no definitive studies on cats.[55]
- The risk is augmented by maternal smoking patterns and rising outdoor pollution levels.[38,55]

- **Genetics:** The relationship between the disease and mutations in the barrier protein is confirmed by recent research into the genetic roots of AD.[57] The FLG gene null mutation is thought to be the most considered factor for AD.[58] Strong correlations have also been found with polymorphism of the high-affinity IgE receptor gene, FCR1.[31] The mother's history of atopy has a more substantial impact than the father's on the development of atopy in children.[59] More concordance occurs between monozygotic twins than dizygotic twins. Chromosome 1q21.3, which carries the filaggrin gene, is where the most vital relationship is found.

  Chromosome 5q31.1 and Chromosome 11q13.5 are two other significant associated loci.[58]

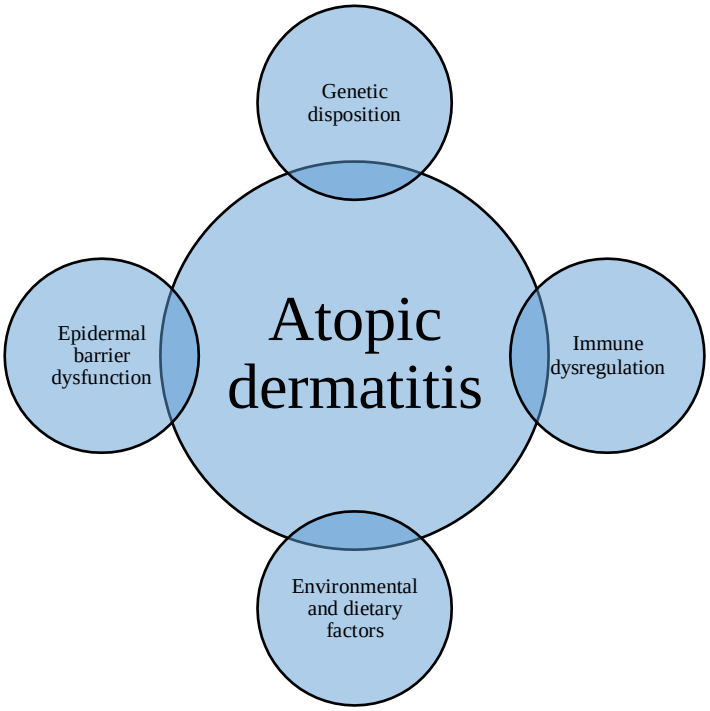

Figure 3: Atopic dermatitis pathogenesis

CLINICAL FEATURES:[29,2,33.]

AD constitutes numerous clinical presentations. They are divided into four categories:

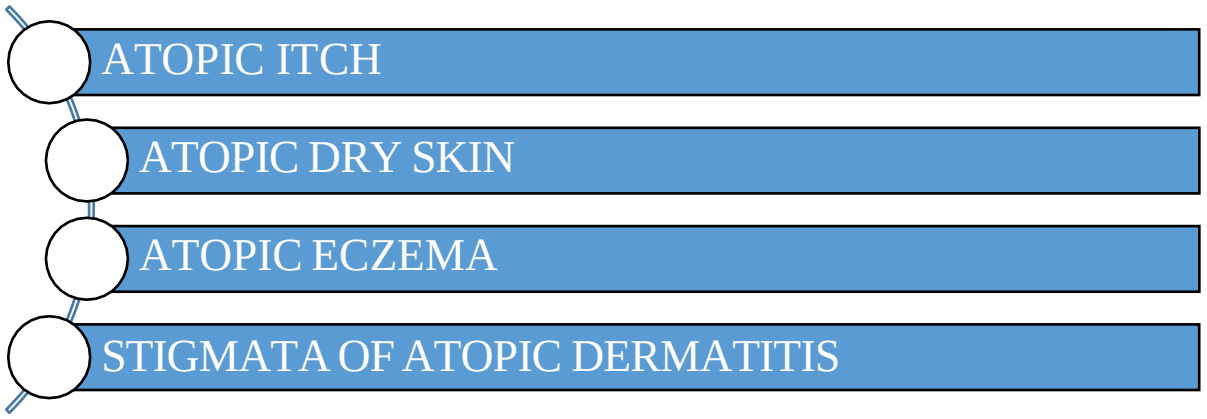

Figure 4: Clinical Presentations Of Atopic Dermatitis

- **Atopic itch:** It is one of the most characteristic features of the disease, which is persistent in nature. Sleep disturbances, agitation, and distress may result from it. Sweating, bathing, mental anguish, exercise, and wool clothing aggravate the condition. It causes lichenification, eczematous skin lesions, excoriations, and prurigo papules.
- **Atopic dry skin:** It results from increased water loss through the epidermis. Also, among the contributing reasons is a reduction in the number of lipids, particularly ceramide.
- **Atopic dermatitis:** It is categorised into three phases:
  - **Infantile stage:** It manifests with erythema and edematous papules over the face, minimally involving the napkin region. Once the baby starts to crawl, the knee and elbows' extensor aspects are affected.
  - **Childhood stage:** Edematous and erythematous papules are succeeded by lichenification. Flexural aspects of the elbow and knee show warty lichenification, redness, crusting, excoriation, and pigmentary alterations,

including hyper- and hypopigmentation. Despite the possibility of neck, ankles, and wrist flexors being impacted.

- **Adult Stage:** Flexures and hands may show lichenification. This age group is most affected by localised dermatitis, with hand, nipple, and eyelid eczema being particularly common. These people might develop photosensitivity.

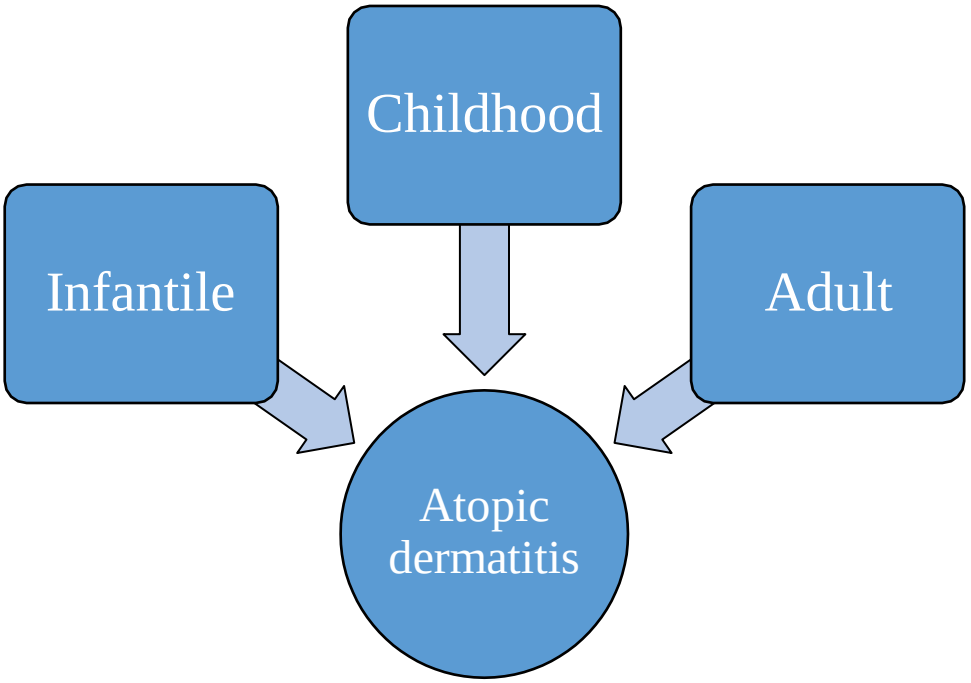

Figure 5: Stages of atopic dermatitis

- **Atopic stigmata:**
  - Below the margin of the lower eyelids is a Dennie-Morgan fold, a linear longitudinal fold that crosses the pupillary midline.
  - Prominent nasal crease.
  - Ichthyotic skin is present in the majority of patients.[60]
  - Dry skin and scaling are observed in low-grade dermatitis.
  - Palm hyperlinearity is frequently noticed.

- Pityriasis alba (P.alba) is an ill-defined hypopigmented patch in subclinical dermatitis.
- Keratosis pilaris, or horny follicular lesions, commonly affect the outer surface of the upper and lower extremities, cheeks, and gluteal region.
- Patients with AD frequently have perifollicular prominences and prurigo nodularis.
- AD affliction to lips results in cheilitis. Perioral dermatitis results from adjacent skin involvement and is worsened by lip-lick dermatitis.[61]
- The periorbital brown-grey pigmentation is described as "atopic shiners."[62]
- Hyperpigmentation and hyperkeratosis typically cause a "dirty neck" appearance.
- "Headlight sign" can develop from periorbital, perinasal and perioral pallor.
- Other stigmata are white dermographism, which results from capillary vasoconstriction and causes skin blanching when a location is stroked with a blunt object.
- Xerosis may cause perianal dermatitis and periocular dermatitis.[61]
- Predominant thinning of the lateral portion of eyebrows, or Hertoghe's sign, can occasionally be seen.
- Atopic hand eczema: The dorsal surface of the hands is particularly susceptible to non-specific hand dermatitis, which manifests as dry, scaly eczematous lesions.[60] Eczema with vesicles and lichenification are frequently noted.[2]

- Most individuals claim that wearing woollen garments and perspiring cause or worsen itching. Eczematous lesions can develop due to environmental factors such as food and allergies, which were covered under etiopathogenesis earlier.

- **Viral infections:** AD individuals exhibit a propensity toward the following:
  - **Eczema herpeticum:** Sometimes referred to as a Kaposi's varicelliform eruption. It is an "Acute disseminated herpes simplex virus (HSV) infection in a patient with atopic dermatitis, frequently with systemic symptoms."[63]
  - **Eczema coxsackium:** Coxsackie virus infection (hand, foot, and mouth disease) that has developed in AD-affected areas.
    In typical sites of childhood dermatitis, it is characterised by the presence of pustules and erosions over eczematous lesions.[61]
- **Bacterial infections:** AD individuals are more likely to develop a staphylococcal infection. The secondary infections are impetigo (most common), folliculitis, abscess (mainly caused by a methicillin-resistant strain of S.aureus), and cellulitis.[43]
- **Ophthalmic features:** The minor criteria of Hanifin and Rajka include specific ophthalmic disorders like keratoconus, anterior subcapsular cataract, and keratoconjunctivitis, as they are linked to AD.[60]

Diagnostic criteria used in atopic dermatitis:

Various diagnostic criteria have evolved to help in AD diagnosis. Hanifin and Rajka first enumerated a list of characteristics to diagnose AD in 1977, then reformed in 1980.[64] The U.K. Working Party criteria consist of a concise set of one major and five minor criteria for population-based surveys.[7] Due to their simplicity and lack of intrusive testing, these criteria have been thoroughly evaluated in clinical studies and shown to be comparable to Hanifin and Rajka criteria in terms of sensitivity and specificity, with good repeatability in a clinical environment.[65]

Major criteria	Minor criteria (three or more of the following)
1. An itchy skin	1. Prolonged history of having generally dry skin. 2. History of affliction for flexures like popliteal fossae, cubital fossae and the fronts of the ankles and cheeks in younger age group. 3. Personal History of asthma or hay fever (or an atopic condition in a first-degree relative in the pediatric age group less than four years). 4. Evident flexural eczema. 5. Onset before two years.

Table 1: Demonstrates U.K. Working Party Diagnostic Criteria:[7]

A. 1989→ Kang and Tian diagnostic criteria
B. 1992→ Schultz-Larsen criteria
C. 1995→ ISSAC questionnaire
D. 1995→ Japanese Dermatology Association criteria
E. 1996→ Criteria of Diepgen
F. 1998→ Millennium diagnostic criteria
G. 2005→ Danish Allergy Research Centre criteria

Table 2: Elaborates Other criteria used in the diagnosis of atopic eczema:[66]

Scoring systems in assessing the severity of atopic dermatitis:

The quality of life (QOL) affected by AD individuals can be significantly impacted by uncomfortable aspects such as itching, severity, and location of the lesions. Hence, assessing the condition's severity is essential for efficient management in clinical practice. To date, no gold standard has been formulated to evaluate the severity of patients living with AD.[67]

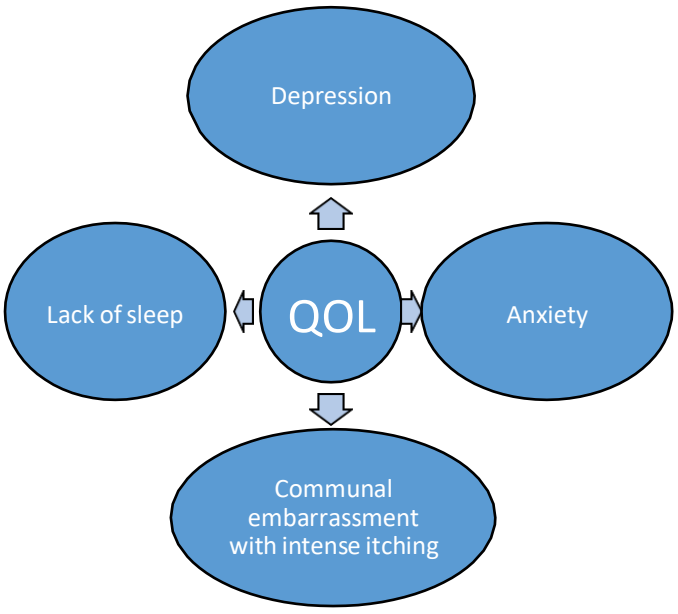

Figure 6: Factors influencing the quality of life

Several significant grading methods include:[68]

(SCORAD) SCORing Atopic dermatitis[12,13]:

The most accurate scoring system for atopic dermatitis is the SCORAD (Index) (AD). The rule of nine was implicated in illustrating the patient's inflammatory lesions to evaluate AD severity. Grading for extent range from 0 to 100. Erythema, excoriations, oedema/papules, lichenification, oozing/crusts, and xerosis are the six components that constitute the SCORAD's intensity. Each item can be scored from 0 to 3 on a scale. The subjective components include itching and sleep disturbances.

A/5 + 7B/2 + C is the formula for the SCORAD Index. In this formula, the term "A" stands for "extent" (0-100), "B" for "intensity" (0-18), and "C" for "subjective symptoms" (0-20). The SCORAD Index has a maximum score of 103.

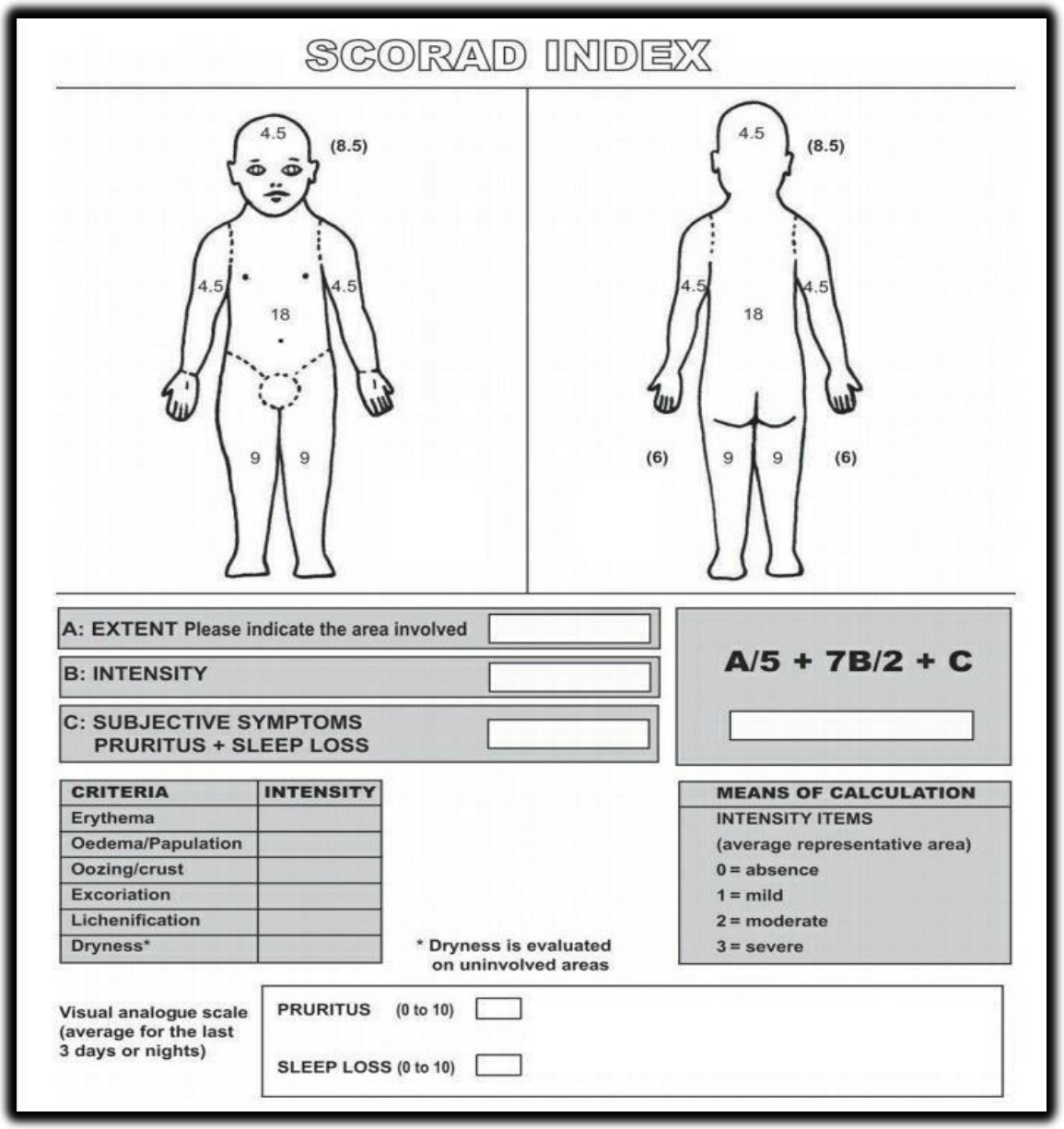

Figure 7: SCORAD INDEX[12,13]

Other scoring systems used are:[68]

1. EASI→ Eczema Area and Severity Index.[69]

2. POEM→Patient-Oriented Eczema Measure.[70]

3. SASSAD→Six Area, Six Sign Atopic Dermatitis.[71]

4. IGA→ Investigator Global Assessment.[68]

5. TISS→ Three-Item Severity score.[72]

Evolution and prognosis of the disease:

Most individuals indicate early disease onset, with 60% displaying symptoms within infancy and 90% up to five years of age.[73] The condition could be chronic, prolonged, or relapsing.[2] With an increment in patient age, the severity of the condition reduces.[30] The disease severity and familial history of atopy are the best indicators of persistent illness.[2] High AD persistence is associated with filaggrin gene mutations.[30]

Poor prognostic variables include:[2,30]

1. Early onset of AD.
2. Severe in intensity during childhood.
3. Personal experience with concomitant hay fever, allergic rhinitis, or bronchial asthma.
4. History of hay fever, bronchial asthma, or atopic dermatitis in the family
5. Raised IgE concentrations.

INVESTIGATIONS:[74]

Several tests are available about AD to find allergies or sensitisations associated with it.[2,68,]

- **Atopy Patch Test**[75,76]: The APT fundamentally aids in the identification of delayed reactions to allergens, more frequently aeroallergens and occasionally food allergies. Similar to the standard patch testing for contact dermatitis, allergens (such as pollen, cat dander and house dust mites) are applied epicutaneously to the trunk, utilising Finn chambers. Based on the appearance of erythema, papules, and vesicles, readings are obtained at 48 and 72 hours, and positive outcomes are scored from + to ++++.
- **Oral Food Challenge:** Tests using oral provocation may be blinded or open. The DBPCFC is the gold standard for determining whether a person has a food allergy**.** The best way to do this is using "masked" foods in neutral formulae and after at least a week of following an elimination diet.

  Patients are watched for both early (within 2 hours) and late (between 2 and 48 hours or over a few days) reactions as food items are given one at a time, two days apart. Single-Blind or open food challenges might be used in circumstances where the DBPCFC is impractical. In the clinical situation, challenge tests that rely on daily exposure to a specific cuisine may be more helpful. It shouldn't be banned whenever an oral challenge test is negative, but a meal is positive for specific IgE antibodies and a skin prick test. Strict elimination diets should only be administered to kids with actual food allergies (based on the oral challenge), especially when there are potentially fatal reactions.
- **Skin prick test (SPT)**[75,77,78]: The results of SPT support the diagnosis of acute hypersensitivity reactions. The immune response mediated by IgE depends upon neurogenic and chemical mediators at the skin's surface. A complex signal

transduction cascade is triggered after intracutaneous injection of allergens because they pass synthesised Immunoglobulin E bound to the high-affinity FcERI receptor on mast cells. In the end, already-formed inflammatory mediators are released, starting with mast cell degranulation in a matter of seconds. Histamine, a transient vasoactive amine that immediately increases local blood flow and vascular permeability, is one of them, along with enzymes like serine esterases, mast-cell chymase, and tryptase. After a superficial antigen administration into the epidermis, a wheal and flare reaction starts to appear within minutes and can last up to half an hour. Mast cells produce and generate chemokines, lipid mediators including prostaglandins, leukotrienes, platelet-activating factors, and other cytokines like IL 13 and 4, all of which support the Th2 response when mast cells are activated.

A delayed reaction which is exceedingly rare and virtually exclusively seen in patients allergic to mould, grass, and parietara pollens, may occasionally follow these alterations. Histamine can only be seen in the middle of the wheal during a positive reaction, not on the edges. Therefore, it is proposed that following a challenge by an allergen, the mediators generated by the mast cell directly stimulate c-fibres to cause an axon reflex. As a result, “the next” mast cell releases neurogenic peptides and mediators, which play a crucial role in the immediate flare and wheal reaction. Skin prick test’s clinical applicability, however, is bitterly debated.

On the one hand, skin prick tests make it possible to identify those who are at risk for food allergies as well as the allergen that is causing an eczematous flare-up. Conversely, when carried out by a generalist, positive skin prick tests on foods may inadvertently result in protracted elimination diets, resulting in nutritional deficits and possibly a lack of tolerance to the prohibited foods. Additionally, skin-prick tests raise the expense of healthcare. There is not yet clarity on this issue.

- **Radioallergosorbent Test (RAST)**[79]: The RAST solid-phase sandwich radio immunosorbent assay measures physiologically active allergen-specific IgE sandwiched between allergen and Fc-specific anti-IgE antibodies while eliminating non-specific serum effects.

  Fadal and Nalebuff altered the procedure by reducing the diagnostic cutoff point to boost sensitivity with only a little decrease in specificity, known as modified RAST. Additionally, the incubation period was lengthened.[80]

  Compared to skin testing, the RAST is less sensitive and has a less direct association with the relevant history of allergies to certain drugs. Furthermore, the reporting laboratory's analysis of the findings and sufficient controls are crucial for the RAST's validity.[80]

- **Total Serum IgE**[81]: Total serum immunoglobulin (Ig) E does not provide a significant predictive value to diagnose these illnesses. The predictive value of this test is relatively low due to the high overlap between total IgE values in normal asymptomatic individuals and allergic rhinitis, atopic dermatitis, and allergic asthma, despite epidemiologic studies showing that these conditions are associated with increased levels of total IgE.

MANAGEMENT:

Non-pharmaceutical interventions:

- **Douching:** It aids in moisturising the skin and removes crusts, sweat, and pollutants. In the event of superadded infection, it facilitates the exfoliation of bacterial toxins.[82]

  It is advised to take a warm water bath once a day for no longer than five to ten minutes. It is recommended to implicate the "soak and smear" technique, which

involves immersing the affected areas in regular water for about 20 minutes before applying any topical medicaments without drying them out if the inflammation is severe and the site is not responding to simple anti-inflammatory medication.[83] Syndets or soap-free cleansers that are hypoallergic, odourless, and have an ideal pH of 5.5 are recommended.[82,83] The severity of AD can be lessened by taking a bleach bath (body below the neck is submerged in a tub with around 150 gallons of water and half a cup of commercial bleach at a concentration of 6 per cent), thereby decreasing bacterial colonisation.[82]

- **Wet-wrap therapy:** When intense eruptions occur, this approach is tried. Here, a topical substance is applied to the skin, followed by two layers of covering that can be left on for up to a day. Soaked gauze, tube bandages, or cotton wrap make up the first/inner layer, while a dried covering makes up the second/outer layer. This method benefits by creating a physical barrier, enhancing topical ingredient penetration, and retaining moisture.[83]
- **Garments:** Wearing long-sleeved, cotton apparel that is smooth, supple, and loose is recommended. Avoiding rough, irritating materials like wool is beneficial.[82]
- **Environment:** Proper ventilation is necessary to reduce sweating in warm climates because it can exacerbate AD. Swimming can aggravate skin inflammation or induce xerosis; hence it should be avoided during flare-ups.[82]
- **Airborne allergens:** HdM functions as both an allergy and a general irritant. The only defences against them are routine cleaning, dusting, and scrubbing.[82]
- **Emollients:** It promotes the repair of defective epidermal barrier function by replenishing skin barrier lipids.[82] It contributes significantly to flare prevention and maintenance.[83] Ideally, it has to be smeared swiftly after showering while the skin is moist.[82] Emollients have to be applied adequately and repeatedly throughout an acute

flare.[83] The usage of greasy crème emollients has increased in AD. Coconut oil and sunflower oil are two beneficial vegetable oils.[82] A more recent line of topical medicaments called prescription emollient devices (PEDs) is created to address skin barrier function deficits in AD. They include creams containing palmitoylethanolamide, glycyrrhetinic acid, or other hydro lipids and preparations for having specific ratios of lipids that imitate endogenous components. Based on the particular agent, they are typically advised to use it twice or thrice daily.[83]

Pharmacological Treatment:

Topical agents:

- **Topical corticosteroids (TCS):** These anti-inflammatory medications are prescribed when the lesions do not improve after receiving good skincare and regular moisturising. They improve acute and chronic symptoms of AD, as well as pruritis. Active inflammatory lesions are managed with TCS. It is used briefly to manage symptoms during acute flares promptly.[83] It is advised to apply one or two times daily. Mid to high-potent steroids are recommended during acute flare-ups. They should be continued until eczema clears up before being progressively discontinued or tapered with TCS of lower potency.[82] TCS with the least potency that is effective helps minimise adverse effects when used in long-term treatment.[83] To extend the period without symptoms, it is advised to take a "proactive" strategy, which involves intermittent (one or two times per week) application of TCS to areas most susceptible to recurrence despite the absence of any lesions.[82]
- **Topical calcineurin inhibitors (TCI):** The two TCIs offered are tacrolimus (0.03% and 0.1%) ointment and pimecrolimus (1%) cream. Both active inflammatory conditions and relapse prevention are addressed by their use. There are no reported

adverse effects of TCI with their use.[83] Patients under the age of two can use tacrolimus 0.03% ointment and pimecrolimus cream, but ≥ 16 years can only use tacrolimus 0.1%.[82,83] Application is advised two times daily. Proactive use of TCI over recurring areas of lesions up to 2-3 times per week minimizes resurgence.[83]

- **Topical antibiotics and antiseptics:** Not frequently advocated, except for those with a secondary bacterial illness, in whom a bleach bath and intranasal mupirocin are advised.[83]
- **Crisabarole:** It is a phosphodiesterase four inhibitors available in a concentration of 2% (20 mg per gram) ointment formulation. Approved by the United States Food and Drug Administration (US-FDA) for use in patients aged two years and above with mild-to-moderate conditions. Twice daily, a thin coating should be applied to the affected area.[84] It has few adverse effects, such as a burning or stinging sensation, and is well tolerated.[85,86]
- **Tapinarof:** It is a novel non-steroidal anti-inflammatory agent being tested in clinical settings that could be beneficial for AD.[57]
- **Topical jak inhibitors:** Ruxolitinib 1.5% cream has been US-FDA approved for use in patients 12 years and older with mild to moderate AD. It possesses both anti-inflammatory and antipruritic properties.[87] Topical delgocitinib ointment of 0.5% and 0.25% has been approved in japan for adults and the paediatric age group. Twice daily application not exceeding 5 g per dosing is recommended.[88]

TOPICAL JAK INHIBITORS	AGE GROUP
Ruxolitinib 1.5% Cream	12 Years And Older
Deglocitinib O.5% Ointment	Adult
Deglocitinib 0.25% Ointment	Paediatric

Table 3: Showing Topical Jak Inhibitors[87,88].

Systemic agents:

- **Antihistamines:** H1 receptor-mediated properties like vasodilation, oedema, and erythema are inhibited by histamine-1 (H1) receptor antagonists. They are implicated in controlling pruritis. Due to their lipophilic nature, first-generation antihistamines penetrate the blood-brain barrier and cause drowsiness. This property enhances the patient's sleep quality. First-generation antihistamines should, therefore, only be used temporarily and infrequently in AD. Antihistamines of the second generation are less drowsy and don't pass the blood-brain barrier. They can be used on a long-term basis until subjective symptoms are improved.[89]
- **Antibiotics:** Systemic antibiotics should not be used in cases of non-infected AD and are advised only for individuals displaying symptoms of bacterial infection.[90]
- **Corticosteroids:** It only plays a constrained part in treating severe AD exacerbations and are used in shortened courses when an acute flare occurs. The dose must be gradually lowered over weeks to avoid steroid withdrawal, which could trigger intense eczema flare-ups. Systemic corticosteroid use over an extended period has serious side effects.[89]
- **Cyclosporine (CsA):** It is an immunosuppressive medication that works by inhibiting T-cell function. As a result, it helps with AD by inhibiting Th2 and Th1 responses during the disease's acute and chronic phases.[89] It is an effective medication for severe AD resistant to topical therapies.[90] CsA enhances the Patient's quality of life by reducing itch and clinical lesion progression.[89] The dosage is 3-6 mg/kg/day, which is advised. Once the lesions have healed, they must be reduced or stopped.[90]
- **Azathioprine (AZA):** It is a purine analogue used to treat resistant AD and selectively targets B and T-cells. AZA has been shown to reduce AD symptoms and

enhance QOL. Depending on thiopurine methyltransferase enzyme levels, the dosage might range from 1-3 mg/kg/day. Children can get doses ranging from 2.5 mg/kg/day to 4 mg/kg/day. The drug should be reduced and stopped once the lesions have healed; then moisturisers and topical treatments should be used to maintain the condition.[90]

- **Methotrexate (MTX):** AD is among the off-label uses for MTX. It is suggested for the management of severe and resistant patients. It usually takes ten weeks to get the actual response.[90]
- **Mycophenolate mofetil (MMF):** MMF is favoured in cases of refractory AD and is used off-label for AD. Yet, there is not enough information on its use in AD.[90]
- **Dupilumab:** US-FDA-approved medication for patients 12 years of age and older with moderate-to-severe AD. Subcutaneous injection is the method of administration. It is administered to adults at a 600 mg dose (two injections of 300 mg), then with a dose range of 300 mg once every other week.[91] Dosage in adolescents is divided based on the weight of the patient. If the patient weighs less than 60kgs initial dose of 400mg (200mg injections two times) is followed by 200mg every other week, and if the weight is more than or equal to 60kgs initial dose of 600mg (300mg injection two times) followed by 300mg every other week is given.[92]
- **JAK inhibitors:** Upadacitinib, available in 15mg and 30mg doses, is US-FDA-approved for use in greater than or equal to 12 years of age with resistant moderate to severe AD.[93] Abrocitinib has been approved in 100 mg and 200 mg for adult patients with resistant moderate to severe AD; patients who don't react to the 100 mg dose are advised to take the 200mg dose.[94]

Other systemic treatments (both existing and in assessment):[86,95]

Molecule	Directed against
Tezepelumab[91]	Anti-TSLP
Apremilast	Phosphodiesterase-4 (PDE4) inhibitor
Fezakinumab[96]	Anti-IL-22
Ustekinumab	Anti-IL-12/23
Nemolizumab	Anti-IL-31/31 Receptor
Secukinumab	Anti-IL-17A
Tralokinumab, Lebrikizumab	Anti-IL-13
Dupilumab[97]	Anti-IL-4/13
Omalizumab	Anti-IgE
Interferon ɣ (IFN- ɣ)[90]	Interferon ɣ (IFN- ɣ)

Table 4: Oral biologics and other substances used in AD

Phototherapy: Several types of phototherapy are effective for treating AD, including natural sunshine, narrowband (NB) ultraviolet (UV) B (NBUVB) therapy, broadband (BB) UVB therapy, UVA therapy, psoralen plus UVA (PUVA) therapy, UVA with UVB (UVAB) therapy, and Goeckerman therapy. The most frequently suggested of these approaches is NB-UVB. The dosage is chosen based on the Fitzpatrick skin type and the minimal erythema dose. Phototherapy is generally advised as a treatment option for kids who don't respond well to multifaceted topical therapy.[90]

Role of NLR, PLR AND MPV in other inflammatory conditions:

- Individuals with allergic rhinitis were shown to have higher NLR levels, which also elevated as the condition got severe.[98]
- NLR was higher in asthma patients, and it was associated with hospitalization.[99]
- NLR and PLR were significantly elevated with the severity of SLE and psoriasis. [25,26,100]
- MPV levels were positively correlated with the severity of chronic urticarial and SLE.[101,102]

Jiang Y *et al.* found that NLR, PLR, and eosinophils were all considerably greater in AD patients than in healthy people after comparing 80 AD patients and 45 healthy controls. When comparing eosinophils, NLR and PLR among AD patients showed a positive correlation with the SCORAD score.[103]

Batmaz S B *et al.* found that AD patient's mean NLR and median PLR levels were more significant than controls in a study comprising 252 AD patients and 75 controls. NLR and PLR levels were positively correlated to disease duration, while NLR was positively associated with disease duration after adjustment. The extrinsic group likewise had a higher NLR value than the intrinsic group.[27]

Gayret O B *et al.* conducted a study with 154 children aged 1 to 60 months, with 79 among the AD group and 75 in the healthy individuals. MPV levels in children with AD were considerably more significant than in the control group and positively correlated with disease severity.[104]

Gunes H S *et al.* did a study with 64 children with AD aged 2-12 months and 50 healthy infants of similar age and gender as controls. The MPV values of the individuals were compared between groups. The MPV values of the AD group were significantly lower than the control group, and there was a positive correlation between platelet counts and the

SCORAD index. Therefore, a decrease in MPV and platelets could be considered an indicator of inflammation in infants with AD.[105]

METHODOLOGY

1. SOURCE OF DATA

Patients suffering from atopic dermatitis presenting to the Dermatology, Venereology and Leprosy OPD at Shri B.M. Patil Medical College Hospital and Research Centre, Vijayapura, were enrolled for the study.

Period of study:

This study was conducted from January 2021 to June 2022.

Study design:

A hospital-based cross-sectional study.

Sample size:

With the anticipated proportion of Atopic dermatitis severity according to SCORAD 18.8%, the study required a sample size of 165 with a 95**%** level of confidence and 6% absolute precision**.**

Formula used

- $\mathbf{n=\frac{z^2\ p*q}{d^2}}$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

Statistical Analysis:

- The data obtained were entered into a Microsoft Excel sheet, and statistical analysis was performed using a statistical package for the social sciences (Version 20).
- Results are presented as Mean (Median) ±SD, counts and percentages and diagrams.
- Pearson/Spearman's Correlation was used to find the correlation between quantitative variables.
- Association of categorical variables was computed using the Chi-square test.
- $p<0.05$ was considered statistically significant. All statistical tests were performed in two-tailed.

METHOD OF COLLECTION OF DATA:

Patients suffering from atopic dermatitis, irrespective of gender, aged up to 18 years, were enrolled in the study after obtaining consent.

Inclusion criteria:

1. Patients of age group up to 18 years with atopic dermatitis confirmed clinically based on U.K. working party criteria.

Exclusion criteria:

1. Patients not willing to give consent
2. Patients with co-existing conditions, e.g. eczema herpeticum, molluscum contagiosum, impetigo, hand, foot and mouth disease.

METHOD:

- An initial clinical examination was done, and clinical symptoms and signs with skin lesions were recorded in the proforma; the diagnosis was made in accordance with U.K. Working party criteria.

- Disease severity was calculated using SCORAD [sum of extent (A)/5 + 7 x intensity (B)/2+C (subjective symptoms)] – A: affected area calculated by the rule of nine, B: Intensity of the lesions assessed as none (0), mild (1), moderate (2), severe (3), C: Subjective symptoms such as itching, sleeplessness with a maximum score of 20%.
- After obtaining consent, the blood sample of 3ml was collected in an EDTA tube and sent for a complete blood count.
- Neutrophil lymphocyte ratio (NLR) was obtained by dividing the total number of neutrophils by the total number of lymphocytes.
- Platelet lymphocyte ratio (PLR) was obtained by dividing the total number of platelets by the total number of lymphocytes.
- Mean platelet volume (MPV) was obtained from the laboratory blood report.
- These values were represented in a table, and their values were correlated with the severity and duration of AD.

ETHICAL CLEARANCE :

Institutional ethical clearance was obtained for the study.

RESULTS

A hospital cross-sectional study was conducted from January 2021- June 2022. A total of 165 patients diagnosed with atopic dermatitis belonging to the paediatric age group of up to 18 years were included.

Distribution of age:

The mean age of the AD patients was 6.21 ± 5.125 years. A total sum of 165 patients was included. The majority of the patients belonged to 2-12 years of age, followed by less than 2 years and more than 12 years of age, as mentioned in the figure and table below:

Age group	No. Of. Patients	Percentage
< 2 years	32	19.4
2 – 12 years	109	66.1
More than 12 years	24	14.5
Total	165	100.0

Table 5: Age distribution

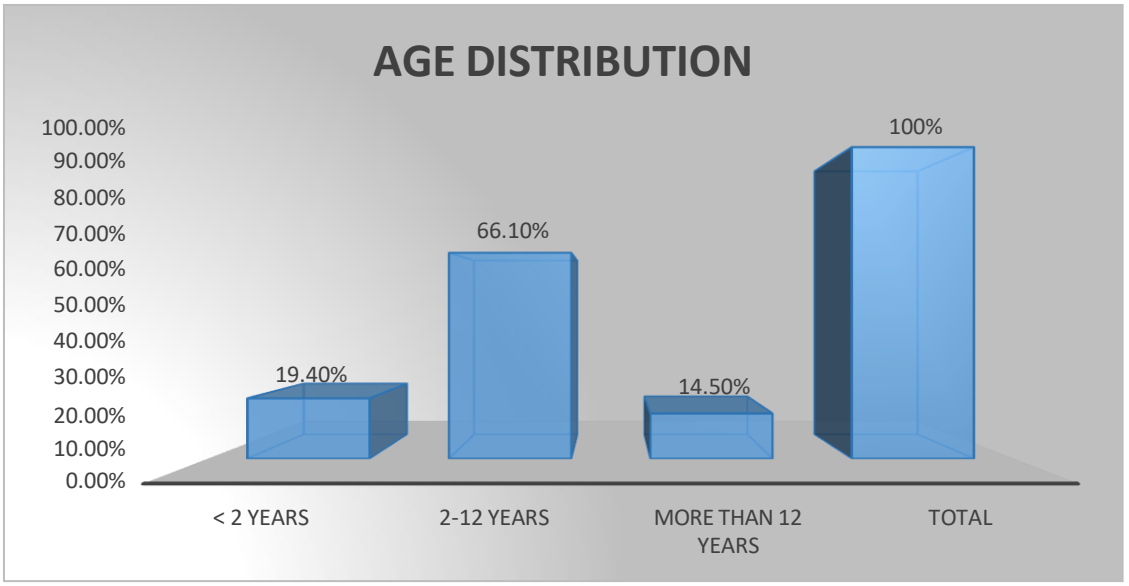

Figure 8: Distribution of age

Gender distribution:

Among 165 patients, 89 (53.9%) were male, and 76 (46.15%) were female, with a sex ratio of 1.17:1, as demonstrated in the figure and table below:

Parameters	No. Of. Patients	Percentage
Male	89	53.9%
Female	76	46.15
Total	165	100%

Table 6: Gender distribution

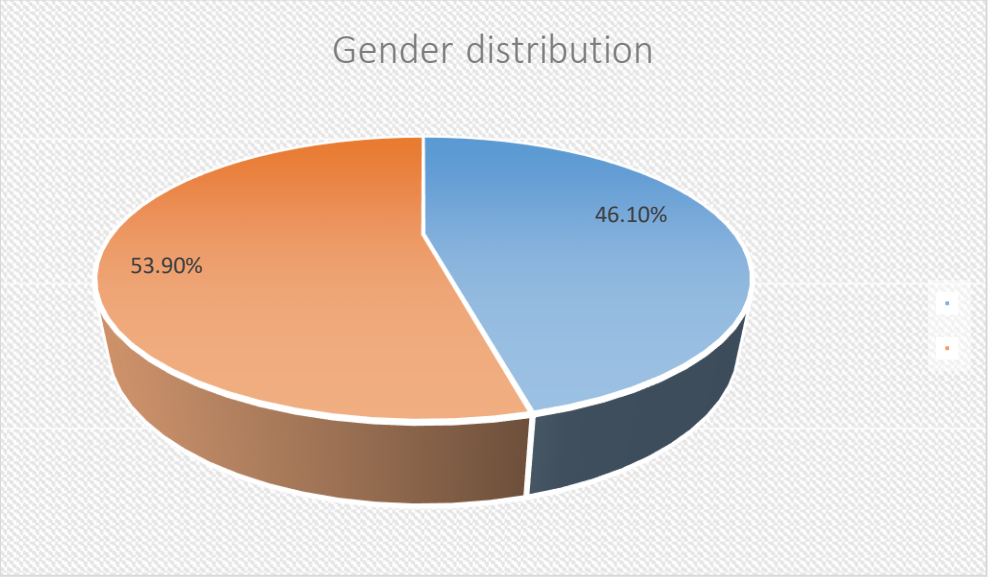

Figure 9: Distribution of gender

Relation between NLR, PLR and MPV:

When correlation analysis was performed between these three parameters, NLR had a positive correlation with PLR, but surprisingly MPV had a negative correlation with both NLR and PLR.

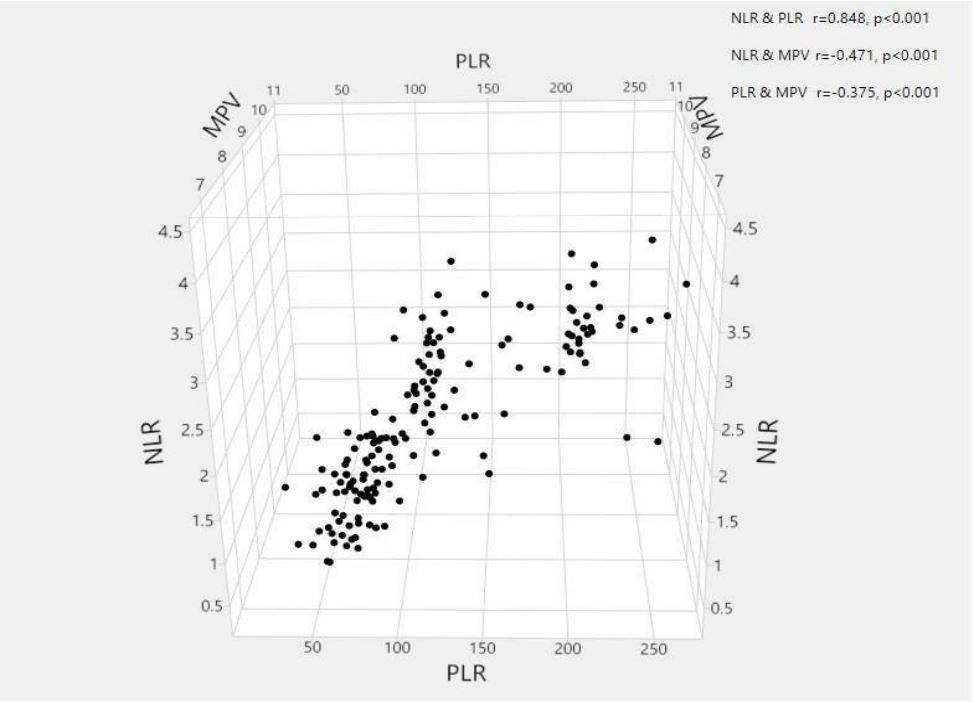

Figure 10: Scattered plot showing the Correlation between NLR, PLR and MPV.

Severity groups:

Based on the SCORAD index, they were classified as mild, moderate and severe. Among them, 78 (47.3%) were mild, 52 (31.5%) in moderate, and 35 (21.2%) were in the severe group.

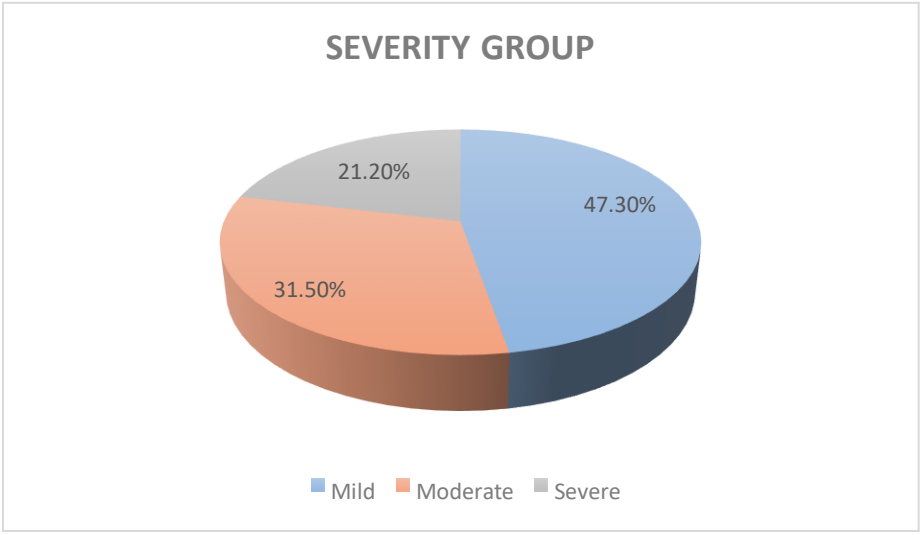

Figure 11: Severity groups

The mean NLR value was 0.64 ± 0.259, 2.20 ± 0.373, and 3.10 ± 0.427 in mild, moderate and severe groups. The mean PLR value was 63.31 ± 12.73, 122.73 ± 19.33, and 217.67 ± 23.639 among mild, moderate and severe groups. The mean MPV value was 8.77 ± 0.923, 8.43 ± 0.918 and 7.60 ± 0.559 among mild, moderate and severity groups. There were significant differences in the mean/standard deviation of NLR, PLR, and MPV values between these groups, as shown in Table 7. NLR and PLR values increased according to severity, while MPV values decreased with severity, as shown in Fig 12, 13, and 14.

	N	Mean	Std. deviation	p-value
NLR				
Mild	78	.641154	.2595700	0.000
Moderate	52	2.202115	.3732703	
Severe	35	3.106000	.4276626	
PLR				
Mild	78	63.318333	12.7334057	0.000
Moderate	52	122.739808	19.3360721	
Severe	35	217.676286	23.6393483	
MPV				
Mild	78	8.776923	.9232809	0.000
Moderate	52	8.436538	.9188716	
Severe	35	7.600000	.5599370	
STATISTICALLY SIGNIFICANT				

Table 7: Demonstrates the differences between NLR, PLR and MPV values among severity groups.

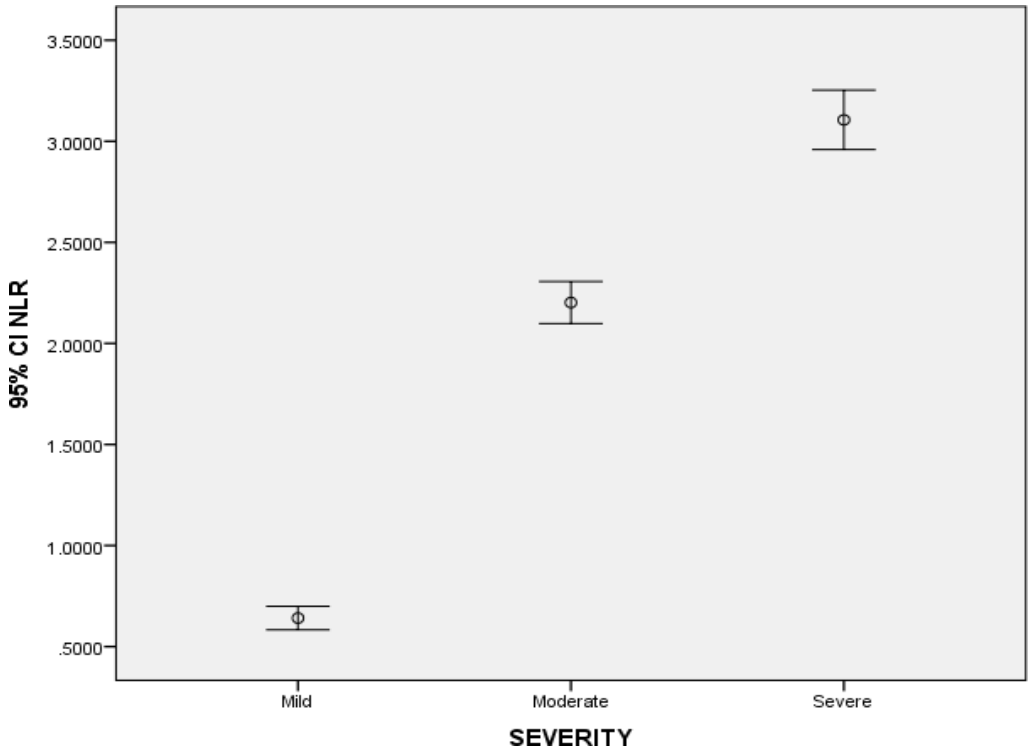

Figure 12: NLR increasing in severe groups

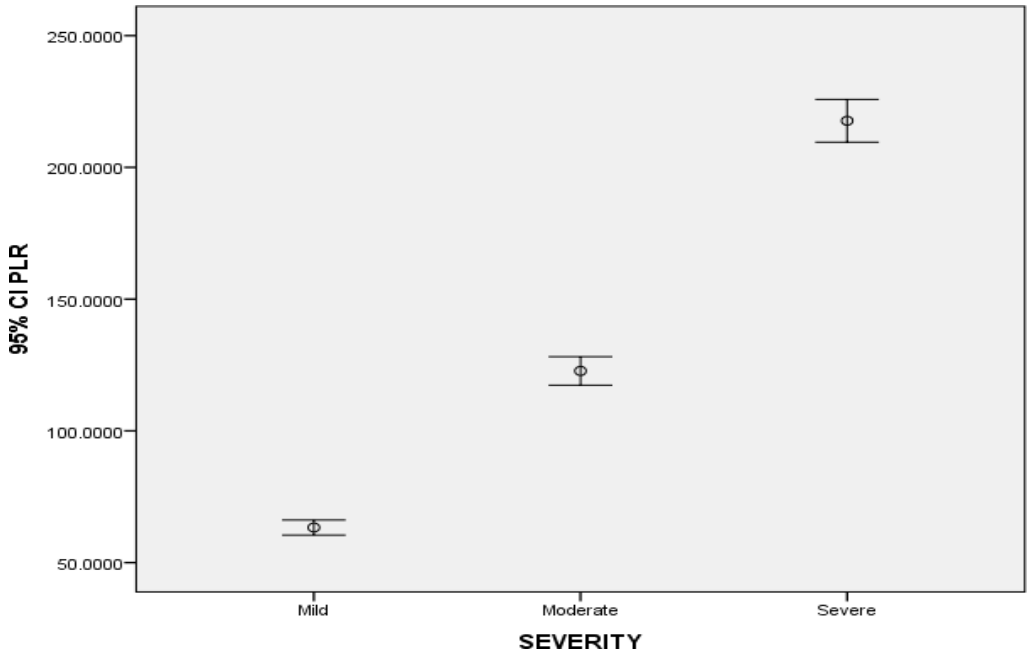

Figure 13: PLR increasing with severity groups

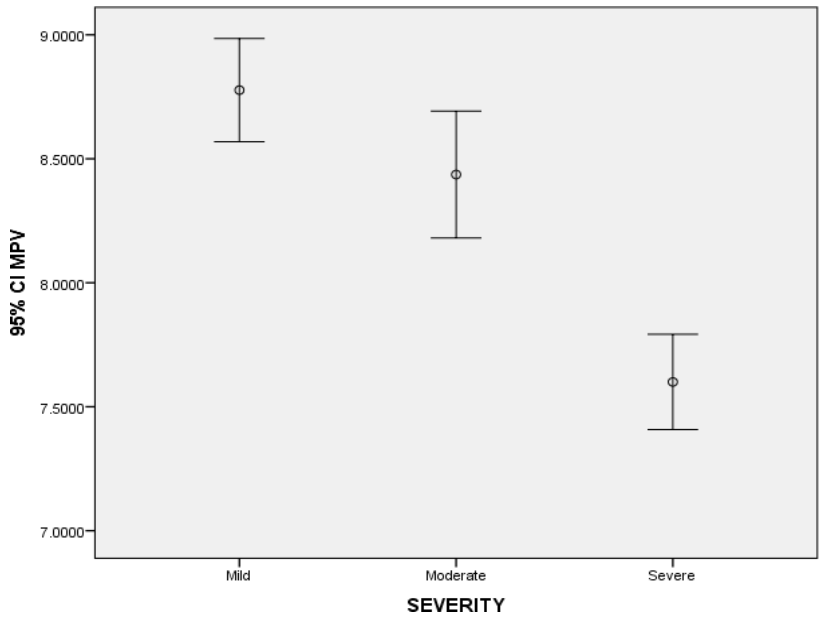

Figure 14: MPV values decreasing with severity.

NLR ($p<0.001$, $r=0.868$) and PLR ($p<0.001$, $r=0.836$) showed a positive correlation with the SCORAD Score, whereas MPV ($p<0.001$ $r=-0.405$) had a negative correlation with SCORAD Score, as shown in Figures 15, 16 and 17.

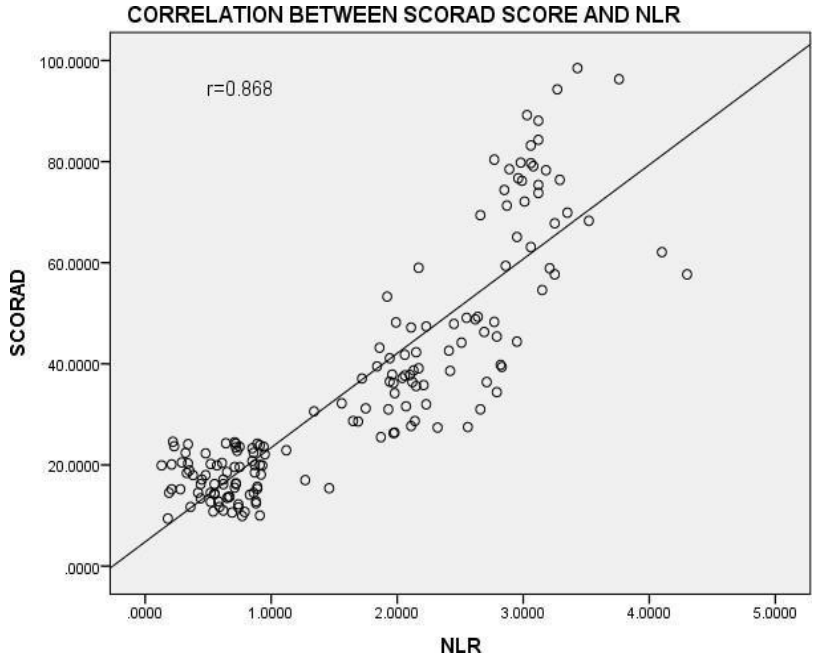

Figure 15: NLR with SCORAD

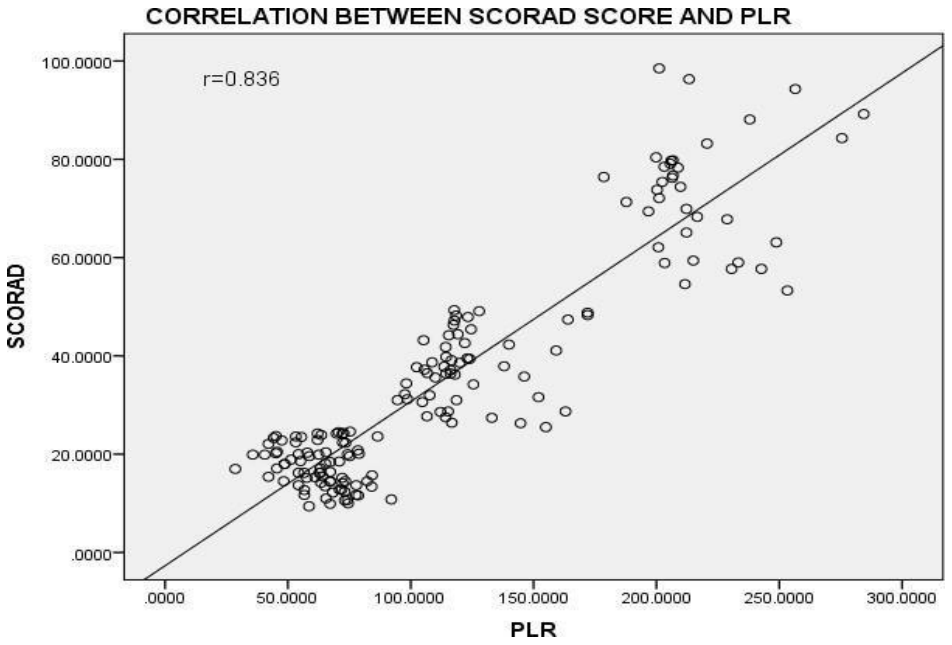

Figure 16: PLR and SCORAD

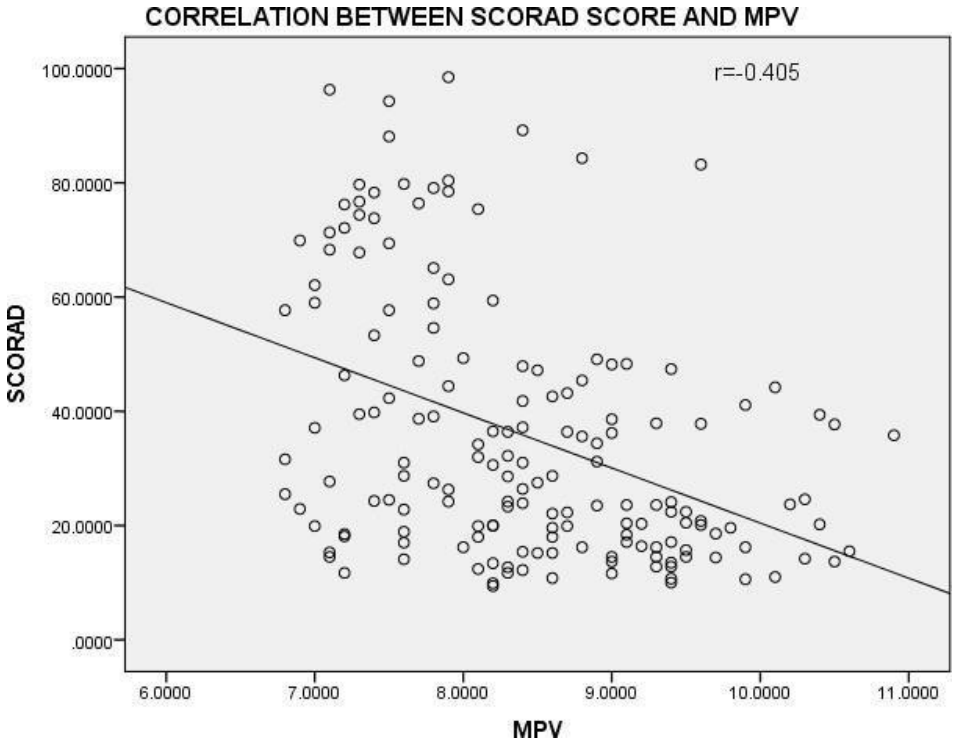

Figure 17: MPV with SCORAD

Disease Duration:

When correlated with duration, NLR ($p<0.033$, $r=0.166$) had a positive correlation with statistical significance, whereas PLR ($p< 0.212$ $r= 0.098$) had a positive correlation without significance. But, MPV ($p<0.586$, $r= -0.043$) did not correlate with duration.

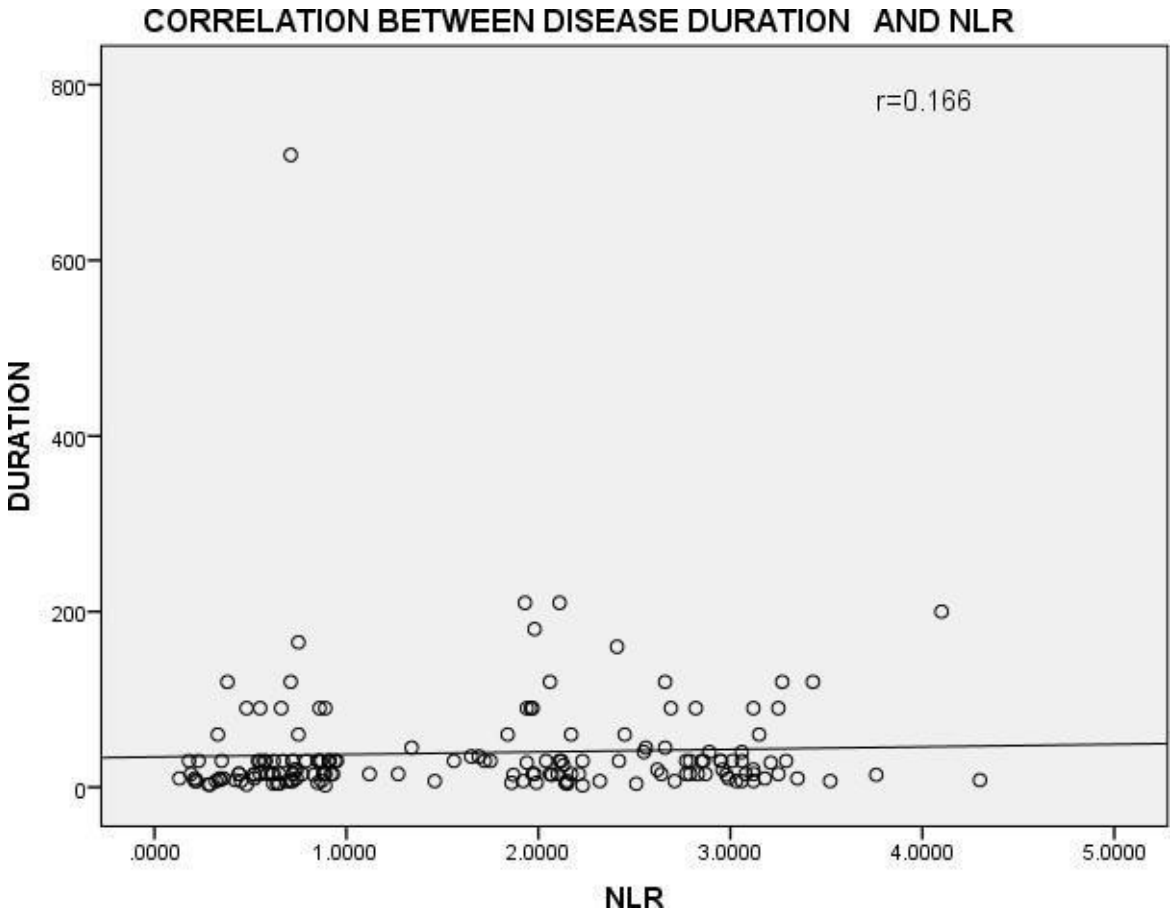

Figure 18: NLR with duration

Parameters	p	r
NLR	0.033	0.166
PLR	0.212	0.098
MPV	0.586	-0.043

TABLE 8: Correlation with duration

ROC Curve:

"In the Receiver Operating Characteristics (ROC) curve for diagnostic accuracy of severity index (SCORAD more than 50), the area under ROC (AUROC) of NLR is 0.982 (95% of Confidence Interval =>2.71 to >2.95%), and the optimal cut-off value is >2.83." Using this cut-off value, the sensitivity and specificity are 88.57% and 99.23%.

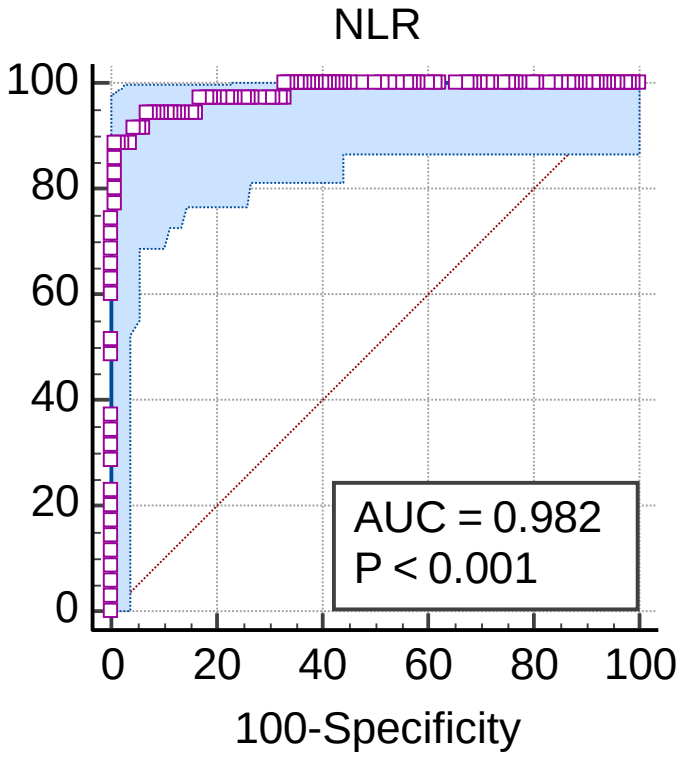

Figure 19: AUROC OF NLR

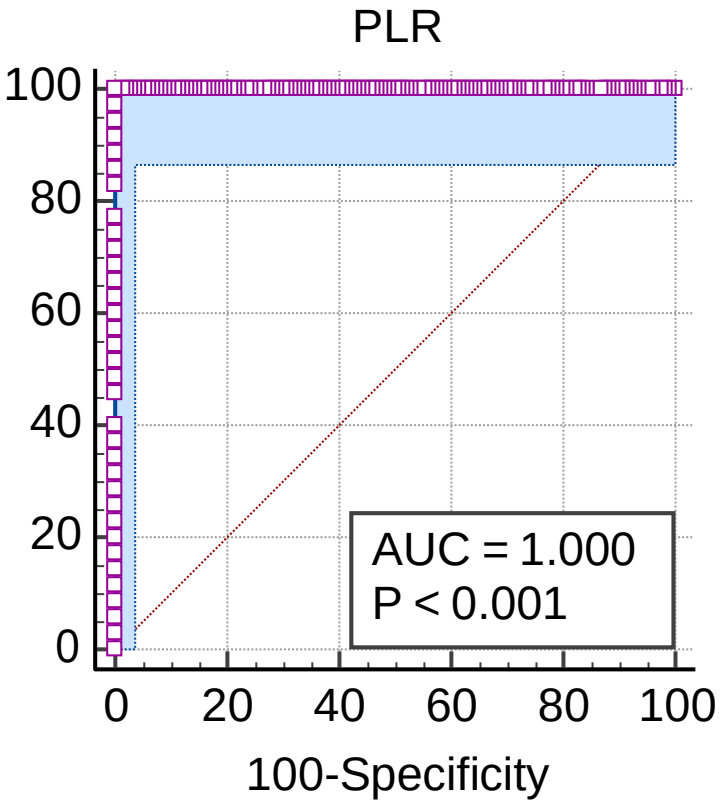

Figure 20: AUROC OF PLR

The area under ROC (AUROC) of PLR is 1.000 (95% of Confidence Interval = >164 to >172%), and the optimal cut-off value is >172. Using this cut-off value, the sensitivity and specificity are 100% and 100%.

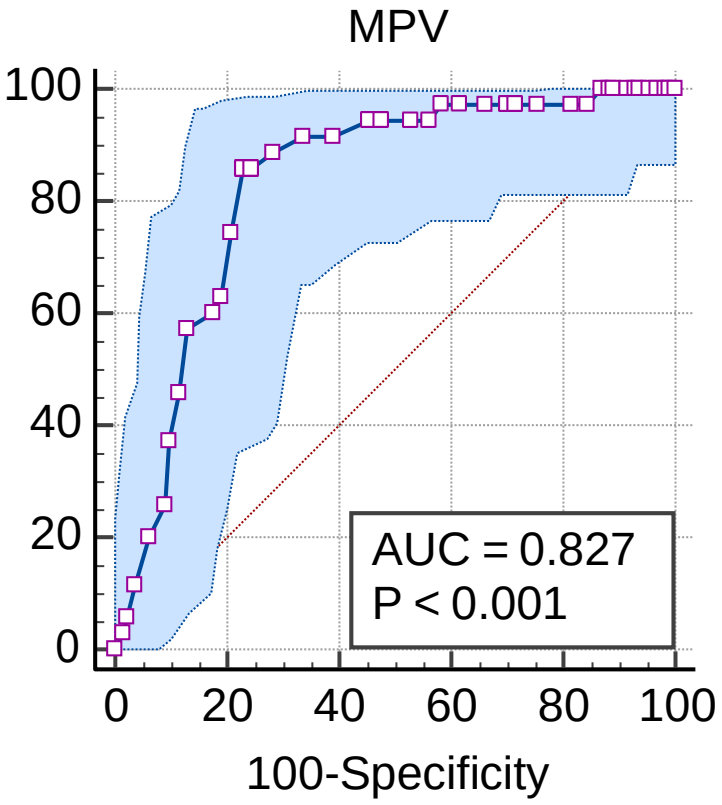

Figure 21: AUROC OF MPV

The area under ROC (AUROC) of MPV is 0.827 (95% of Confidence Interval = ≤7.7 to ≤8.2%), and the optimal cut-off value is ≤7.9. Using this cut-off value, the sensitivity and specificity are 85.71 and 76.92. When comparing the diagnostic accuracy of these three parameters in predicting severity, PLR had a higher AUROC (1.000 and p<0.001) than NLR and MPV, with 100% Sensitivity and Specificity.

Parameters	AUROC	SENSITIVITY	SPECIFICITY	CUT OFF VALUE	95% Confidence interval
NLR	0.982	88.57	99.23	>2.83	>2.71 to >2.95
PLR	1.000	100.00	100.00	>172	>164 to >172
MPV	0.827	85.71	76.92	≤7.9	≤7.72 to ≤8.2

Table 9: Diagnostic accuracy in terms of severity between three Parameters.

DISCUSSION:

Atopic dermatitis is a prevalent, persistent, recurring, inflammatory skin condition that primarily affects children, with few cases progressing into adulthood.[1] It is characterised by intense itching, dryness and eczematous regions with crusting manifesting in an age-dependent pattern, with face, scalp, and extensor involvement in infants and flexural predominance in the older age group.[2,3] Familial and Personal history of "atopic diathesis" is present in most affected patients. Mere existence like allergic rhinitis, bronchial asthma, or atopic dermatitis is referred to as "atopic diathesis."[4]

There is no gold standard diagnostic laboratory marker or diagnostic criteria for atopic dermatitis.[6] But, we have opted U.K working party criteria to diagnose atopic dermatitis in our study as it is relatively easier to apply and the only criteria which have undergone multiple validation trials in hospital and population-based settings.[7,9,10,11]

Recently, the development of systemic and local inflammation has been implicated in the pathophysiology of atopic dermatitis.[27] In our study, we intended to correlate the levels of NLR, PLR and MPV values with disease duration and severity and assess the accuracy of these inflammatory biomarkers in determining the severity.

The prevalence of AD is generally higher in women.[37] However, recent research has shown a male majority at an earlier age.[103] In our study, the sex ratio was 1.17:1, with a male predominance which aligned with a study done by Jiang Y *et al.*[103] We also found that the majority of the patients belonged to 2-12 years of age (66.1%), followed by less than 2 years of age (19.4%) signifying that most of them belonged to childhood stage of atopic dermatitis.

The severity of Atopic dermatitis must be analysed to assess the disease process and quantify intervention by treatment. As a result, it must be objective as possible.[12] The most accurate

scoring system for atopic dermatitis is the SCORAD (Index).[12,13] Based on the severity assessed through the SCORAD index, our study constituted a majority of the patients in the mild group (47.3%) followed by moderate (31.5%) and least in the severity group (21.2%).

In our study, interestingly, the intervariable relationship between NLR, PLR and MPV showed a positive association between NLR and PLR. An inverse correlation between MPV, NLR and PLR were similar to the association observed with the SCORAD index.

NLR is a marker of systemic inflammation. Increased NLR values have been shown in the literature to be linked with disease presence and outcome in various nonallergic conditions. Asthmatics had higher NLR than the healthy controls, which was related to hospitalisation.[99,106] In a study done by Dogru M *et al.* determining the association between NLR and severity of allergic rhinitis, NLR values were more significant in allergic rhinitis individuals than in the control group, and NLR values increased with disease severity.[98] Furthermore, the severity of AD, as measured by the SCORAD index, is associated with the incidence of asthma or allergic rhinitis.[107]

In the literature, only two studies were done by Batmaz SB *et al.* and Jiang Y *et al.* in determining the association between NLR with disease duration and severity, showed a positive correlation between the same, which was in line with our results. The mean NLR values were 0.64, 2.202, 3.106 in mild, moderate and severe groups, and we observed significant differences in mean NLR values in the severity groups.[27,103] This might suggests systemic inflammation in AD may align with the length of duration and severity of the cutaneous manifestation, which is reflected by NLR value being directly proportionate to increased duration and severity associated with significant statistical correlation found in our study. The AUROC of NLR in our study was 0.982, and the optimal cut-off value is >2.83. Using this cut-off value, the sensitivity and specificity were 88.57% and 99.23%.

Many studies in the literature have focused on the role of platelets in inflammation. During inflammation, platelets become activated, and the rate of platelet synthesis is accelerated. By engaging with endothelia, platelets produced chemotaxis signals and increased the production of adhesion molecules. They augmented the inflammation by promoting the release of pro-inflammatory mediators.[108,109]

A study done by Kim DS *et al.* in assessing PLR with psoriasis vulgaris and psoriatic arthritis and a study by Wu Y *et al.* in determining PLR with disease activity in patients with systemic lupus erythematosus (SLE) showed that PLR was associated with disease severity in SLE and psoriasis.[25,100] In our study, PLR was positively correlated with the SCORAD index but did not have any association with duration.

A study was done to assess the role of NLR and PLR in patients with atopic dermatitis by Jiang Y *et al.* also found similar results in their research with PLR and disease severity.[103] But a study by Batmaz SB *et al.* to assess the systemic inflammation using simple markers in atopic dermatitis of the paediatric population concluded that PLR had a positive correlation with duration.[27]

The mean PLR values were 63.31, 122.7, 217.7 in mild, moderate and severe groups and statistically significant differences was found among the mean PLR values in the severity groups. PLR had a higher ROC (1.000) in predicting severity (SCORAD >50) with 100% sensitivity and specificity, and the optimal cut-off value was >172.

The role of MPV in inflammation demonstrates that cytokines lowered platelet sizes during inflammation, allowing smaller platelets to be discharged into the bloodstream and making decreased MPV a sign of inflammation.[110] Other studies have suggested that more giant platelets released to the bloodstream due to enhanced platelet turnover brought on by platelet activation serve as a signal of inflammation.[27] A study was done by Aleem S *et al.* to

correlate the levels of MPV with the severity of chronic urticaria, and a study by Yavuz S *et al*. to find the role of MPV indicating Juvenile SLE concluded that MPV positively correlated with disease activity in chronic urticaria and SLE.[101,102]

In our study, MPV had a negative correlation with the SCORAD index and no association with duration. The mean MPV values are 8.77, 8.43 and 7.6 in the mild, moderate and severe groups. There were differences in MPV values between severity groups, which were significantly lower when the severity increased. Gunes H S *et al.* conducted a study to evaluate MPV in patients with AD of age group less than 1 year and concluded that MPV values decreased in AD patients compared to healthy controls but did not find any correlation with disease severity.[105] In a study done by Gayret O B *et al.* to determine the role of NLR and platelet indices as an indicator for assessing severity in children with AD showed that MPV was positively correlated with disease severity and was significantly higher in the AD group compared to controls which contrasted the finding observed in our study. The area under ROC (AUROC) of MPV is 0.827, and the optimal cut-off value is ≤7.9 in predicting severity (SCORAD > 50). Using this cut-off value, the sensitivity and specificity were 85.71% and 76.92%.

In this study, we sought to correlate the levels of NLR, PLR and MPV levels with disease duration and severity in paediatric atopic dermatitis and conclude that as the duration and intensity of cutaneous manifestation increases, there is a probability of systemic inflammation accumulating in the body paving the way towards the atopic march, i.e., bronchial asthma and allergic rhinitis.[2] We found statistically significant differences between the severity groups among NLR, PLR and MPV. Secondly, NLR and PLR increased with SCORAD, whereas MPV decreased, reflecting inflammation and severity of the disease. Third, NLR increased with disease duration, denoting chronic inflammation. Higher NLR value might suggest the

inclusion of systemic immunosuppressants as the treatment modality in addition to topical emollients, corticosteroids and calcineurin inhibitors. Fourth, a comparison between inflammatory markers like NLR, PLR and MPV showed that PLR carries a sensitivity and specificity of 100% with a statistically significant association ($P<0.001$). This may reflect that PLR is a better inflammatory biomarker than NLR and MPV. Hence, inflammatory markers like NLR, PLR and MPV could be used to assess the systemic inflammation associated with atopic dermatitis.

However, there are a few limitations in this study which include the following;

1. Absence of control group.

2. Few numbers of patients in the severe group.

3. Absence of intrinsic and extrinsic group

CONCLUSION:

Atopic dermatitis is a chronic inflammatory condition with frequent remissions and relapses. There is no gold standard diagnostic laboratory marker or criteria for atopic dermatitis. But, we have opted U.K working party criteria to diagnose atopic dermatitis in our study as it is relatively easier to apply and the only criteria which have undergone multiple validation trials in hospital and population-based settings. SCORAD was used to assess the severity and extent of the disease.

This was a hospital-based cross-sectional study consisting of 165 patients belonging to the paediatric age group. The mean age of the study population was 6.21 ± 5.125 years, and the majority of the patients were 2-12 years of age. Among them, 89 are male and 76 were female.

Correlation analysis between NLR, PLR and MPV revealed NLR having a positive correlation with PLR and MPV displaying a negative correlation between both NLR and PLR. Based on the SCORAD index, 78 (47.3%) were mild, 52 (31.5%) moderate and 35 (21.2%) belonged to the severe group.

There were significant differences between the severity groups among NLR, PLR and MPV values.

NLR had a positive correlation with the SCORAD index, i.e., severity score and duration. PLR had a positive correlation with the SCORAD index but not with duration, whereas MPV had an inverse correlation with severity but no association with duration.

The AUROC of NLR in our study was 0.982, and the optimal cut-off value is >2.83. The sensitivity and specificity were 88.57% and 99.23%.

PLR had a higher ROC (1.000) in predicting severity (SCORAD >50) with 100% sensitivity and specificity, and the optimal cut-off value was >172. The AUROC of MPV is 0.827, and the optimal cut-off value is ≤7.9 in predicting severity (SCORAD > 50), with the sensitivity and specificity being 85.71% and 76.92%. This may reflect that PLR is a better inflammatory biomarker than NLR and MPV in predicting systemic inflammation respective to high SCORAD.

Even though there are numerous sophisticated biochemical assays available to assess the systemic inflammatory response in AD for poorly resourced and economically challenged clinical infrastructures, NLR, PLR and MPV are cost-effective, feasible and readily available alternative tests to detect systemic inflammation in AD with good sensitivity and specificity. Additionally, it provides insight into the inclusion of therapeutic approaches like systemic immunosuppressants alongside conventional management techniques like topical therapy.

SUMMARY:

A Hospital-based cross-sectional study to correlate the levels of NLR, PLR and MPV values with disease duration and severity in paediatric atopic dermatitis was conducted between January 2021 to June 2022.

- 165 patients aged up to 18 years diagnosed with atopic dermatitis were included in the study.
- The mean age of the patients was 6.21 ± 5.125 years. The majority of the patients belonged to 2-12 years of age.
- Predominantly were males who were 89 in number, and male to female ratio in the study population was 1.17
- Based on SCORAD, they were classified as mild, moderate and severe.
- Among them, 78 (47.3%) were mild, 52 (31.5%) in moderate and 35 (21.2%) were in the severe group.
- There were statistically significant differences between the severity groups among NLR, PLR and MPV values.
- NLR was positively correlated with the SCORAD index and increased with disease duration.
- PLR had a positive correlation with the SCORAD index and had no association with disease duration.
- MPV had an inverse correlation with the SCORAD index, decreased when severity increased and did not have any association with disease duration.
- AUROC of PLR is 1.000, and the optimal cut-off value is >172. Using this cut-off value, the sensitivity and specificity were 100%, with better diagnostic accuracy in predicting high SCORAD.

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ANNEXURE- I

IEC/no-09/2021
Date-22/01/2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A study to correlate the levels of NLR, PLR and MPV ratio with duration and severity of the disease in paediatric atopic dermatitis

Name of PG student: Dr Mohnish Sekar, Department of Dermatology

Name of Guide/Co-investigator: Dr Arun.C.Inamadar, Professor & HOD of Dermatology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

3

ANNEXURE –II

B.L.D.E. (Deemed to be University)

SHRI B. M. PATIL MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE,

VIJAYAPURA.

DEPARTMENT OF DERMATOLOGY, VENEREOLOGY AND LEPROSY

SCHEME OF CASE TAKING

A STUDY TO CORRELATE THE LEVELS OF NLR, PLR AND MPV RATIO WITH DURATION & SEVERITY OF THE DISEASE IN PAEDIATRIC ATOPIC DERMATITIS PATIENTS

S.No: **Date:**

Name: **Hospital Number:**

Age / Sex:

Address and Contact Details:

Presenting Complaints & duration:

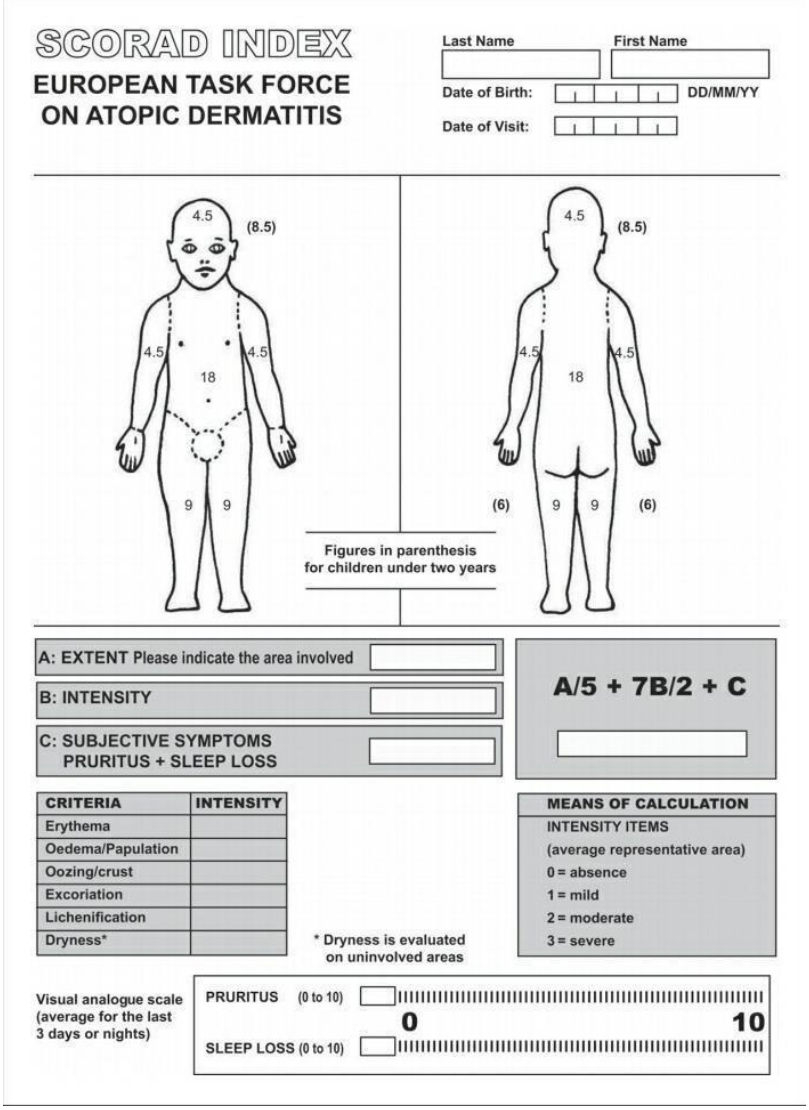
History of Present Illness:

Personal History:

Family History:

Cutaneous Examination:

SCORAD:



Clinical Diagnosis:

Investigations:

Complete blood count:

Parameters:

NLR	PLR	MPV

APPENDIX – III

B.L.D.E. (Deemed to be University)

SHRI B.M PATIL

MEDICAL COLLEGE HOSPITAL AND RESEARCH CENTRE,

VIJAYAPURA-586 103

RESEARCH INFORMED CONSENT FOR

TITLE OF THE PROJECT:- A STUDY TO CORRELATE THE LEVELS OF NLR, PLR AND MPV RATIO WITH THE DURATION & SEVERITY OF THE DISEASE IN PAEDIATRIC ATOPIC DERMATITIS.

PG GUIDE :- DR. ARUN. C. INAMADAR

PG STUDENT :- DR. MOHNISH SEKAR

PURPOSE OF RESEARCH: -

I have been informed that this project will correlate the levels of NLR, PLR and MPV ratio with the duration & severity of the disease in paediatric atopic dermatitis at Shri BM Patil Medical College and Research Centre, VIJAYAPURA.

BENEFITS:-

I understand that my participation in this study will help the investigator to know the association of NLR, PLR and MPV ratio with disease duration and severity in paediatric atopic dermatitis patients.

PROCEDURE:-

I understand that relevant history will be taken, and I will undergo a detailed clinical examination, after which relevant investigations will be done whenever required.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the hospital's confidentiality and privacy regulation. Information of a sensitive personal nature will not be a part of the medical records but will be stored in the investigator's research file.

Suppose the data are used for publication in the medical literature or teaching. No names will be used in that case, and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs and videos and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time. Dr Mohnish Sekar is available to answer my questions or concerns. I will be informed of any significant new findings discovered during this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary, and I may refuse to participate or withdraw consent and discontinue participation in this study at any time without prejudice. I also understand that Dr Mohnish Sekar may terminate my participation in this study at any time after he has explained the reasons for doing so and helped arrange my continued care by my physician if this is appropriate.

INJURY STATEMENT:-

I understand that in the unlikely event of injury resulting directly from my participation in this study. If such an injury were reported promptly, then medical treatment would be available to me, but no further compensation will be provided. I understand that I am not waiving my legal rights by my agreement to participate in this study.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in the patient's language.

_____ _____

Investigator / P. G. Guide Date:

I confirm that ……. (Name of the PG guide / chief researcher) has explained the research, the study procedures I undergo, and the possible risks, discomforts, and benefits I may experience. I have read and understand this consent form. Therefore, I agree to consent to participation as a subject in this research project.

_____ _____

Participant /Guardian Date:

_____ _____

Witness to signature Date:

KEY TO MASTER CHART

Y - Years

M - Male

F - Female

D - Days

SCORAD- Scoring Atopic Dermatitis

NLR - Neutrophil lymphocyte ratio

PLR - Platelet Lymphocyte Ratio

MPV – Mean Platelet Volume

MASTERCHART

S. No.	AGE (Y)	SEX	DURATION (D)	SEVERITY	SCORAD	NLR	PLR	MPV
1	6	F	15	Moderate	35.8	2.21	146.2	10.9
2	0.9	M	15	Moderate	39.4	2.83	124	10.4
3	6	F	90	Moderate	37.9	1.96	138	9.3
4	17	M	90	Moderate	41.1	1.94	159.2	9.9
5	7	F	160	Moderate	42.6	2.41	122	8.6
6	0.5	F	30	Moderate	47.4	2.23	164	9.4
7	2	M	20	Moderate	48.8	2.62	172	7.7
8	0.7	F	15	Moderate	36.2	1.97	118	9
9	1	M	60	Moderate	39.5	1.84	123	7.3
10	0.6	F	30	Moderate	34.4	2.79	98.2	8.9
11	0.1	M	120	Moderate	31	2.66	94.6	8.4
12	0.9	F	7	Moderate	27.4	2.32	133	7.8
13	4	M	14	Moderate	25.5	1.87	155	6.8
14	3	M	5	Moderate	28.7	2.14	163	7.6
15	2	F	15	Moderate	48.3	2.77	172	9.1
16	0.3	M	30	Moderate	38.6	2.42	120	9
17	10	F	4	Moderate	42.3	2.15	140	7.5
18	2	M	14	Moderate	31.6	2.07	152	6.8
19	8	M	210	Moderate	31	1.93	118.6	7.6
20	10	F	30	Moderate	37.1	1.72	116.2	7
21	7	M	15	Moderate	37.7	2.06	102.4	10.5
22	7	M	210	Moderate	27.7	2.11	106.6	7.1
23	0.4	F	2	Moderate	32	2.23	107.7	8.1
24	7	M	60	Moderate	39.1	2.17	116.6	7.8
25	2	F	60	Moderate	47.9	2.45	123.3	8.4
26	18	M	4	Moderate	44.2	2.51	115.5	10.1

27	7	F	15	Moderate	49.3	2.64	117.7	8
28	14	M	7	Moderate	36.4	2.71	116.2	8.3
29	0.1	F	90	Moderate	39.8	2.82	114.4	7.4
30	0.4	M	30	Moderate	44.4	2.95	119.2	7.9
31	3	M	90	Moderate	46.3	2.69	117.4	7.2
32	9	M	90	Moderate	26.3	1.97	144.7	7.9
33	14	M	90	Severe	88.1	3.12	238	7.5
34	2	F	30	Severe	59.4	2.86	215	8.2
35	5	M	30	Severe	79.7	3.06	206	7.3
36	0.8	F	14	Severe	96.3	3.76	213.3	7.1
37	4	M	7	Severe	68.3	3.52	216.6	7.1
38	13	F	120	Severe	98.5	3.43	201.1	7.9
39	5	M	15	Severe	75.4	3.12	202.4	8.1
40	5	F	15	Severe	79.1	3.08	205.7	7.8
41	10	M	7	Severe	84.3	3.12	275.5	8.8
42	2	F	7	Severe	89.2	3.03	284.4	8.4
43	9	M	120	Severe	94.3	3.27	256.5	7.5
44	12	M	7	Severe	63.1	3.06	248.8	7.9
45	3	F	200	Severe	62.1	4.1	200.8	7
46	2	F	8	Severe	57.7	4.3	242.7	6.8
47	6	M	7	Severe	53.3	1.92	253.3	7.4
48	3	F	15	Severe	59	2.17	233.3	7
49	4	M	15	Severe	67.8	3.25	228.8	7.3
50	3	M	10	Severe	69.9	3.35	212.2	6.9
51	3	M	10	Severe	78.3	3.18	208.8	7.4
52	5	F	30	Severe	76.4	3.29	178.6	7.7
53	3	F	30	Mild	14.5	0.86	48.3	7.1
54	4	M	20	Mild	22.8	0.73	47.5	7.6
55	3	M	30	Mild	16.2	0.62	56.6	8

56	5	F	15	Mild	11.7	0.59	56.7	7.2
57	1	M	15	Mild	18.1	0.92	65.3	7.2
58	0.3	M	15	Mild	22.9	1.12	62.1	6.9
59	9	F	30	Mild	20	0.87	54.3	8.2
60	0.3	M	90	Mild	18	0.48	48.6	8.1
61	7	M	4	Mild	24.3	0.64	72.7	7.4
62	0.9	F	120	Mild	24.5	0.71	70.6	7.5
63	9	F	15	Mild	15.3	0.89	61.1	7.1
64	4	M	15	Mild	19.9	0.93	40.6	7
65	17	M	5	Mild	23.3	0.85	44.2	8.3
66	16	F	15	Mild	17	1.27	28.6	7.6
67	3	M	7	Mild	15.4	1.46	42.1	8.4
68	9	F	15	Mild	12.7	0.52	56.7	8.3
69	9	M	3	Mild	15.2	0.28	72.1	8.5
70	7	M	7	Mild	17.1	0.45	63.2	9.4
71	6	F	7	Mild	15.2	0.21	57.7	8.6
72	2	F	10	Mild	19.9	0.13	62.5	8.1
73	0.9	F	3	Mild	20.5	0.29	45.6	9.5
74	5	M	30	Mild	18.9	0.35	51.3	7.6
75	4	F	30	Mild	13.7	0.67	54.3	9
76	6	F	60	Mild	23.6	0.75	53.2	9.1
77	3	M	15	Mild	12.8	0.88	71	9.4
78	4	M	30	Mild	23.9	0.91	63.6	8.4
79	9	M	30	Mild	22.1	0.95	42.1	8.6
80	17	M	7	Mild	23.5	0.72	55.5	8.9
81	0.1	M	10	Mild	20.3	0.34	57.9	9.2
82	6	F	120	Mild	18	0.38	48.7	8.6
83	18	F	15	Mild	16.2	0.44	63.2	9.3
84	16	F	30	Mild	19.9	0.57	35.7	8.7

85	12	M	2	Mild	24.2	0.89	62.1	8.3
86	18	F	30	Mild	16.2	0.55	54.3	8.8
87	11	M	15	Mild	13.4	0.44	84.1	8.2
88	6	F	10	Mild	11.7	0.36	77.7	8.3
89	12	F	8	Mild	14.5	0.42	73.3	9
90	17	F	30	Mild	10.8	0.54	92.1	8.6
91	4	M	4	Mild	11	0.62	65.5	10.1
92	17	M	15	Mild	16.2	0.72	62.8	9.9
93	7	M	30	Mild	10	0.91	74.5	9.4
94	1	F	15	Mild	9.9	0.77	67.2	8.2
95	10	F	90	Mild	13.7	0.66	77.8	10.5
96	14	M	14	Mild	14.5	0.52	82.3	9.5
97	15	M	30	Mild	9.4	0.18	58.61	8.2
98	18	F	15	Mild	14.5	0.19	67.32	9.3
99	7	M	30	Mild	20	0.91	74.32	8.2
100	3	M	14	Mild	14.1	0.83	72.23	7.6
101	4	F	7	Mild	18.5	0.87	70.91	7.2
102	10	M	20	Mild	12.2	0.74	68.3	8.4
103	8	F	30	Mild	24.2	0.72	69.8	7.9
104	9	F	7	Mild	19.6	0.71	75.12	8.6
105	5	M	15	Mild	12.4	0.88	73.1	8.1
106	1	M	15	Mild	14.4	0.55	67.12	9.7
107	0.6	F	7	Mild	22.4	0.32	53.22	9.4
108	4	M	10	Mild	20.1	0.21	78.92	9.6
109	3	F	60	Mild	18.4	0.33	67.22	9.1
110	7	M	7	Mild	24.6	0.22	75.32	10.3
111	4	M	10	Mild	20.2	0.52	45.12	10.4
112	1	F	4	Mild	18.6	0.65	55.12	9.7
113	4	F	720	Mild	15.5	0.71	64.12	10.6

114	10	M	8	Mild	24.1	0.34	72.14	9.4
115	12	F	90	Mild	14.2	0.55	63.51	10.3
116	8	F	30	Mild	23.7	0.23	45.12	10.2
117	2	M	30	Mild	10.7	0.79	74.23	9.4
118	0.8	M	3	Mild	22.3	0.48	73.45	8.7
119	13	F	15	Mild	13.5	0.65	65.12	9.4
120	0.1	F	15	Mild	17.1	0.62	45.52	9.1
121	0.7	F	30	Mild	23.6	0.94	86.5	9.3
122	3	F	30	Mild	20.8	0.85	78.5	9.6
123	14	F	7	Mild	10.6	0.69	73.1	9.9
124	5	F	30	Mild	16.4	0.72	67.23	9.2
125	3	F	30	Mild	12.8	0.58	71.84	9.3
126	4	F	90	Mild	15.7	0.89	84.23	9.5
127	18	M	165	Mild	19.6	0.75	58.75	9.8
128	3	M	15	Mild	20.4	0.61	65.43	9.1
129	11	M	90	Mild	22.4	0.86	72.36	9.5
130	13	M	10	Mild	11.6	0.74	78.63	9
131	3	M	35	Moderate	28.7	1.65	115.23	8.6
132	2	M	180	Moderate	34.2	1.98	125.5	8.1
133	9	F	30	Moderate	36.4	2.12	114.4	8.7
134	17	M	30	Moderate	37.2	2.04	105.6	8.4
135	1	M	15	Moderate	26.4	1.98	116.7	8.4
136	12	M	45	Moderate	27.5	2.56	114.2	8.5
137	3	M	30	Moderate	31.2	1.75	98.6	8.9
138	6	M	7	Moderate	35.6	2.15	110	8.8
139	8	F	15	Moderate	37.8	2.1	113.55	9.6
140	0.3	F	15	Moderate	45.4	2.79	124.56	8.8
141	0.4	M	5	Moderate	43.2	1.86	105.24	8.7
142	15	F	28	Moderate	36.5	1.94	106.75	8.2

143	5	M	30	Moderate	47.2	2.11	117.78	8.5
144	3	M	5	Moderate	48.2	1.99	118.45	9
145	3	F	40	Moderate	49.1	2.55	127.89	8.9
146	1	F	120	Moderate	41.8	2.06	114.23	8.4
147	5	F	30	Moderate	32.2	1.56	97.62	8.3
148	7	M	45	Moderate	30.6	1.34	104.7	8.2
149	6	M	35	Moderate	28.6	1.69	112.1	8.3
150	2	M	25	Moderate	38.7	2.13	108.67	7.7
151	2	F	30	Severe	65.1	2.95	212.2	7.8
152	4	M	20	Severe	73.8	3.12	200.28	7.4
153	1	M	10	Severe	76.2	2.99	206.4	7.2
154	10	F	40	Severe	83.2	3.06	220.6	9.6
155	15	M	60	Severe	54.6	3.15	211.6	7.8
156	17	F	90	Severe	57.7	3.25	230.6	7.5
157	1	F	30	Severe	74.4	2.85	209.8	7.3
158	12	M	40	Severe	78.5	2.89	203.2	7.9
159	2	M	14	Severe	79.8	2.98	206.67	7.6
160	1	M	30	Severe	80.4	2.77	199.87	7.9
161	4	F	45	Severe	69.4	2.66	196.75	7.5
162	3	M	15	Severe	71.3	2.87	187.75	7.1
163	2	F	20	Severe	76.7	2.96	206.72	7.3
164	11	M	28	Severe	58.9	3.21	203.33	7.8
165	5	F	30	Severe	72.1	3.01	201.1	7.2