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FROM AUTOIMMUNITY TO INNOVATION: A NARRATIVE REVIEW OF VITILIGO AND ITS MANAGEMENT

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ABSTRACT

Background: Vitiligo is a chronic skin disorder characterized by the development of hypopigmented or depigmented macules and patches, resulting from the loss of functional melanocytes in the affected areas. It is estimated to affect approximately 0.5% to 4% of the global population. Although the exact etiology remains unclear, vitiligo is considered an acquired, multifactorial condition involving complex interactions.
Aim: To summarize current knowledge on vitiligo, focusing on its pathogenesis, clinical presentation, diagnostic principles, and therapeutic strategies.
Methodology: Literature review was conducted using PubMed, the Cochrane Library, and Google Scholar databases.
Results: Vitiligo is now widely regarded as an autoimmune disorder. Current management centers on immune modulation through topical and systemic agents, phototherapy, and, in selected cases, surgical intervention. Adjunctive measures including camouflage techniques, nutritional optimization, and psychological support play an important role in improving quality of life.
Conclusions: Vitiligo results from complex autoimmune and oxidative processes leading to melanocyte destruction. First-line treatment typically includes topical corticosteroids or calcineurin inhibitors, with phototherapy serving as an effective and well-established adjunct. Combination and targeted immunomodulatory therapies, such as JAK inhibitors, represent promising future directions. Despite notable advances, complete and durable repigmentation remains uncommon, highlighting the need for continued research and individualized patient care.

KEYWORDS

Vitiligo, Melanocytes, Melanin, Glucocorticosteroids, Calcineurin Inhibitors, Phototherapy

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1. Introduction

Vitiligo is a dermatological condition characterized by the appearance of discolored patches on the skin, which can occur in various areas of the body. The condition can also involve changes in the nail apparatus (leukonychia), the scalp (leukotrichia), and the mucous membranes. Epidemiological studies estimate its prevalence to be between 0.5% and 4.0% of the general population. Although onset can occur at any age, most cases develop before the age of 20, with similar incidence observed in both sexes [1]. Vitiligo is not a life-threatening condition and does not pose a direct risk to physical health, however, it can have a significant psychological impact, often affecting patients' emotional well-being and quality of life. The psychosocial burden of vitiligo is particularly pronounced in individuals with darker skin tones, where the contrast between depigmented and normally pigmented areas is more visually apparent. Vitiligo can significantly reduce quality of life, negatively affect self-esteem, and impair social functioning [2]. In pediatric population, especially among children and adolescents with vitiligo affecting more than 25% of the body surface area, challenges such as difficulty forming friendships, learning impairments, and experiences of bullying or social exclusion are frequently reported [3]. Although no definitive cure currently exists, modern therapeutic approaches can slow disease progression and promote repigmentation, often achieving results that patients consider satisfactory [4].

This literature review aims to summarize current knowledge on vitiligo by presenting up-to-date information regarding its etiology, pathogenesis, clinical presentation, diagnostic methods, and therapeutic strategies.

2. Methodology

A literature search was conducted to identify studies related to the etiology, diagnosis, and treatment of vitiligo. The electronic databases PubMed, Google Scholar, and the Cochrane Library were screened using combinations of the following keywords: vitiligo, melanocytes, autoimmunity, oxidative stress, phototherapy, JAK inhibitors, corticosteroids, and surgical treatment.

3. Causes and mechanisms of vitiligo development

Vitiligo is a chronic skin disease characterized by the selective loss of melanocytes, resulting in the formation of clearly demarcated, chalky-white patches, typically without signs of scaling. Current knowledge suggests that the interaction of numerous factors contributes to the destruction of pigment cells. The etiology remains unknown, but several major theories have been described to explain the mechanism of this process.

One proposed mechanism is the autocytotoxic hypothesis, which postulates that intermediates generated during melanin biosynthesis exert cytotoxic effects on melanocytes, ultimately leading to their destruction. The neuronal theory suggests that the accumulation of specific neurochemical mediators may disrupt melanin production. Another concept, related to autoimmune processes, is the most common and widely accepted, and is based on the presence of antibodies capable of destroying melanocytes [5]. In recent years, significant progress has been made in understanding the pathogenesis of vitiligo, which is currently classified as an autoimmune disease. Numerous scientific reports suggest that vitiligo may coexist with other autoimmune diseases, further supporting the hypothesis of its immunological basis. Several factors have been implicated in the pathogenesis of vitiligo, including biochemical disorders, oxidative stress, and nervous system dysfunction. Studies have also indicated the significant role of genetic predisposition to vitiligo in individuals who are predisposed to the condition [6]. Moreover, various environmental and physiological factors may precipitate the onset of the disease, including trauma, such as vaccinations, radiation therapy, and sun exposure; malignant tumors and their treatment, such as lymphoma or melanoma; bone marrow transplantation; interferon, interleukin, and other medications; psychological factors; endocrine diseases; and cytotoxic compounds [7].

4. Histology

Vitiligo lesions show marked depletion of melanin and a significant reduction in the number of melanocytes. Histopathological analysis reveals that the morphological alterations extend beyond the epidermis, involving subtle structural changes in the superficial dermis as well. Most cases demonstrate loss of pigmentation within the basal layer, and approximately half exhibit varying degrees of inflammatory infiltrate. In active vitiligo, characteristic lichenoid inflammatory changes are observed at the dermoepidermal junction, indicating an autoimmune process that targets basal melanocytes. Perilesional inflammatory infiltrates are mostly composed of T lymphocytes, especially cytotoxic $CD8^+$ cells that cluster around dermal vessels and skin appendages [8]. These cells recognize melanocyte differentiation antigens such as Melan-A/MART-1, tyrosinase, and gp100 [9]. Ex vivo studies have confirmed that such autoreactive T lymphocytes can induce vitiligo-like melanocyte destruction within a physiological tissue microenvironment [10].

5. Clinical findings

The clinical presentation of vitiligo is characterized by well-demarcated depigmented macules or patches, sometimes accompanied by leukotrichia. Although the condition is typically asymptomatic, pruritus occurs in approximately 20% of patients, most often coinciding with the appearance of new lesions. Depigmented areas are most frequently located on the face, hands, around body orifices, and in the genital region. Some patients exhibit a positive Koebner phenomenon, in which new lesions develop at sites of prior mechanical trauma. This response is particularly evident in areas exposed to chronic friction, such as the neck, elbows, and ankles, where new hypopigmented patches may form secondary to repetitive irritation [11]. In early stages, lesions appear as small, depigmented macules that may progressively enlarge and merge to form more extensive patches over time [12]. Wood's lamp examination can aid diagnosis, particularly in individuals with lighter skin phototypes, by revealing sharply demarcated, bright white fluorescence of affected areas [13].

6. Laboratory tests

The diagnosis of vitiligo is primarily clinical, supported by characteristic skin findings and Wood's lamp examination. However, because vitiligo frequently coexists with other autoimmune disorders, a detailed medical history and systemic evaluation are essential [7]. Vitiligo has been associated with a broad spectrum of autoimmune comorbidities, including autoimmune thyroid disease, alopecia areata, type 1 diabetes mellitus, pernicious anemia, systemic lupus erythematosus, rheumatoid arthritis, Addison's disease, inflammatory bowel disease, Sjögren's syndrome, dermatomyositis, and systemic sclerosis. In addition, ocular and auditory abnormalities, as well as dermatologic conditions such as psoriasis and atopic dermatitis, have been reported in affected patients. Educating patients about potential comorbidities is an essential part of comprehensive disease management, as early recognition and treatment of associated conditions can reduce the overall disease burden and improve quality of life [14]. When laboratory testing is indicated, recommended investigations include measurement of thyroid-stimulating hormone (TSH) and anti-thyroid antibodies, particularly anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG), which are sensitive markers of autoimmune thyroid disease. Additional tests, such as antinuclear antibodies (ANA), vitamin B_{12}, and fasting glucose or HbA1c, may be considered based on clinical context [15].

7. Classification of vitiligo

Vitiligo is broadly classified into two major types: non-segmental vitiligo (NSV) and segmental vitiligo (SV). Mixed forms exhibiting features of both categories have been described, while certain atypical cases that do not conform to these definitions are designated as unclassified vitiligo [16]. The non-segmental type is the most common, accounting for approximately 85-90% of all cases. It typically manifests in adulthood, although initial symptoms may appear in childhood. NSV is frequently associated with a personal or family history of autoimmune disease, and the Koebner phenomenon is often observed. Relapses are common, and surgical treatment usually offers limited benefit in this subtype. NSV encompasses several clinical variants, Including focal, mucosal, acrofacial, generalized, and universal forms. The segmental type generally presents earlier, most often during childhood. SV is characterized by a rapid onset of depigmentation followed by a stable, non-progressive course. Lesions usually occur unilaterally, following dermatomal or Blaschko lines, and are most frequently located on the face. Leukotrichia is commonly observed. In contrast to NSV, surgical treatment tends to produce more favorable results in SV, particularly when the disease is stable. SV can be subclassified into uni-segmental, bi-segmental, and multi-segmental types.

8. Vitiligo in children

In children, vitiligo often affects common predilection sites such as the face and neck, but depigmentation in the diaper area is also characteristic in infants. Pediatric lesions typically involve less than 20% of the total body surface area, with scalp involvement occurring in approximately 25% of cases [1]. The disease usually begins in early childhood or adolescence. About half of all patients develop vitiligo before the age of 20, and approximately one-quarter before the age of 8, with the mean age of onset being around 4-5 years [17]. The appearance of vitiligo during childhood can be emotionally distressing for both the patient and their caregivers, leading to a reduced quality of life and potential psychosocial challenges [18]. Comprehensive management in pediatric cases should therefore include not only early medical intervention aimed at halting disease progression and promoting repigmentation, but also psychological and social support to help maintain the child's functional and emotional well-being.

9. Treatment

A wide range of therapeutic options is currently available for the management of vitiligo, and new treatment modalities continue to emerge. Despite these advances, therapeutic challenges persist, as not all patients respond satisfactorily to existing interventions [19]. Current therapeutic approaches include topical and systemic treatments, phototherapy, laser therapy, surgical techniques, cosmetic camouflage, supportive measures, and psychological care. Most pharmacologic agents used in vitiligo are prescribed off-label, requiring proper documentation and adherence to ethical and regulatory standards. At present, no available therapy guarantees complete or permanent repigmentation. Therefore, the optimal treatment strategy should be individualized, considering factors such as the patient's age, disease duration, activity status, clinical type (SV or NSV), comorbidities, contraindications, and patient preferences. Treatment goals should focus on halting disease progression, achieving maximal repigmentation, and improving quality of life [1].

10. Local treatment

Topical therapy represents the cornerstone of vitiligo management, particularly for localized forms of the disease. Commonly used topical agents include corticosteroids, calcineurin inhibitors, Janus kinase (JAK) inhibitors, pseudocatalase, and microdermabrasion as an adjunctive procedure [20]. Vitamin D analogues, such as calcipotriol and tacalcitol, have also been utilized for disorders of pigmentation, including vitiligo [21]. Psoralen and khellin, both photosensitizing agents, may be applied topically in combination with ultraviolet (UV) radiation, although they are not recommended as monotherapy. Less commonly used or ineffective topical agents include melagenin, phenylalanine, L-DOPA, coal tar, anacardic (babchi) oil, and topical minoxidil [22].

10.1. Topical corticosteroids

Topical corticosteroids (TCs) are among the most frequently prescribed agents in dermatology. When used appropriately, they are both safe and effective [23]. Potent (betamethasone valerate) and very powerful (clobetasol propionate) corticosteroids are considered first-line treatments for localized vitiligo [24]. Their efficacy is supported by histological evidence demonstrating repopulation of active melanocytes in previously depigmented epidermis following therapy with betamethasone valerate or 0.05% clobetasol propionate cream [25]. Continuous use of potent corticosteroids should be restricted to a maximum of 6 to 8 weeks, followed by intermittent or weekend application to minimize adverse effects such as skin atrophy, telangiectasia, and striae.

10.2. Calcineurin inhibitors

Topical calcineurin inhibitors (TCIs), including pimecrolimus and tacrolimus, are widely accepted as alternatives to potent corticosteroids, especially for sensitive areas such as the face, neck, and intertriginous regions [26]. Although originally approved for atopic dermatitis, numerous studies have confirmed their efficacy in vitiligo as off-label agents.

In monotherapy, tacrolimus 0.1% ointment has demonstrated comparable repigmentation efficacy to clobetasol propionate 0.05% cream [27]. Similar outcomes have been observed in pediatric populations. The best responses are typically seen in facial lesions, where ≥75% repigmentation has been achieved in a substantial proportion of patients. Common transient adverse effects include burning, stinging, erythema, and local irritation [28].

10.3. Janus Kinase Inhibitors

In July 2022, the U.S. Food and Drug Administration (FDA) approved topical ruxolitinib (Opzelura) as the first JAK inhibitor indicated for the treatment of vitiligo. Ruxolitinib, a selective JAK1/JAK2 inhibitor, promotes repigmentation through modulation of the interferon-γ signaling pathway and has shown particularly favorable outcomes in facial lesions. This formulation is approved for use in both adults and adolescents (≥12 years old) and is generally well-tolerated, with minimal systemic absorption and infrequent mild local reactions, such as acneiform eruptions or pruritus [29,30]. Other topical JAK inhibitors remain under clinical investigation for potential use in vitiligo.

11. Phototherapy

According to current recommendations, the most common phototherapy methods include heliotherapy, NB-UVB, PUVA, and UVA1. Phototherapy is based on the therapeutic use of ultraviolet (UV) radiation. It can be performed with exposure to sunlight, ultraviolet A radiation (UVA), or ultraviolet B radiation (UVB). Based on the recommended guidelines, the wavelengths and doses of UV radiation may vary. Ultraviolet radiation (UVR) covers wavelengths from 200 to 400 nm. It is divided into UVA (320-400 nm), which is further subdivided into UVA2 (320-340 nm) and UVA1 (340-400 nm), and UVB, which is further subdivided into broadband UVB (290–320 nm) and narrowband UVB (NB-UVB), from 311 to 313 nm. Phototherapy is most often combined with topical or systemic pharmacological agents to increase the overall effectiveness of treatment. Adverse reactions, typically transient and including erythema or burns, may occur during therapy; therefore, close monitoring of the treatment course is essential [31]. In the management of generalized non-segmental vitiligo (NSV), particularly when >20% of total body surface area is affected, whole-body narrowband UVB (NB-UVB, 311 nm) phototherapy remains the first-line treatment due to its favorable efficacy and safety profile. In contrast, localized forms, especially in pediatric patients or in the case of recent-onset, limited lesions, are more appropriately treated with targeted phototherapy modalities, including focal NB-UVB and 308 nm excimer laser or non-laser light. These approaches reduce unnecessary UV exposure

and are preferable when full-body irradiation is contraindicated. Psoralen plus UVA (PUVA) therapy is reserved as a second-line option, primarily in adult patients with extensive NSV. However, it demonstrates lower efficacy compared to NB-UVB and is associated with a higher incidence of adverse effects. For PUVA bath therapy, psoralen concentrations should not exceed 0.01%. Phototherapy should be discontinued if no clinical response is observed after three months or if repigmentation remains below 25% after six months of treatment. The cumulative exposure should be carefully monitored, not exceeding 2000 J/cm² for PUVA or two years of NB-UVB therapy. At present, maintenance phototherapy is not routinely recommended. Nevertheless, regular dermatologic follow-up is advised. During periods of increased natural sunlight exposure, supervised heliotherapy may serve as a temporary alternative to artificial phototherapy [1]. The effectiveness of narrowband UVB phototherapy (NB-UVB) has been confirmed in studies. Analysis of therapy efficacy by lesion location revealed the highest incidence of repigmentation in the face and neck. Lesser effects were observed on the trunk and limbs, while no significant clinical improvement was achieved in the hands and feet [32].

12. Surgical treatment

Surgical approaches are primarily indicated for patients with stable vitiligo who have not responded to medical or phototherapy modalities. Two major categories are recognized: tissue grafting and cellular transplantation. Tissue grafts involve the transfer of thin split-thickness skin or epidermal fragments to depigmented areas without the use of enzymes or chemical processing. Donor sites are typically chosen from areas not exposed to sunlight, such as the inner thighs, buttocks, back, or retroauricular region especially for facial reconstruction. These techniques yield the most favorable results in segmental vitiligo (SV), although success has also been reported in stable non-segmental vitiligo (NSV) when combined with adjuvant therapy.

Cell-based techniques utilize suspensions of melanocytes and keratinocytes. They can be performed using cultured methods (transplantation of cultured melanocytes or epidermal sheets) or non-cultured methods. Disease stability for at least 6 to 12 months is essential for optimal outcomes. The main objective is restoration of pigmentation, however, complications may include infection, scarring, color mismatch, or donor-site morbidity [33]. In systematic analyses, >90 % repigmentation was achieved in over half of patients, with the best results seen using thin split-thickness grafts. Suction-blister grafts and epidermal cell suspensions also achieved ≥50 % repigmentation in most cases. Clinical outcomes depend on patient age, disease type, lesion site, and cost considerations [34].

13. Systemic treatment

Systemic therapy aims to halt disease progression and induce repigmentation, generally with acceptable safety. Commonly used agents include oral mini-pulse corticosteroid therapy (OMP), methotrexate, azathioprine, cyclosporine, mycophenolate mofetil, simvastatin, apremilast, minocycline, afamelanotide, and JAK inhibitors such as tofacitinib and baricitinib. Oral or injectable corticosteroids and antioxidants are also employed. Despite experimental interest, zinc supplementation and alefacept have not produced consistent clinical benefits [35]. Ritlecitinib, an oral inhibitor of JAK3 and Tec kinases, has demonstrated efficacy and good tolerability in patients with active, particularly non-segmental, vitiligo [36].

14. Combined Treatment

14.1 Topical Corticosteroids and Phototherapy

Combining potent corticosteroids with NB-UVB 311nm or 308nm excimer laser/light enhances repigmentation and allows reduction of cumulative UV exposure. This strategy is particularly useful for new or active lesions and for areas prone to therapeutic resistance (elbows, knees).

14.2 Calcineurin Inhibitors and Phototherapy

Topical tacrolimus or pimecrolimus combined with phototherapy produces synergistic effects, outperforming either modality alone. The regimen is well tolerated, though long-term data on photocarcinogenicity remain limited.

14.3 Phototherapy and surgery

Postoperative NB-UVB or PUVA phototherapy accelerates repigmentation following surgical procedures. Progress should be documented with serial photographs or planimetric measurements [1].

14.4 Vitamin D analogues and adjuncts

Topical calcipotriol and tacalcitol, when used with NB-UVB, may enhance repigmentation. Tacalcitol appears slightly more potent. Combination therapy with corticosteroids and vitamin D analogues increases efficacy while reducing steroid-related side effects. Emerging data also support cholecalciferol plus microneedling for stable disease [37].

15. Additional therapeutic approaches

For localized, stable vitiligo, adjunctive modalities such as microneedling, fractional YAG laser, and platelet-rich plasma (PRP) injections have shown promise. Microneedling disrupts the epidermis mechanically, promoting regeneration and facilitating penetration of topical agents. Laser-assisted drug delivery (LADD) with fractional YAG laser creates microscopic ablation zones that enhance drug diffusion while minimizing thermal injury. PRP, an autologous concentrate rich in growth factors, stimulates melanocyte proliferation and survival. Clinical trials indicate that YAG and PRP produces greater repigmentation and higher patient satisfaction than PRP + microneedling alone [38].

16. Camouflage and photoprotection

At the outset of treatment, patients should receive counseling on disease mechanisms, realistic expectations, and sun protection. Cosmetic camouflage and self-tanning products can substantially improve appearance and quality of life, especially in exposed areas. Regular sunscreen use helps prevent contrast enhancement between depigmented and normal skin. In selected patients, camouflage therapy alone may suffice during the initial management phase [26].

17. Depigmentation therapy

Depigmentation is reserved for patients with extensive, treatment-refractory vitiligo who desire uniform skin tone. The principal agent is the monobenzyl ether of hydroquinone (MBEH), while 4-methoxyphenol and phenol (≤88%) may be alternative options. Physical modalities include Q-switched ruby or alexandrite lasers, as well as cryotherapy. Experimental or second-line options such as imatinib mesylate, imiquimod, and diphenylcyclopropenone (DPCP) remain investigational. Depigmentation requires many months and is irreversible; local irritation, uneven bleaching, and paradoxical repigmentation may occur [39]. Thorough counseling and informed consent are essential.

18. Psychological support

Patients with vitiligo exhibit higher rates of anxiety, depression, and hopelessness than healthy controls [40]. Routine use of validated instruments such as the Dermatology Life Quality Index (DLQI) or VitiQoL questionnaire is recommended to assess psychosocial burden and identify those needing psychological or psychiatric referral [41]. Integrating camouflage therapy with psychotherapy has been shown to significantly enhance quality of life and may beneficially modulate the psycho-neuro-endocrine-immune-cutaneous axis, supporting holistic disease management [42].

19. Diet and lifestyle factors

Recent studies suggest that elevated body-mass index (BMI) and unhealthy dietary patterns may contribute to vitiligo onset and progression, with distal extremities often most affected. Deficiencies in micronutrients such as vitamin D, manganese, and dietary fiber may exacerbate oxidative stress and inflammation. Dietary optimization and weight control can therefore serve as valuable adjunctive measures in comprehensive care [43].

20. Skin cancers and vitiligo

Epidemiological and genome-wide association studies indicate an inverse relationship between vitiligo susceptibility and the risk of melanoma, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC). Certain genetic variants that increase autoimmunity appear to confer protection against tumor development. Patients with advanced melanoma who develop vitiligo-like depigmentation during immunotherapy often experience improved survival, supporting this immune-protective link [44]. Nevertheless, photoprotection remains essential, especially for individuals receiving phototherapy.

21. Future directions

Advances in vitiligo treatment are primarily focused on the use of targeted therapies that modulate the immune response and support melanocyte regeneration. Patients with vitiligo are encouraged to actively participate in current clinical trials to contribute to the development of increasingly effective therapeutic strategies. Following the approval of topical ruxolitinib, oral JAK inhibitors baracitinib, upadacitinib, povorcitinib, and rilecitinib are currently being studied in this area. Inhibiting the onset of the disease may be an important element of future therapeutic strategies for vitiligo. The HSP70i protein is an important signal that can trigger the disease, so blocking its action may prove an effective strategy, as confirmed by animal studies. Furthermore, preventing the damage and shedding of skin pigment cells by using therapeutic agents that inhibit matrix metalloproteinase-9 may also yield beneficial results. New data also suggest a role for gut-dermal dysbiosis in the pathogenesis of vitiligo, opening therapeutic avenues related to microbiome modulation [45].

Prostaglandin F2α analogues, such as latanoprost and bimatoprost, show potential as topical treatments for vitiligo due to their ability to stimulate melanogenesis. Preliminary studies suggest their efficacy in promoting repigmentation with minimal side effects, but further studies are needed to confirm their effectiveness and safety. Another medication under investigation is afamelanotide, a synthetic analogue of α-MSH, which enhances the effects of phototherapy in vitiligo, particularly in darker-skinned individuals, by accelerating and enhancing repigmentation.

Another promising therapeutic approach is inhibiting the IL-15 pathway. The cytokine IL-15 plays a key role in the survival and maintenance of resident memory T lymphocytes (TRMs), which contribute to the destruction of melanocytes. IL-15 pathway inhibitors have the potential to prevent disease progression and relapse. Preclinical studies confirm the efficacy of this therapy, and further data on its safety and effectiveness are being developed [46]. Studies also indicate that IFN-γ plays a key role in the progression of vitiligo by recruiting autoreactive CD8+ T cells to the skin via the chemokine CXCL10, and that blocking IFN-γ or its signaling pathways could represent a potential therapeutic strategy. Additionally, simvastatin, a drug approved for hypercholesterolemia, has been shown to both prevent and reverse vitiligo in mice, likely by inhibiting STAT1 activation [47]. Numerous promising therapeutic strategies are currently being investigated, which may lead to the development of increasingly effective treatment options in the future.

22. Conclusions

Vitiligo is a chronic, acquired depigmenting disorder caused by the selective loss of melanocytes through complex autoimmune and oxidative mechanisms. Genetic and biochemical factors further modulate susceptibility and disease course. Although not physically harmful, vitiligo has a significant psychosocial impact, requiring management that addresses both medical and emotional aspects. Current treatment options including topical and systemic therapies, phototherapy, and surgery can slow progression and induce repigmentation, though complete and lasting results remain uncommon. The emergence of targeted immunomodulatory agents, particularly JAK inhibitors, offers promising prospects for more effective and individualized therapy. Adjunctive measures such as dietary optimization, psychological support, and camouflage techniques contribute to improving patients' quality of life. Continuous research and patient participation in clinical trials are essential to refine existing treatments and develop new strategies aimed at achieving durable repigmentation and better long-term outcomes.

Authors' contribution statement:

Conceptualization, K.M., and E.S.; methodology, K.M., and E.S.; check, L.S., J.B., D.G., M.C.,R.S.,M.A., and M.M.; formal analysis, E.S., J.B., L.S., and M.M.; investigation, K.M.; resources, K.M., and E.S.; writing - rough preparation, K.M., E.S., and L.S.; writing - review and editing, J.B., M.A., M.C., R.S., D.G., and M.A.; visualization, L.S.; supervision, J.B.,L.S., M.C.,R.S., D.G., and M.A.; project administration, L.S., K.M., and E.S.

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