Indian Journal of Pharmacy Practice., 2024; 17(2):93-101.
https://www.ijopp.org

Review Article

A Review on Unraveling the Complexity of Autoimmune Skin Disorders: Genetic Influences, Environmental Triggers and Innovative Management Approaches

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ABSTRACT

An autoimmune condition arises when the immune system erroneously targets and eliminates healthy bodily tissues. This can be preceded by a prolonged asymptomatic phase marked by the presence of auto antibodies. Especially in individuals with a genetic predisposition, these auto antibodies can significantly increase the likelihood, severity, and organ-specific impacts of the disease. There are various autoimmune disorders affecting both mucocutaneous and systemic functions, including conditions like psoriasis, vitiligo, dermatitis herpetiformis, systemic lupus erythematosus, bullous pemphigoid, lichen planus, and alopecia areata. These disorders are characterized by identifiable autoantibodies and susceptibility genes. Identifying individuals at the highest risk and avoiding triggering factors could potentially prevent the development of apparent illnesses. Numerous environmental triggers for autoimmunity have been recognized, including insufficient vitamin D levels, exposure to ultraviolet (UV) radiation, smoking, medications, and others. Treatment for these conditions involves the use of sunscreens, topical or systemic corticosteroids, antimalarials, oral immunosuppressants, and intravenous immunoglobulins.

Keywords: Autoimmune disorders, Psoriasis, Vitiligo, Bullous phemigoid, Systemic Lupus Erythematous, Dermatitis Herpetiformis, Alopecia areata, Immunosuppressant, Corticosteroids.

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Received: 02-09-2023;
Revised: 26-12-2023;
Accepted: 12-02-2024.

INTRODUCTION

Autoimmune diseases are the leading contributors to global morbidity and mortality, as evidenced by various sources.[1] Over the past three decades, these diseases have become more prevalent and frequent. They encompass a range of chronic conditions where the immune system mistakenly attacks the body's own healthy tissues.[2] The interplay between genetic factors and environmental influences plays a significant role in increasing an individual's susceptibility to various ailments, including skin disorders.[3] Although the root cause of most immune-related conditions remains unidentified, it's established that a combination of environmental, genetic, and epigenetic triggers play a role.[4] The term "epigenetics" refers to mechanisms that can modify gene expression, thereby altering cellular characteristics. Auto antibodies can serve as indicators predicting the likelihood and onset timing of a disease. Other immune systems might mediate the actual disease process.[5] The development of autoimmune diseases often involves a complex interplay of immune system activation, genetic predisposition, and environmental triggers over the course of years in an individual.[6] This study highlights common autoimmune skin conditions like psoriasis, vitiligo, bullous pemphigoid, systemic lupus erythematosus, lichen planus, alopecia areata, and dermatitis herpetiformis. It delves into their prediction, prevention, and management strategies.

The etiological factors that cause autoimmune disease

Genetics

An extensive amount of study suggests that genetic predisposition plays a significant part in the mosaic of autoimmune disease. Numerous skin diseases have been linked to greater concordance in monozygotic compared to twins with dizygotic traits as well as increased frequency of an infected family member.[7] A concordance rate of 25% between monozygotic twins and dizygotic twins for lupus suggests genetic predisposition, but it is not sufficient to be the only cause of the illness. The Major Histocompatibility Complex (MHC) is the genetic factor that has the greatest genetic influence on immune system. A relative risk of 2-12% is related with numerous HLA-alleles (Table 1) with Systemic Lupus Erythromatosus (SLE).[8] The relative risk of 15% for pemphigus

DOI: 10.5530/ijopp.17.2.16

vulgaris is connected with the genes DRB1 and DQB 1.90% of patients with celiac disease and dermatitis herpetiformis have HLA DQ2 gene and the remaining patients have HLA DQ8 gene (relative risk is 11.6%). Vitiligo is linked to the HLA-DR gene and others. Psoriasis is linked to PSORS 1, and early beginning of the condition was linked to HLA-Cw6.[9] Additionally, there are non-MHC autoimmune susceptibility alleles, although it is difficult to discover these genes, mostly because of the high genetic variation. The probability of developing an autoimmune disease in the future is significantly increased by the identification of a vulnerable locus in combination with certain auto-antibodies, even if hereditary susceptibility is an unalterable element.

Environmental triggers

Autoimmunity can be triggered or made worse by environmental variables such as UV radiation, lack of vitamin D, infections, vaccinations, adjuvants, xenobiotics, dietary habits, stress, smoking, and other medicines.[10] Once a person's personal risk of autoimmunity is established, the majority of these environmental variables are modifiable and can be avoided. Sunlight is a frequent cause of autoimmune skin manifestations since Ultra-Violet B [UVB] appears to have a pro-autoimmune effect. Apoptosis, an anti-inflammatory mechanism during times of low UVB exposure. On the other hand, necrosis, an inflammatory mechanism when UVB exposure is overly high, can reveal autoantigens to presenting cells and exacerbate autoimmune responses. A connection has been established between some antibodies, such as anti-Ro, sunlight exposure, and cutaneous and systemic SLE exacerbations. Numerous pathogens that cause illness, such as the Epstein-Barr virus in SLE, the Herpes virus in pemphigus, and streptococcal, staphylococcal, and Candida albicans infections in psoriasis, have been related to autoimmune skin illnesses. On the other hand, immunisations protect against infections and may stop autoimmunity from being triggered; on the flip side, vaccines have been linked to an increased incidence of SLE, dermatomayositis, and other disorders.[11]

Predictive role of autoantibodies in skin disease

For the purpose of identifying, categorization, and prognosis assessment of diseases, the detection of autoantibodies has been employed. Autoantibodies now play a new function known as the predictive function.[10] Numerous antibodies can be found before the initiation of a disease and used to predict a diagnosis, particularly in those at greater risk. There are two categories for mucocutaneous autoantibodies: type I, which refers to autoimmunity mediated by self-antigens presented at both cutaneous and extra cutaneous sites; type II, which refers to self-antigen presented solely by mucocutaneous cells.[12] The majority of type I autoantibodies target prominent autoantigens that were first identified in patients with "dermatologic" conditions such as SLE, scleroderma, Sjogren's syndrome, dermatomyositis, etc. Contrarily, type II autoantibodies, such as those to adhesion molecules in immunoblistering skin eruptions and pigmented cells in vitiligo, appear to be not only limited to the muco-cutaneous tissues (epidermal and dermal autoantigens) but also directly associated to disease. Keratocytes generate epidermal antigens, which can cause non- blisters-forming disorders like vitiligo as well blistering conditions like the pemphigoid group. Dermatitis herpetiformis, cutaneous-SLE, and other illnesses target dermal antigens. Although other immunological systems are also involved in the development of illnesses, both types of antibodies can be employed as diagnostic and possibly prognostic markers.[13]

Mechanisms of ASD

In order to establish accurate predictions and targeted therapies, it is essential to recognize the distinctive cellular and molecular characteristics. Immune cells such as T cells, B cells, self-antibodies and different cytokines can target cellular elements of tissues in the skin. Characteristic cellular and molecular features or signatures for particular skin conditions can be found by using cellular and molecular approaches, such as microarray testing, flow cytometry, immunofluorescence or immunohistochemistry, proteomics, metabolomics, and single-cell RNA sequencing, in conjunction with cutting-edge data analysis (bioinformatic analysis). These discoveries might lead to new and improved immunotherapies or tailored treatments for ASD patient (Figure 1).[14,15]

Psoriasis

Psoriasis, an eternal immune-related systemic illness that is impacted by both heredity and the environment, affected over 125 million individuals globe-wide. Sharply defined, silvery scaly, and erythematous plaques are typical clinical symptoms. Individuals with mild to critical psoriasis are more likely to develop the metabolic syndrome, atherosclerotic heart disease, and anxiety, all of which have profound effects on their level of living.[16] External factors have been identified and recognized as having significant effects on both the predisposition and the progression of psoriasis. Stress, surgery, alcohol misuse, smoking, and infection are some examples of environmental factors that cause psoriasis.[17] The main reason of psoriasis include bacterial infections, viral infections, and fungal infections, according to literature. While concrete data is currently insufficient, infection may be connected to a high frequency of anxiety and depression in psoriasis patients. Through inflammatory mediators, sickness may increase the frequency of psychiatric symptoms in psoriasis patients. Pro-inflammatory cytokines in psoriasis, namely IL-6, IL-17, and TNF-α, have been linked to mental disorders, according to numerous research. Despite a genetic propensity, psoriasis is an immune-driven illness for which no specific immunogen has been found. On the external surfaces of the limbs, the head, thighs and trunk, plaque psoriasis lesions develop. Heat, trauma, and inflammation may be factors

Table 1: Characteristic autoantibodies, genes and triggering factors of autoimmune skin diseases.

Autoimmune disorder	Auto-antigens	Genetic factors	Triggering factors
SLE	Nuclear (DsDNA) Phospholipids Ribosomal P Ro Nucleosome.	A1 B8 C4AQO DR2 DR3 DQ3	Cigarette Crystalline silica Infection (EBV) Smoking Sunlight (UVB) Vitamin D deficiency.
PEMPHIGUS	Acetylcholine-receptor Collagen XVII Desmoglein 1-4 Desmocollins Desmoplakins E-cadherin Laminin 5 annexing.	DRB1*0402 DQB1*0503	Drugs: penicillamine, captopril, rifampicin Diet: garlic, onion and leek Gardening materials Heat Metal vapour Pesticides Sunlight (UVB) Viral infection (Herpes).
VITILIGO	Pmel17 Tyrosinase TRP-1 TRP-2.	A19 B13 CTLA-4 Cw6 DR4 Dw7 DR7 DR1 DR53	Cytotoxic compounds Psychological factors Radiotherapy Sunlight (UVB) Trauma. Vaccination
DERMATITIS HERPETIFORMIS	Endomysia-reticulin Fibrillin Gliadin Transglutaminase.	DQ2 DQ8 (11%)	Diet: gluten
PSORIASIS	Calpastatin HSP60-strep Nuclear RNP Sn.	CTLA-4 PSORS 1	Alcohol Drugs: lithium, beta-blockers, anti-malarial, NSAID, angiotensin-converting enzymes Obesity Smoking Sunlight (UVB) Stress.

in the development of inverse psoriasis, which is less scaly than the plaques form and typically affects folds in the skin such contracture areas and the perineal, inframammary, axillary, inguinal, and intergluteal areas. Widespread erythema, scaling and edema are the describing feature of erythrodermic psoriasis, which is frequently accompanied by generalized symptoms. It might emerge suddenly in persons with moderate psoriasis or progressively evolve from chronic psoriasis. Individuals less than thirty years old are at greater risk to develop guttate psoriasis, and lesions are typically found on the upper part of the body.[18] Psoriasis is characterized by an intricate interaction between the natural immune system, which is primarily activated by TNFα, and the adaptive immune system, which includes dendritic cells, T-cells, mostly Th1-cells, and associated cytokines like INF α.While autoimmunity including antinuclear, antiSn, and anticytoplasmic ribonucleoprotein antibody are produced during psoriasis, which is thought to be a T cell-driven autoimmune disorder. In order to apply protective measures to both normal and affected individuals, future investigations are required to evaluate the prognostic usefulness of various autoimmunity and combinations, genetic screening, and environmental variables in autoimmune skin diseases.[13]

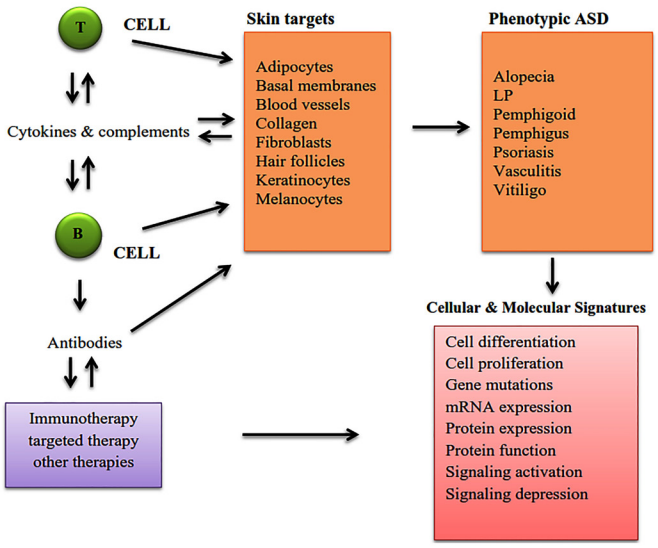

Figure 1: Mechanism of autoimmune skin Disorders.

Management

The purpose of medical care is to improve lesions on the skin, nails, and joints while also enhancing the quality of living. External treatments, such as corticosteroids, vitamin D analogues, tazarotene and calcineurin inhibitors, are frequently effective in the treatment of these individuals.[19] Non-medicated moisturizers, salicylic acid, coal tar, and anthralin are examples of uncommon external treatments. Psoriasis is frequently treated with topically applied corticosteroids. The treatment of choice for patients with advanced psoriasis, which affects more than 5% of the body's skin surface or the hands, feet, face, or genitalia, is radiation therapy in conjunction with systematic therapies. Methotrexate, cyclosporine, acitretin and biologic therapy are examples of systemic treatments. Azathioprine, hydroxyurea, sulfasalazine, leflunomide, tacrolimus and thioguanine are second-tier medications with less convincing evidence.[20]

Vitiligo

Vitiligo, a depigmenting disorder can be defined as a specific decline in melanin-producing resulting in the diminution of pigmentation within the epidermis's regions. The distinctive defect consists of a completely amelanotic, nonscaly, chalky-white macule in definite edges.[21] It is particularly prevalent depigmenting disorder, affecting approximately five percent and one percent of people worldwide. Primarily, restricted, or generalised cutaneous and mucosal discoloration associated with vitiligo is influenced by genetics, absence of melanoma, inflammatory substances, autoimmune, and oxidative damage. Segmental and nonsegmental vitiligos were the well-known manifestations of the condition. Segmental vitiligo is defined with a unidirectional, confined pattern of vitiligo spots, and it frequently characterised as initial follicles of hair activation and a quick start and stabilisation. Nonsegmental vitiligo, which is distinguished by the symmetric collection of vitiligo spots across the skin, is additional usually characterised as a gradual beginning of several episodes, subsequent appearance of scalp hair follicles, and an unpredictability outcome. Nonsegmental vitiligo is the most frequent type of the condition, with segmental vitiligo being the least frequent variant that affects five percent to sixteen percent of those with vitiligo. The acquired, amelanotic, nonscaly, chalky-white macules with clear edges is a common dispersion yields a simple identification of vitiligo. The upper and lower lips proximal extremity points, segmental, periorificial, and regions on contact.[22]

Management

One of the greatest challenging skin issues today is vitiligo therapy. Recognising because vitiligo is a serious illness and rather than a superficial condition with accessible, secure, and successful therapies is an essential initial step in managing vitiligo. A combination of these therapies, which involve topical, light therapy, external and systematic immune suppressants, might be able to arrest the progression of the condition, stabilise spots that have lost their pigment, and promote pigmentation regrowth.[23] The elements that influence therapy selection include the individual's age, skin category, how the condition affects their general living, and why they want therapy, along with the disorder's category, its scope, delivery, and action. At present, a large number of JAK inhibitors are utilised for treating numerous illnesses. The four JAKs (JAK1, JAK2, JAK3, and TYK2) can be selected depending on the specificity of the individual drug, or simply a certain enzyme can get restricted. JAK inhibitors prevent disease-causing T lymphocytes from attacking melanin cells as the therapy of vitiligo. Dermal ruxolitinib is the newest JAK inhibitor recognised by the US Food and Drug Administration (FDA). This is now approved for the therapy for nonsegmental vitiligo in individuals who are over twelve years old that affects a maximum of ten percent of the individual's Body Skin Area (BSA). In a newly released review, different cell-based treatments utilised for curing vitiligo were compiled. The Melanocyte-Keratinocyte Cell Transplantation (MKCT) appears to be the best possible therapeutic option among non-cultured epidermal cell transplants, and mixed treatment.[24] When MKCT is used, a minimum of ninety percent from the original coloration is restored, that is better than previous techniques. In individuals who have vitiligo, Wnt/-catenin transmission are suppressed, while its elevation could serve to regulate the immunological reaction protecting melanin cells against oxidative damage, blocking CD8+ T cells that are cytotoxic, while activating lymphocytes. Simvastatin and lithium chloride are two examples of stimulants and up regulators within this signalling system that could additionally have a part in the management of vitiligo. The Melanocyte-Stimulating Factor (MSH) derivative afamelanotide activates its MC1R, which in turn promotes the movement of a pigment. Due to the effects of MC1R in cells that are inflamed, it is additionally known can significantly activate antioxidant

functions, promote the repair of DNA techniques, and control aggravation. For both researchers and dermatology doctors, the prevention and therapies of vitiligo continues to be an unsolvable problem. Many of the therapy philosophies used today is general. Therapies for those with vitiligo are becoming further specialised, efficient, and secure because to the latest developments in our understanding of the pathophysiological mechanisms underlying this condition.[25]

Dermatitis herptiformis

An inflammation skin condition called dermatitis herpetiformis features pruritic polymorphic lesions, a chronic, relapsing course, and characteristic histological and immunopathological findings. There is mounting evidence that dermatitis herpetiformis is the distinct dermatological manifestation of a gluten disease-like gluten-sensitive enteropathy. Both dermatitis herpetiformis and celiac disease are complicated illnesses where particular lesions in the small bowel and skin are caused by a combination of genetic and environmental triggers. The symptoms of dermatitis herpetiformis include erythema, urticarial plaques, papules, herpetiform vesicles and blisters that are followed by erosions, excoriations, and darkening. These lesions are widespread, symmetrical, and clustered polymorphic in pattern. The lateral portions of the elbows (90%), knees (30%), shoulders, buttocks, sacral region, and face are the areas that are most frequently affected.[26] Variable-intensity itching, scratching, and feeling of burning are frequent in the moments before lesions appear. Since dermatitis herpetiformis frequently presents clinically in an uncommon manner, this diagnosis might not be obvious. Atopic dermatitis, scabies, papular urticaria, and impetigo are the main differential diagnoses in children, whereas eczema, other autoimmune blistering diseases (especially IgA linear disease and bullous pemphigoid), nodular prurigo, urticaria, and polymorphic erythema should be taken into account in adults. The clinical trajectory, histology, and, most importantly, DIF, will aid in making the diagnosis.[27]

Management

The foundation of treatment for spectrum DH/CD is a rigorous gluten-free diet. The maximum amount of gluten that can be present in a product is 20 ppm (gluten-free); nevertheless, in some nations, items with 100 ppm (extremely low gluten) are permitted. Both gastrointestinal and signs of skin inflammation can be treated with a gluten-free diet, and it can also stop the growth of lymphomas and other disorders linked to gluten-induced enteropathy and malnutrition. Dapsone is seen as a viable therapeutic option for people with DH during the 6- to 24-month window before the gluten-free diet becomes successful, but the absence of reports from randomised controlled trials about its usage in the literature.[26] To reduce the likelihood of adverse effects, the initial dose should be 50 mg/day. In the maintenance phase, 0.5-1 mg/kg/day typically controls itching and the emergence of new skin lesions. The dosage can then be increased up to 200 mg/day until the disease is under control. Sulfasalazine (1-2 g/day), sulfapyridine (2-4 g/day), and sulfamethoxypyridazine (0.25-1.5 g/day) can be effective alternatives in order to cure for patients with DH if dapsone is unable to control the symptoms or in the event of side effects. Renal examination with urinalysis and a complete blood count should be performed before the treatment is started.[28] Following the initial three months, the same exam should be done monthly, then every six months after that. For patients with DH, other medications can be utilised to manage their skin issues. Among them, powerful topical steroids (clobetasol propionate or betamethasone valerate) or very powerful ones (betamethasone valerate or dipropionate) are useful in cases of localised disease to lessen itching and the emergence of new lesions.[29] Topical dapsone, immunosuppressants such azathioprine or cyclosporin A, colchicine, heparin, tetracyclines, nicotinamide, mycophenolate, and rituximab are extra medications that have been demonstrated to be successful in some studies.[30]

Systemic lupus erythematous

The multisystem long term autoimmune illness known as Systemic Lupus Erythematosus (SLE) has a relapsing and remitting course. With a 9:1 female predominance, it is more prevalent in women of childbearing age. It is unclear exactly what causes this condition. Epigenetic, genetic, ecological, and environmental variables are all involved in this complex condition. It predominantly causes adaptive as well as innate immunity to be activated, which in turn causes autoreactive B lymphocytes to be activated by T lymphocytes and immune complexes to accumulate in tissues, which sets off an autoimmune sequence that might be restricted to a single part or may result in wide-ranging systemic contribution.[31] Antibodies against nuclear and cytoplasmic antigens are a defining feature of SLE. Other autoantibodies, such as anti-Scl-70 antibodies (present in systemic sclerosis), anti-La, anti-Ro antibodies (present in Sjogren disease), anticardiolipin antibodies, and anti-phospholipid antibodies, may also be present in SLE patients, indicating a broad connection between SLE and various autoimmune conditions. The symptoms of SLE can vary from mild to intense, affecting either a single organ system or multiple systems, and changing over time, posing difficulties in making a diagnosis. Skin rashes, such as the malar "butterfly rash," arthritis, pleurisy and serositis, alopecia, and lupus nephritis are among the typical signs. Because of the disease's unpredictable nature, the range of its symptoms, and the limited understanding of its origins, diagnosing SLE can frequently be challenging. So, diagnostic standards are applied.[32] SLE is diagnosed based on both clinical and test results. The most recent and accurate classification standards are those employed by the American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR). Early detection of Systemic Lupus Erythematosus (SLE) is crucial to prevent both flare-ups and the resulting tissue harm. It's important to note that

the route to SLE begins before clinical illness. Prior to diagnosis, autoantibodies werse discovered in the serum of SLE patients for a period of three to nine years. The earliest serum antibodies to be found include Antinuclear Antibody (ANA), anti-Ro, anti-La, and antiphospholipid antibodies. Autoantibody accrual normally halts once a disease manifests itself. However, people who are susceptible to developing SLE and LE-skin manifestation, such as those who are related to SLE patients and those who have suspected autoantibodies, should be recommended to avoid certain substances and drugs and to think about taking Vitamin D supplements.[33]

Management

A multi-organ illness with heterogenic manifestations, systemic lupus erythematosus varies in severity and organ involvement from patient to patient, making disease management difficult and necessitating an integrated strategy. The purpose of treatment is to minimise the pharmacological adverse effects while preventing disease flare-ups, promoting remission and maintenance, and preventing recurrence. The Systemic Lupus Erythematosus Disease Activity Index-2000 (SLEDAI-2K), the Systemic Lupus Activity Questionnaire (SLAQ), the Physician Global Assessment (PGA), the British Isles Lupus Assessment Group (BILAG 2004 index), and the Lupus Foundation of America Rapid Evaluation of Activity in Lupus (LFA-REAL) are among the scoring systems used to evaluate the disease activity.[31]The selection of medications and their efficiency in treating diseases are significantly influenced by these grading systems. Hydroxychloroquine is the predominant antimalarial drug employed in the maintenance phase of Systemic Lupus Erythematosus (SLE) treatment, and while its effectiveness is promising, ongoing patient supervision is essential due to the potential risk of retinal damage associated with extended medication use.[34] Prednisolone is administered intravenously during the acute phases; depending on the severity of the disease, prednisolone may then be gradually tapered off and replaced by an immunosuppressant or an antimalarial. The goal of using glucocorticoids during a flare-up of the disease is to achieve remission while reducing the dose and switching to hydroxychloroquine or an immunosuppressant. For minimal side effects, the minimum tolerable dose must be equal to or lower than 7.5 mg per day. When a patient is unresponsive to the maximal tolerable dose of glucocorticoids and hydroxychloroquine, methotrexate and azathioprine should be considered. Mycophenolate mofetil and cyclophosphamide, which are typically used in organ-threatening and rescue treatment in resistant instances, are also included.[35]

Bullous Phemighoid

Bullous Pemphigoid (BP) is the most common autoimmune blistering skin disease worldwide, typically affecting the elderly population. The circulating autoantibodies that target structural dermal-epidermal junction components, such as bullous pemphigoid antigen-1 (BP230) and bullous pemphigoid antigen-2 (collagen XVII, BP180), are the cause of chronic Bullous Pemphigoid (BP),which is characterised clinically by pruritic tense blisters imposed on normal skin or erythematous urticaria-like plaques.[36] A lack of tissue-bound and circulating autoantibodies directed against the structural elements of the Brachial subcutaneous Membrane Zone (BMZ) is a defining feature of BP. At the dermal-epidermal junction of perilesional skin, these anti-hemidesmosomal antigens and complement elements are deposited along the base barrier. The majority of BP cases appear to have no clear cause, although in several instances, an extensive medical record reveals the presence of inducing drugs. No dietary factors are thought to be implicated in the onset of BP, unlike pemphigus. Antigliadin antibodies found in the sera of BP patients may suggest that some of these individuals are gluten sensitive. However, there have been no instances of BP decreasing with a gluten-free diet.[37]

Management

Based on the quantity of daily new blisters, the management of BP has typically been categorised into mild/localized and moderate/severe/extensive disease. There is no universal agreement on this classification since some specialists believe that body surface area participation plays a significant role in determining the course of treatment.[38] The Bullous Pemphigoid Disease Area Index (BPDAI), a severity index that includes cutaneous and nasal blisters/erosions, as well as cutaneous urticaria/erythema, is specifically recommended by the JDA, EDF/EADV, and SIDeMaST.[39] The first-line treatment for mild or localised disease is to apply clobetasol propionate cream or ointment to the affected areas or the entire body, avoiding the face. The systemic corticosteroid use should be started at 0.5-1.0 mg/kg/day in cases with severe illness. Although certain individuals have recognized the advantages of using topical corticosteroids as a sole remedy for moderate, severe, or extensively spread Bullous Pemphigoid (BP), limitations might exist in applying this approach to certain patients and within various healthcare systems.[40]

Lichen planus

Lichen Planus (LP) is a chronic inflammatory condition that can affect the skin, mucus membrane hair and nails. The wrists, lower back, and ankles are the most prevalent places where it manifests as itchy, violaceous papules and plaques. Overlying the lesions appear as an interlacing pattern of white lines referred to as Wickham striae, most prominently visible on the inner cheek lining (buccal mucosa), where further deterioration can also be noticed. Its pathophysiology is unclear; however, it seems to be an autoimmune condition that is T-cell-mediated. According to the current idea, contact allergens, drugs, and viruses are exogenous agents that can modify epidermal self-antigens and activate cytotoxic CD8+ T cells. When the altered self-antigens engage with the regular self-antigens on basal keratinocytes,

leading to the assault by T lymphocytes and subsequent cellular death. In rare and severe cases, the diagnosis can be confirmed through skin biopsy and subsequent microscopic analysis, as the histopathological features remain consistent regardless of the specific pattern or classification. Pruritic, purple, polygonal, planar, papules, and plaques are the "Six Ps," which are frequently used to recall the symptoms of LP.[41] There are distinct categories of LP that may develop anywhere on the human body, including oral, hypertrophic, vesiculobullous, annular, linear, zoster form, nail, inverted, eruptive, vulvovaginal, pigmentosus, planopilaris and erythematous overlap syndrome LP.[42]

Management

The initial course of therapy for LP is thought to be high-potency topical corticosteroids, especially in patients with localised cutaneous LP (e.g., clobetasol, halobetasol, betamethasone dipropionate, fluocinolone acetonide, prednisolone, triamcinolone acetonide). Topical calcineurin inhibitors (TCI; for example, tacrolimus, pimecrolimus) have established themselves as a second-line therapy primarily for mucosal erosive LP. Relapses commonly occurred within a timeframe of 3-9 weeks after discontinuing treatment, making it necessary to use topical calcineurin inhibitors (TCI) over an extended period to maintain the initial clinical improvement. Oral steroids, such as prednisone, prednisolone, methylprednisolone, betamethasone, and dexamethasone, are utilized for treating lichen planus.[43] The rationale for incorporating topical vitamin D derivatives (like calcipotriol) in lichen planus treatment is founded on their capacity to reduce inflammation and regulate the growth and differentiation of keratinocytes. These topical medications can be applied individually or in combination with topical steroids.[44] Phototherapy is also used to treat lichen planus. It Utilises a "sweet spot" between the therapeutic and sunburning ranges at a wavelength of 311 nm, narrowband UVB phototherapy emits light over a very small range of wavelengths that are concentrated in the therapeutic range and barely in the sunburning region. Theoretically, narrowband UVB is safer and more effective than broad-band UVB, but longer treatment times are needed to achieve the maximal dose. Although the exact mechanism by which narrowband UVB enhances LP is unknown, it has been hypothesised that it may be linked to photo-induced T cell death or to the anti-inflammatory and immunosuppressive properties of the radiation.[45]

Alopecia areata

The prevalent chronic autoimmune disease Alopecia Areata (AA) is characterised by non-scarring hair loss and hair follicle preservation. It is a non-scarring T-cell-mediated form of hair loss that affects the body, face, and/or scalp and has an underlying immunoinflammatory aetiology.[46] Alopecia Areata (AA) commonly presents as a recurring and intermittent condition characterized by the spontaneous onset of patchy hair loss that appears and disappears unpredictably. This is followed by periods of irregular remission. However, the illness often persists in those with more severe hair loss. Clinical observation is frequently used to make the diagnosis of AA. The diagnosis of AA can occasionally be made with the aid of a positive hair pull test or trichoscopy; histology is infrequently required. In addition to hair loss, up to 44% of patients also have atypical nails, which are frequently found in more severe cases of AA.[47] Dermatoscopy is particularly important for differentiating between hair illnesses that do not leave scars and those that do, as well as for verifying the diagnosis of AA and assessing the severity of the disease. The hair pull test is useful for making a differential diagnosis and assessing the disease's activity. At the boundary, a bundle of 50-60 hairs is gripped firmly near to the scalp and pulled moderately hard in the direction of growth. Spotty lesions and on the clinically unaffected opposite side.[48]

Management

Present treatments for Alopecia Areata (AA) primarily focus on suppressing or modulating the immune system's response associated with the condition. However, these approaches frequently yield unfavorable outcomes and exhibit a notable recurrence rate, particularly in cases of greater severity. Oral zinc and vitamin D effectiveness in treating AA are still debatable, and the majority of the research is made up of case reports and tiny case-control studies that have produced conflicting findings.[49] It is generally known that patches of alopecia in AA can regenerate in the absence of active therapy, and this is probably influenced by the disease subtype. These regrowing nonpigmented hairs have fewer melanocytes and less melanization, according to electron microscope examination. This may be due to incomplete or partial melanocyte activation during the early stages of these follicles' anagen, while the illness is still active. The majority of the time, AA places a severe psychosocial burden on patients due to its high visibility and unpredictable clinical course. Despite the fact that it can be difficult at any age, young children and teenagers are more susceptible to bullying and social exclusion from others.[50]

CONCLUSION

Numerous autoantibodies have a predictive value, which implies that they can be identified through serology far in advance of the diagnosis of a clinical condition. As a result, it may be possible to identify an autoimmune process in the preclinical stage and execute the primary strategies for prevention. Autoantibodies may be able to forecast the scope and severity of ailments in patients with explicit disease, allowing for both tertiary and secondary preventive measures. The advantages of a course of medical care must be assessed with its possible drawbacks, as well as its implications for independence, mobility, everyday activities, clothes, and other aspects of living. Corticosteroids,

immunosuppressants, are necessary for the majority of immunological dermatological conditions to be controlled.

ACKNOWLEDGEMENT

First and foremost, we would like to express our thanks to the Almighty for providing us the strength and guidance. We are very grateful to acknowledge our Principal Dr. G. Muruganantha, M.Pharm., Ph.D., of Swamy Vivekanandha College of Pharmacy for his guidance.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

ABBREVIATIONS

ASD: Autoimmune skin disease; **UV:** Ultraviolet Rays; **SLE:** Systemic Lupus Erythromatosus; **MHC:** Major Histocompatibility Complex; **UVB:** Ultra-violet B; **FAD:** Food and Drug Administration, **BP:** Bullous Pemphigoid; **IF:** Immunofluorescence, **ELISA:** Enzyme-Linked Immunosorbent Assay; **SLEDAI-2K:** Systemic Lupus Erythematosus Disease Activity Index-2000; **SLAQ:** Systemic Lupus Activity Questionnaire, **PGA:** Physician Global Assessment; **BILAG:** British Isles Lupus Assessment Group; **LFA-REAL:** Lupus Foundation of America Rapid Evaluation of Activity in Lupus; **ANA:** Antinuclear Antibody; **MKCT:** Melanocyte-Keratinocyte Cell Transplantation; **BSA:** Body Skin Are; **DH:** Dermatitis Herpetiformis; **BPDAI:** Bullous Pemphigoid Disease Area Index; **IVIG:** Intravenous Immunoglobulin; **MMF:** Mycophenolate Mofetil; **BMZ:** Brachial Subcutaneous Membrane Zone; **SCS:** Systemic Corticosteroids; **TCS:** Topical Corticosteroids; **ACR:** American College of Rheumatology; **EULAR:** European League Against Rheumatism; **JDA:** Japanese Dermatological Association; **EDF:** European Defence Fund; **EADV:** European Academy of Dermatology and Venerology; **IL-6:** Interleukin-6; **IL-17:** Interleukin-17; **TNF-α:** Tumor Necrosis Factor; **LE:** Lower Extremity; **CSU:** Chronic Spontaneous Urticaria; **LP:** Lumbar Puncture; **JAKs:** Janus Kinases; **MC1R:** Melanocortin 1 Receptor.

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Cite this article: Nirojini PS, Vijay A, Amrutha BR, Murugan A. A Review on Unraveling the Complexity of Autoimmune Skin Disorders: Genetic Influences, Environmental Triggers and Innovative Management Approaches. Indian J Pharmacy Practice. 2024;17(2):93-101.