

**FROM MELANIN TO MEDICINE: MODERN INSIGHTS INTO VITILIGO****Om Pandekar\*, Samiksha Dadas, Sakshi Khot, Sanskruti Pandekar, Ravi Barkade**

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Article Received on 28 March 2026,

Article Revised on 17 April 2026,

Article Published on 01 May 2026,

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**How to cite this Article:** Om Pandekar\*, Samiksha Dadas, Sakshi Khot, Sanskruti Pandekar, Ravi Barkade (2026). From Melanin To Medicine: Modern Insights Into Vitiligo. World Journal of Pharmaceutical Research, 15(9), 47-64.

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**• ABSTRACT**

Vitiligo is a common skin condition that affects about 0.5% to 2% of people worldwide. In this condition, the pigment-producing cells of the skin, called melanocytes, are gradually lost. As a result, smooth, chalky-white patches appear on the skin. These pale or colorless areas, known as achromic macules and patches, occur because of loss of normal skin pigmentation.<sup>[2]</sup> The most common treatments for vitiligo include phototherapy (both systemic and topical) and medications that help regulate the immune system, such as corticosteroids, calcineurin inhibitors, and vitamin D analogues. Many people also use cosmetic products to cover the affected areas and boost their confidence. Although vitiligo is often seen as a cosmetic condition, it can have a significant impact on both

the physical and emotional well-being of those who live with it.<sup>[3]</sup>

**Vitiligo (vi-ti-LEYE-goh)** is a chronic autoimmune disorder that causes patches of skin to lose pigment or color.<sup>[1]</sup>

**Figure No. 1: Vitiligo.**

## ● INTRODUCTION

Vitiligo is a long-term skin condition that develops over time and often recurs. It is marked by the appearance of pale or white patches on the skin due to the destruction of melanocytes—the cells responsible for skin pigmentation. This loss of color can cause visible changes that may affect a person's confidence, sometimes leading to emotional and social challenges and a reduced quality of life.

In recent years, mesenchymal stem cells (MSCs) have gained attention for their ability to regulate the immune system, support tissue repair, and show low chances of rejection after transplantation. This article highlights the current understanding of how the immune system contributes to vitiligo and explores the advances made in using MSC-based therapies as a potential treatment approach.<sup>[4]</sup>

Vitiligo is usually diagnosed based on its appearance during a clinical examination, often supported by a Wood's lamp test, which helps highlight the depigmented patches on the skin. Although rarely necessary, a skin biopsy may be performed; in established lesions, it typically shows a complete loss of melanocytes, while in actively spreading areas, T cells can be seen near the remaining melanocytes.

Vitiligo itself does not cause serious physical illness, but it can deeply affect a person's social and emotional well-being. Throughout history, the condition has carried a heavy stigma—many ancient cultures viewed it as a punishment from the gods, a sign of demonic influence, or even confused it with leprosy. These misconceptions have contributed to the social and cultural challenges faced by people with vitiligo.<sup>[5]</sup>

Recent studies have found that the levels of certain signaling proteins, such as the chemokines CXCL9 and CXCL10, are higher in the blood of people with active vitiligo and may be linked to how well they respond to treatment. Other studies have also reported increased levels of inflammatory molecules like IL-15, IL-17, IL-1 $\beta$ , and IL-18 in these patients. However, since these blood markers reflect inflammation throughout the entire body, they can be influenced by other inflammatory conditions that a person might have. Therefore, directly studying biomarkers from the skin itself provides a more accurate understanding of the disease process in vitiligo.<sup>[6]</sup>

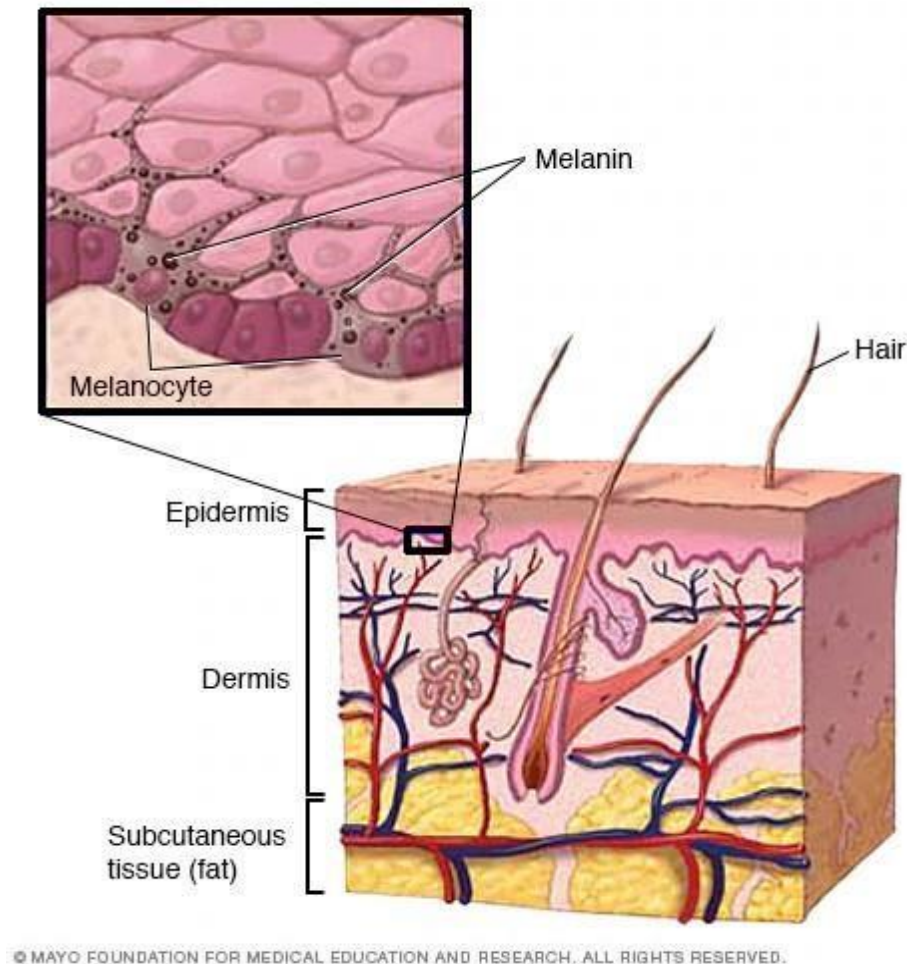
Vitiligo holds particular significance for patients in our country because the loss of skin color is more visible on darker skin tones, and, more importantly, the condition is often burdened by deep social stigma. Research using tools that measure health-related quality of life, such as the Dermatology Life Quality Index (DLQI), has shown that vitiligo can greatly impact a person's well-being. In fact, studies among Indian patients have found that many individuals with vitiligo experience mental health challenges like anxiety, depression, and sleep disturbances, highlighting the emotional toll of the condition beyond its physical appearance.<sup>[7]</sup>

### ● ETIOLOGY

1. Scientists believe that vitiligo is an autoimmune condition, meaning the body's own immune system mistakenly attacks and destroys the melanocytes—the cells responsible for producing skin pigment. Researchers are also exploring how genetics and family history might influence the risk of developing vitiligo. In some cases, triggers such as severe sunburn, emotional stress, or exposure to specific chemicals can cause vitiligo to appear or make existing patches spread more rapidly.<sup>[8]</sup>

Vitiligo develops when the cells produce skin pigment, called melanocytes, either die or stop making melanin — the natural it's pigment is responsible for the color of your skin, hair, and eyes. When it is lost, the affected skin areas appear lighter or may become completely white. The exact reason why these pigment cells stop working or die isn't fully understood, but it's believed to be linked to a few factors, such as.

- \* An autoimmune reaction, where the body's immune system attacks its own pigment cells
- \* A family history of vitiligo, suggesting a genetic connection
- \* Certain trigger events, like emotional stress, severe sunburn, or skin injury caused by exposure to chemicals.<sup>[9]</sup>



**Figure No. 2: Melanin and Melanocyte.**

- **CLINICAL FEATURES**

- **TYPES OF VITILIGO**

- 1. Segmental Vitiligo**

Segmental vitiligo is a distinct form of vitiligo that differs from the more common generalized type. It usually begins early in life and is characterized by the rapid appearance of well-defined white patches or spots on one side of the body, typically following a segmental or band-like pattern. These patches usually develop over a period of 6 to 24 months and then stop spreading on their own. Unlike generalized vitiligo, segmental vitiligo affects only one side and does not cross the body's midline.

The exact cause isn't fully known, but similar to generalized vitiligo, it's thought to happen when the immune system of the body wrongly targets and destroys the pigment-producing cells known as melanocytes. Some researchers also suggest that it may result from a phenomenon called.

\*somatic mosaicism\*, which occurs very early in development and makes a specific group of pigment cells more vulnerable to immune system attack.<sup>[10]</sup>



**Figure No. 3: Segmented Vitiligo.**

## 2. Non-Segmented Vitiligo

Nonsegmental vitiligo is a type of vitiligo where patches of skin lose their natural color because the immune system mistakenly targets and destroys melanocytes — the cells responsible for producing pigment. Both genetic and environmental factors play a role in its development. Recent genetic research has uncovered several genes that may raise the risk of nonsegmental vitiligo, offering scientists a better understanding of the mechanisms behind the condition.<sup>[11]</sup>

Recent histopathological studies shown that in vitiligo-affected skin, especially around the edges of depigmented patches, there is an increased presence of immune cells such as dendritic cells, Th17 cells, and CD8+ cytotoxic T lymphocytes. At the same time, there is a noticeable decrease in regulatory T cells (Treg cells), which normally help keep the immune system in balance. This imbalance triggers the immune system to attack melanocytes, the pigment-producing cells, which result in reducing skin color seen in vitiligo.<sup>[12]</sup>



**Figure 5a:** Nonsegmental vitiligo patch on forehead showing merger with pariaural patch in a lateral view



**Figure 5b:** Nonsegmental vitiligo patch on forehead, a frontal view

**Figure No. 4: Non-Segmented Vitiligo.**<sup>[13]</sup>

### 3. Mixed Vitiligo

Mixed vitiligo (MV) refers to the presence of both segmental vitiligo (SV) and non-segmental vitiligo (NSV) in the same individual. However, research on this form of vitiligo is still quite limited. To better understand it, a retrospective study was conducted using clinical data from patients with MV and SV who visited our pigmentedary clinic between July 2015 and December 2019. The study aimed to compare their clinical characteristics, demographic details, and treatment responses.<sup>[14]</sup>



**Figure No.5: Mixed Vitiligo.**<sup>[15]</sup>

## ■ DISTRIBUTION PATTERN

### 1. Focal Vitiligo

Focal vitiligo is identified by the presence of small, localized patches of depigmentation that do not follow the typical segmental pattern. It is considered an undetermined form of vitiligo because, over time, it may either remain localized or progress into segmental or non-segmental vitiligo. A clearer diagnosis is usually made if the condition does not change or spread within one to two years. However, since the likelihood of progression is still uncertain, deciding on the best treatment approach can be challenging. The aim of the study was to analyze the characteristics of patients with focal vitiligo and identify possible factors that may predict its progression.<sup>[16]</sup>



**Figure No. 6: Focal Vitiligo.**<sup>[17]</sup>

### 2. Acrofacial Vitiligo

In acrofacial vitiligo, the depigmentation typically affects areas such as the face, scalp, hands, and feet. A key feature of this type is the loss of color around the fingertips and facial openings, such as the mouth, eyes, and nose. Over time, the condition may spread to other parts of the body, eventually developing into generalized vitiligo. Studies using latent class analysis have shown that acrofacial vitiligo occurs more frequently in adults who develop vitiligo later in life.



**Figure No. 7: Acrofacial Vitiligo.**<sup>[18]</sup>

### **3. Mucosal Vitiligo**

Mucosal involvement in vitiligo is quite common among people with darker skin tones, with lip depigmentation seen in up to 50% of patients. In lighter-skinned individuals, the occurrence of mucosal vitiligo is likely underreported because loss of colour is harder to notice against their naturally pale mucous membranes. In some cases, a slight darkening around the edges of the depigmented areas may help in identifying and confirming the condition.



**Figure No. 8: Mucosal Vitiligo.**<sup>[19]</sup>

#### 4. Generalized Vitiligo

Generalized vitiligo is an acquired skin condition in which white patches, or depigmented areas, develop due to the immune system attacking and destroying melanocytes—the cells that give skin its color. This form of vitiligo is often linked to other autoimmune disorders, like thyroid diseases (like Hashimoto's thyroiditis and Graves' disease), rheumatoid arthritis, adult-onset type 1 diabetes, psoriasis, pernicious anemia, systemic lupus erythematosus, and Addison's disease.<sup>[20]</sup>



Figure No. 9: Generalised Vitiligo.<sup>[21]</sup>

#### 5. Universal vitiligo

Universal vitiligo refers to complete or near-complete loss of skin tone across most of the body. This condition usually develops when non-segmental vitiligo (NSV) gradually spreads, leading to widespread, loss or absence of skin pigment, resulting in lighter or white areas on the skin., body hair, and sometimes the mucous membranes of the mouth and genitals. Scalp hair is often affected as well, where as in the initial stages, areas such as the scalp, underarms, and pubic region may remain unaffected. In some sun-exposed areas, small patches of pigment may persist around hair follicles or appear as tiny, merged spots.

The difference between vitiligo universalis (VU) that develops from typical NSV and more aggressive, “fulminant” forms of vitiligo that also affect other melanocyte-containing tissues—like those in the ears and eyes, as seen in the rare Vogt-Koyanagi-Harada syndrome—is still not completely known. It’s also essential to note that individuals who lose all skin color due to medical depigmentation treatments should not be classified as having VU.<sup>[22]</sup>



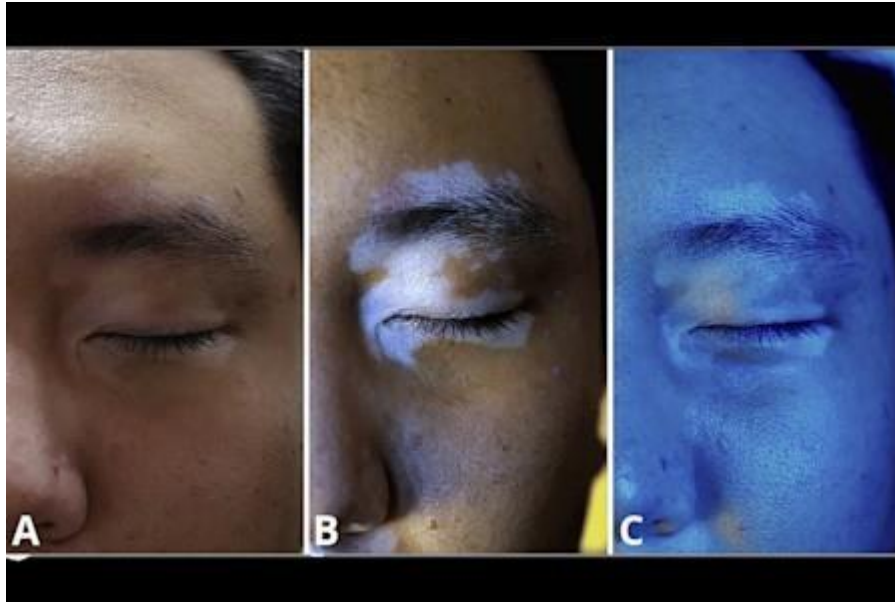
**Figure No. 10: Universal Vitiligo.<sup>[23]</sup>**

#### ● **DIGNOSIS**

A board-certified dermatologist can diagnose vitiligo by carefully examining your skin and reviewing your medical history to understand when and how the patches developed.

#### **1 Wood's Lamp**

To examine your skin more closely, your dermatologist may use a device called a Wood’s lamp. This special lamp gives off ultraviolet (UV) light, also known as blacklight, which causes certain skin cells to glow or change color. The procedure is quick and painless, and it helps the dermatologist clearly identify areas affected by vitiligo. It’s also commonly used to help diagnose other skin conditions, such as fungal or bacterial infections.



**Figure No. 11: Woods lamp method for diagnosis of vitiligo.**<sup>[24]</sup>

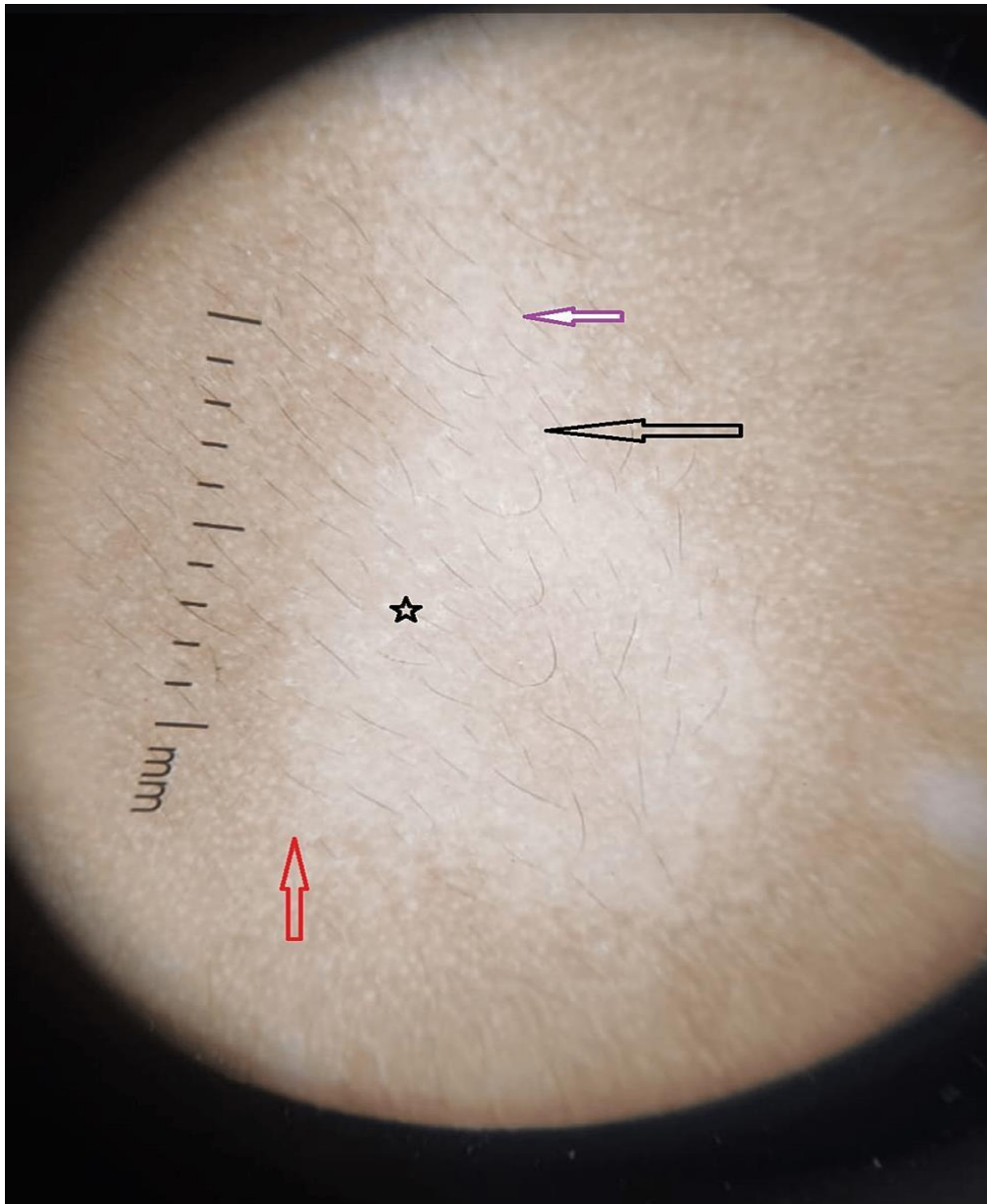
## 2 Dermiscopy

Dermiscopy is a simple, non-invasive technique that helps confirm a vitiligo diagnosis by allowing doctors to see tiny skin structures that aren't visible to the naked eye. It helps detect subtle pigment changes, evaluate how active the vitiligo is, monitor repigmentation efforts, identify white hair (leucotrichia), and distinguish vitiligo from other causes of light-colored skin patches.

Most of the clues seen through dermoscopy are found around hair follicles, both in the center and at the edges of the affected areas. The presence of pigment around hair follicles often indicates either active vitiligo or signs of improvement with treatment. However, complete depigmentation in these areas usually suggests a poor treatment response or prognosis.

In the center of the lesion, dermoscopy typically shows a reduced or missing pigment network in both active and stable cases. If small islands of pigment, redness (erythema), or tiny visible blood vessels (telangiectasias) are seen, it suggests that repigmentation may be starting.

At the borders of the patch, unstable or spreading vitiligo can appear as a blurred or uneven edge, a trichrome (three-tone) pattern, tiny tail-like extensions (comet tail or micro-Koebner phenomenon), small satellite spots, or a tapioca sago-like pattern—features that help dermatologists assess disease activity and predict its course.<sup>[25]</sup>



**Figure No. 12: Typical dermoscopic image showing four distinct patterns.**

### **3 Autoimmuno Pannel**

An autoimmune panel is a helpful blood test used in diagnosing vitiligo because it measures the levels of autoimmune antibodies in the body. This panel typically includes tests for antinuclear antibodies (ANA) and other specific autoantibodies that are often associated with autoimmune conditions linked to vitiligo, like thyroid disorders or rheumatoid arthritis. Increased levels of antibodies suggest that the body's defense system overactive and may be attacking own cells of body, which could lead to or progression of vitiligo.

### **4 Thyroid Function Test**

One common misconception is that thyroid function tests (TFTs) can be used to diagnose

vitiligo. This is not true. TFTs are not diagnostic markers for vitiligo; instead, they help detect other autoimmune conditions—such as thyroid disorders—that are often linked to the disease.

Many people with vitiligo may have underlying thyroid issues that go unnoticed because the symptoms are mild or nonspecific. Therefore, conducting comprehensive thyroid function tests alongside a vitiligo diagnosis is important. It helps identify any related complications early and allows for timely treatment, supporting the patient's overall physical and emotional well-being.<sup>[26]</sup>

## ● TREATMENT

### 1 Topical Corticosteroides

Applying a corticosteroid cream to the affected areas of skin can sometimes help restore color, especially when vitiligo is in its early stages. These creams are easy to use and can be quite effective, though it may take several months before any noticeable improvement appears. Possible side effects include skin thinning or the development of fine streaks or lines on the skin.

For children or individuals with large patches of discolored skin, doctors usually recommend milder forms of corticosteroids to minimize side effects. In cases where vitiligo is spreading quickly, corticosteroid pills or injections may be prescribed to help slow down the progression of the condition.<sup>[27]</sup>

### 2. Calcineurin Inhibitors

Calcineurin (CaN) is a special type of enzyme known as a calcium ( $\text{Ca}^{2+}$ ) and calmodulin (CaM)-dependent serine/threonine phosphatase. It becomes active when the calcium levels inside cells increase. Once activated, calcineurin plays an important role in regulating various cellular processes, including immune responses and inflammation.<sup>[28]</sup>

Topical calcineurin inhibitors (TCIs) — medicines like tacrolimus and pimecrolimus — are commonly used to treat vitiligo, but their effectiveness when used alone is often underestimated. This review looked at prospective studies to measure how well TCIs work by themselves and when combined with phototherapy, and it also examined how these drugs act in the skin. In short: TCIs can help by calming the immune attack on pigment cells, and pairing them with light treatment may improve results — but the exact benefits and why they

work best in some patients more than others are what researchers aimed to clarify.<sup>[29]</sup>

### 3 Phototherapy

Phototherapy is a treatment that uses ultraviolet (UV) light—similar to the light in natural sunlight but carefully filtered—to deliver specific wavelengths that help restore skin color. The focused UVB rays used in this therapy can stimulate the growth of melanocytes, the pigment-producing cells, in areas affected by vitiligo. This process not only encourages repigmentation but can also help prevent new white patches from appearing.<sup>[30]</sup>

During phototherapy, your skin is exposed to controlled amounts of UV light for a specific period, which is carefully determined by your dermatologist based on your skin type and condition. The treatment is usually done using a light box that emits UV light while you stand inside it.

If only certain areas of your skin need treatment, your dermatologist may recommend laser therapy instead. This approach allows focused light to target small, specific patches of skin affected by vitiligo, minimizing exposure to the surrounding healthy skin.<sup>[31]</sup>

### 4. Skin Grafting

For people with stable vitiligo, “skin grafting” can be an effective treatment option. This procedure involves transplanting small sections of healthy, pigment-producing skin (rich in melanocytes) onto the depigmented areas. By restoring color to these patches, skin grafting not only improves the skin’s appearance but can also boost a person’s confidence and emotional well-being. When performed by skilled specialists, many patients experience noticeable and lasting results.

Types of skin grafting include

1. Split-thickness grafting – uses a thin layer of the top skin surface.
2. Composite grafting – combines both the epidermis and a portion of the dermis.
3. Pinch grafting– involves transferring small “pinch-sized” pieces of skin.
4. Punch grafting – uses tiny circular sections of skin, often for smaller patches.<sup>[32]</sup>



**Figure No.13: Skin Grafting method for treatment of vitiligo.<sup>[33]</sup>**

## **5. Stem Cell Therapy**

Stem cell therapy holds potential new approach for treating vitiligo, particularly in patients with stable, non-segmental vitiligo who haven't responded well to conventional treatments. This regenerative focuses on restore lost pigment by repairing or replacing damaged melanocytes and rebalancing the immune response.

### **Types of Stem Cell Therapy Used in Vitiligo**

#### **1. Epidermal Melanocyte Stem Cell Transplantation**

In this method, skin grafts are taken from the patient's normally pigmented areas. The pigment-producing cells are then processed and transplanted into the depigmented patches to help restore color.

#### **2. Mesenchymal Stem Cells (MSCs)**

Collected from bone marrow or fat tissue, MSCs have powerful anti-inflammatory and immune-regulating properties. They help reduce autoimmune activity and promote the healing of damaged skin.

### 3. Adipose-Derived Stem Cells (ADSCs)

Extracted from fat tissue, these stem cells help lower immune system overactivity and support the regeneration of healthy skin cells, aiding in repigmentation.

### 4. Hair Follicle-Derived Stem Cells

These stem cells contain precursors of melanocytes. When transplanted, they can migrate to depigmented areas and repopulate them with new pigment-producing cells, helping restore natural skin color.

- **Psychological and Social Aspects**

- **Quality of Life impact**

Vitiligo is often seen as just a cosmetic condition, but it can deeply affect a person's emotional and psychological well-being, leading to significant challenges in daily life. Many individuals with vitiligo experience feelings of embarrassment and low self-esteem, especially when the patches appear on visible parts of the body. This can result in emotional distress, social withdrawal, and isolation.

The stigma surrounding vitiligo can also impact how people interact with others, sometimes leading to strained relationships and a high risk of depression or other psychological issues. Even though vitiligo is not life-threatening, it can greatly influence overall quality of life and overall mental and emotional health.<sup>[34]</sup>

#### Psychosocial Comorbidities in Patients With Vitiligo: A Systematic Literature Review



**Figure No. 14: Psychological impact of Vitiligo.**<sup>[35]</sup>

- **Role of counselling and supportive groups**

Vitiligo can deeply affect life, particularly among younger individuals, as it influences daily activities, career opportunities, and personal relationships. The emotional and social impact

tends to be more severe when the patches appear on visible parts of the body or in individuals with darker skin tones. However, with time and proper management, many patients develop greater acceptance, which can help improve their overall well-being.

Providing psychological support and counseling is essential, as many people living with vitiligo do not seek medical help due to stigma or lack of awareness. Education plays a powerful role in helping patients understand the condition better, reducing fear and anxiety.

In conclusion, the relationship between vitiligo, psychological health, and quality of life underscores the need to address social stigma, offer emotional support, and promote education and awareness. Together, these efforts can greatly enhance the well-being and confidence of individuals living with vitiligo.<sup>[36]</sup>



**Figure No. 15: Socialisation of the patient.**<sup>[37]</sup>

## CONCLUSION

Vitiligo is a complex, multifactorial skin disorder with an intricate underlying pathophysiology. Although significant advances have been made in understanding this condition, its exact origin and mechanisms remain unclear. The processes that lead to melanocyte damage are still not fully understood, highlighting the need for further research

into the disease's etiology. Gaining insight into the molecular pathways and biological mediators responsible for metabolic dysfunction, melanocyte destruction, and autoimmune reactions is crucial for identifying new therapeutic targets and developing effective treatments to halt disease progression or achieve repigmentation. Recent findings suggest that therapies targeting cytokines may be beneficial for autoimmune skin disorders such as psoriasis and vitiligo. Consequently, interventions directed at the interferon (IFN)-chemokine axis represent a promising area for current and future treatment development. However, treatment outcomes for vitiligo remain inconsistent, and relapse is common. Personalized therapeutic approaches should be tailored according to the type and activity level of vitiligo, as well as potential side effects.

Currently, treatment options are limited, and none guarantee consistent repigmentation in all patients. Continued scientific and clinical research is essential to deepen the understanding of vitiligo and to develop innovative, more effective therapeutic strategies. Many emerging therapies show promise, though most evidence comes from case reports or small studies. Robust randomized controlled trials are needed to confirm their efficacy and safety.

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