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*Original Article*

# A Comprehensive Overview of Vitiligo

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## ABSTRACT

The loss of melanocytes, which are cells that produce colour, is the hallmark of vitiligo, a chronic autoimmune skin condition that causes white spots or patches on the skin. Even though its precise cause is yet unknown, vitiligo most likely results from a complicated interaction between several variables. These include environmental, autoimmune, and hereditary factors. The three primary forms of vitiligo are segmental, non-segmental, and mixed. The symptoms of vitiligo include white or pale spots, skin discolouration, loss of skin pigmentation, itching or redness, and skin sensitivity. Topical corticosteroids, topical immunomodulators, vitamin D analogue, skin grafting, dietary modifications, stress reduction, JAK inhibitors, stem cell therapy, and more are some of the treatments available. This review summarised what is currently known about vitiligo and attempted to provide a forecast for future developments in vitiligo treatment.

**Keywords:** vitiligo, pigmentation, leukoderma, melanocytes, autoimmunity

## INTRODUCTION

The depigmenting skin condition known as vitiligo is brought on by a specific melanocyte depletion that weakens the melanin in the skin's afflicted regions. The macule has distinct edges, is chalky-white, non-scaly, and entirely amelanotic [1]. Depigmentation typically manifests symmetrically, starting on your fingers, toes, forearms, elbows, and upper arms and extending to the area around your lips and eyes. It is impossible to understand such symmetry [2]. Hypopigmented patches are the hallmark of the condition and are often initially observed on the knuckles, fingertips, and the region around the eyes, lips, toes, and reproductive organs [3]. Bilateral or generalized vitiligo can start at any age and frequently advances intermittently throughout a person's lifetime [2]. If less than one centimetre of skin is losing colour, the lesion is called a macule; if more, it is called a patch [4]. Both men and women are equally impacted, however a small number of studies have found a female predominance. This may be due to the fact that women are more prone to suffer from autoimmune disorders or to have self-consciousness about their appearance when they seek medical attention [5]. In 1975, Thomas B. Fitzpatrick developed Fitzpatrick skin phototypes, which are based on an individual's skin tone and how they burn and tan when exposed to sunlight [6]. A prospective population-based and case-control research study has most commonly used the Fitzpatrick skin type to examine sun sensitivity and the factors that contribute to skin cancer, such as UV radiation exposure, tanning, and protective behaviours [7]. Prevalence rates vary geographically, with Africa and India often having higher rates. At 9.98%, the Indian subcontinent has the highest frequency of vitiligo [8], followed by Nigeria at 2.8% and Romania at 2.28% [9]. Numerous Indian studies indicate that the prevalence of vitiligo among dermatological outpatients varies from 0.25 to 4%, with the highest frequency occurring in the states of Gujarat and Rajasthan (8.8%) [10]. The distinctive lesion is a chalky-white, nonscaly, completely amelanotic macule with clear borders. The pathophysiology of vitiligo has been better understood in recent years, and it is now categorically categorised as an autoimmune disease linked to environmental and genetic causes as well as well as problems in metabolism, oxidative stress, and cell detachment [11]. Because the disease causes social isolation, stigmatisation, and low self-esteem in those who are affected, it significantly lowers the quality of life for both adults and children [12]. Originating from the Latin term "vitium," which denotes a "blemishing fault," The complex interaction of autoimmune,

**Relevant conflicts of interest/financial disclosures**: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

environmental, and genetic variables is where it started. [13]

**Etiology:**

The cause of vitiligo is still unknown and the focus of numerous research projects. Since autoantigens recognised by T cells from vitiligo patients have been discovered in recent decades, it is thought to be an autoimmune-related disease. Numerous distinct mechanisms have been implicated in the development of white patches and the death of melanocytes in vitiligo. Neural, genetic, autoimmune, oxidative stress, inflammatory mediator production, and other pathways for melanocyte separation are among them [11].

- **Autoimmune theory:**

The most popular and well-established theory, known as "autoimmune mediation," postulates that when the response is disrupted, autoimmune effector mechanisms—such as memory cytotoxic T cells or autoantibodies directed against melanocyte. The connection between vitiligo and autoimmune diseases is widely acknowledged [14]. The fact that vitiligo is linked to various autoimmune diseases, that organ-specific antibodies are present in vitiligo patients, and that vitiligo treatments indirectly modulate the immune system all lend credence to the autoimmune idea [15]. The finding that checkpoint inhibitor-treated neoplastic patients may also develop the condition lends further credence to the idea that autoimmunity plays a part in vitiligo development. As a result, it has been noted that in patients with metastatic melanoma receiving treatment with inhibitors of the cytotoxic T-lymphocyte antigen-4 (CTLA-4) and programmed cell death-1 protein (PD-1) pathways, vitiligo development may also result in improved response and survival rates [16].

- **Genetic Theory:**

Several candidate genes have been identified as contributing to the polygenic nature of vitiligo, including the major histocompatibility complex (MHC), angiotensin-converting enzyme (ACE), catalase (CAT), cytotoxic T lymphocyte antigen-4 (CTLA-4), protein tyrosine phosphatase, human leukocyte antigen (HLA), and interleukin-2 receptor A (IL2RA). A genetic connection between widespread vitiligo and all of these immune-regulating factors has been investigated [17]. Currently, a number of related genes have been found. Along with other pigmentary, autoimmune, and autoinflammatory illnesses, they play a role in immunological modulation, melanogenesis, and apoptosis. [18] The enzyme tyrosinase, which is encoded by the TYR gene, catalyses the melanin biosynthesis's rate-limiting stages. In generalised vitiligo, tyrosinase is a key autoantigen present [19]. Large protein synthesis during melanin formation raises the possibility that those proteins will misfold, which triggers the unfolded protein response, a stress pathway inside the cell. Vitiligo has been linked to XBP1P1, the gene that codes for X-box binding protein. The 23% concordance rate of monozygotic twins emphasises the significance of extra stochastic or environmental elements in the vitiligo development process [20].

- **Oxidative Stress Theory:**

As per the oxidative stress theory, the main cause of vitiligo is the intra-epidermal accumulation of reactive oxygen species, the most well-known of which is hydrogen peroxide (H2O2), whose concentration at this concentration, the H2O2 changes the mitochondria, causing the melanocytes to perish by apoptosis. Vitiligo patients usually show alterations in redox status markers. MDA is an indication of oxidative stress and a byproduct of lipid peroxidation. The activity of GPx requires selenium, a vital antioxidant present in erythrocytes. SOD neutralises peroxide radicals, reducing their toxicity, and CAT transforms them into oxygen (O2) and water (H2O). Vitiligo patients exhibit low levels of the enzyme CAT, significantly higher levels of SOD, decreased erythrocyte GPx activity, and low levels of vitamins C and E in their blood and epidermis [21]. Melanocytes react to stress by releasing reactive oxygen species (ROS). The antioxidant system is then widely altered as a result [22]. It has been proposed that the heightened sensitivity of melanocytes to external pro-oxidant stimuli in vitiligo is caused by an imbalance between pro-oxidants and antioxidants [23]. Melanocytes are poisoned by melanin synthesis itself. Melanocytes use energy for a process called melanogenesis, which causes the skin to become pro-oxidant [24].

- **Neural Theory:**

According to the neural theory, neurochemicals released by nerve endings have the ability to harm melanocytes or decrease the formation of melanin. It also suggests a link between the catalase gene and the pathophysiology of vitiligo. In practically every living organism, the peroxisome enzyme catalase is found. It shields cells against extremely reactive oxygen radicals by promoting the breakdown of hydrogen peroxide into water and oxygen. Patients with vitiligo have reduced catalase enzyme activity in both their lesional and non lesional skin [11].

- **Biochemical Theory:**

The accumulation of harmful intermediate metabolites of melanin formation and insufficient defence against free radicals, according to the biochemical theory, result in excessive hydrogen peroxide (H2O2), which kills melanocytes. Some hypotheses suggest that the depigmentation process is caused by a combination of hereditary factors, defects in melanocyte structure and function, and a deficiency of melanocyte development factors [11].

**Pathophysiology:**

Melanocyte loss may occur gradually due to a number of causes, including immunological attack or cell degeneration and separation. According to the "convergence theory" or "integrated theory," two or more pathways may cooperate in vitiligo to cause melanocyte loss, which would ultimately result in the same clinical outcome [25]. The inflammatory pathophysiology of SV and NSV, however, appears to overlap, according to more recent data. Vascular dilatation and the immunological response follow the initial release of proinflammatory cytokines and neuropeptides brought on by internal or exterior injury, which appears to be a multistep process in both cases [26]. Known as the "neural hypothesis," some authors have proposed that the nerve system plays a role in the pathophysiology of vitiligo. This theory was predicated on SV's unilateral distribution pattern [27]. Moreover, there is little data to back up such a theory. Possible HLA connections in vitiligo were investigated because of the common correlation between vitiligo and autoimmune disorders. Several studies have linked HLA types A2, DR4, DR7, and Cw6 to vitiligo. The pathophysiology of vitiligo also suggests mutation [28]. Heritable biological characteristics that may make some people's melanocytes vulnerable to environmental triggers or other stressors, potentially leading to melnocyte death by necrosis, apoptosis, or pyroptosis, may be indicated by anecdotal reports of precipitating events by vitiligo patients [29]. Vitiligo can be caused by a variety of reasons, including the buildup of toxic substances, changes in the cellular environment, poor migration and/or proliferation of melanocytes, viral infections, neurological, autoimmune, and autocytotoxic factors, as well as psychological (patients' stress and personality traits) [30]. According to Al-Abadei et al., psychological stress may be the first stage in the pathophysiology of vitiligo since it raises levels of neuroendocrine hormones, impacts the immune system, and changes the amount of neuropeptides. [31] A thorough examination of the borders of active generalised vitiligo lesions has consistently revealed sparse infiltrates of cytotoxic T cells, and many individuals with the condition have serum autoantibodies and circulating autoreactive T cells that are directed against melanocytes and melanocyte components [29] Patients with vitiligo have been shown to have higher levels of soluble interleukin (IL)-2 receptor, IL-6, and IL-8, which further implies that T-cell activation may play a role in the pathophysiology of vitiligo [32],Because melanins are colloidal pigments with a strong affinity for metal ions, pigmented tissues involved in melanin formation were found to contain significant concentrations of specific metal ions, including copper, zinc, and iron. In conclusion, it is expected that the identification of the molecular processes underlying the pathogenesis of vitiligo will yield new therapeutic and preventative targets for upcoming strategies aimed at treating and preventing vitiligo and the autoimmune disorders that are linked to it [33]. Only the genes linked to autoimmune susceptibility—HLA, PTPN22, NALP1, and possibly CTLA4—have significant support at this time. Patients with vitiligo typically score higher on measures of anxiety, sadness, obsessive symptoms, adjustment difficulties, and hypochondria. Therefore, there might be a connection between stress and vitiligo growth

**Epidemology:**

Approximately 0.5 to 2% of adults and children worldwide are thought to have vitiligo, the most

prevalent depigmenting skin condition [34]. But it appears that there are significant regional variations. In the Shaanxi Province of China, for instance, a research found a prevalence of 0.093% [35], but in other parts of India, rates reached 8.8% [36]. A comprehensive analysis of prevalence data from over 50 research conducted worldwide has shown that vitiligo prevalence varies from 0.06% to 2.28% [37]. " In a meta-analysis of 103 research, the pooled prevalence of vitiligo from 82 community- or population-based studies was 0.2%, and from 22 hospital-based studies, it was 1.8% [38]. While both men and women are equally impacted, women and girls tend to seek advice more frequently than men and boys, maybe as a result of the larger negative social impact [39]. In certain South Asian, Mexican, and American groups, the incidence has been observed to reach 4% . About 20% of vitiligo patients have at least one first-degree family who also has the condition, and the relative risk for first-degree relatives of vitiligo patients is seven to ten times higher [28]. The prevalence rates of vitiligo vary widely throughout the world, ranging from 0.004% to 2.28% [40]. The prevalence peaks in early adolescence for young women and between 45 and 60 for men [33].

## CLASSIFICATION:

According to the assessment conducted by the Vitiligo Global Issues Consensus Conference in 2011 and 2012, there are four ways that Vitiligo might manifest clinically. mixed (SV+NSV), segmental, non-segmental, and unclassified. These subcategories vary in their aetiologies in addition to clinical symptoms, which include the onset of the first skin lesions, their location and extent, the presence of concomitant autoimmune illnesses, and the dermatosis's natural course [73]. The face (periorificial), hands (dorsal surfaces), nipples, axillae, umbilicus, sacrum, and inguinal/anogenital areas are among the areas that are frequently hyperpigmented and typically affected by vitiligo. It prefers the digits, flexor wrists, knees, and elbows on the extremities [41].

| Type of Vitiligo | Subtype of Vitiligo |
|---|---|
| SV | a) Focal<br>b) Unisegmental<br>c) Bi-Or Multisegmental |
| NSV | a) Focal<br>b) Mucosal<br>c) Acrofcial<br>d) Generalized<br>e) Unisersal<br>f) Rare Variants of Vitiligo (Leukoderma Punctata, Hypochromic Vitiligo, Follicular Vitiligo) |
| Mixed (SV+NSV) | Concomitant occurrence of SV and NSV According to severity of SV |
| Unclassified | Focal at onset, multifocal asymmetrical nonsegmental, mucosal (one site), |

**Segmental Vitiligo:**

Segmental vitiligo is an acquired chronic pigmentation disease characterised by unilaterally distributed white patches that may resemble a dermatome entirely or in part. Hair bleaching is caused by its rapid impact on the follicular melanocyte reservoir [14]. One or more white, depigmented macules are dispersed on one side of the body in monosegmental vitiligo. It is SV's most prevalent form [42].

**1) Focal Vitiligo:**

The term "focal vitiligo" describes a small, isolated, depigmented lesion that has not changed over the course of one to two years and lacks a clear distribution pattern. It can develop into either SV or NSV [11].

**2) Mucosal Vitiligo:**

Oral and/or genital mucosae are usually affected by mucosal vitiligo. It might manifest as a separate ailment or as part of a larger case of vitiligo. A solitary case of mucosal vitiligo that persists for at least two years [11].

**Non-Segmental Vitiligo:**

The lesions are symmetrically dispersed across the body or bilaterally distributed in an acrofacial pattern. There are six other categories for this type: NSV, or nonsegmental vitiligo, is the most prevalent kind of vitiligo, accounting for 80–90% of all instances. It is a long-term acquired pigmentation condition characterised by bilateral, usually symmetrical white spots that gradually get bigger and usually reflect a significant decrease in the number of melanocytes in the epidermis and some in the hair follicles that are still functional. NSV encompasses acrofacial, generalised, universal, mixed, localised, mucosal (when affecting many mucosal locations), and others [43].

**1) Acrofacial Vitiligo:**

Depigmented macules restricted to the face and/or distal extremities are a characteristic of acrofacial vitiligo. Depigmentation of the distal fingers and facial orifices is a characteristic. It might eventually spread to other bodily parts and be more appropriately categorised as universal or generalised [11].

**2) Genralized Vitiligo:**

Bilateral, frequently symmetrical, depigmented macules or patches that appear randomly across the body surface are the hallmark of generalised vitiligo. It frequently impacts regions that are prone to pressure, friction, and/or trauma. It could start in early adulthood or youth. Focal vitiligo, which may be a prelude to generalised vitiligo, is defined as a single macule or patch that lacks a segmental distribution and remains consistent over a period of two years [11].

**3) Universal Vitiligo:**

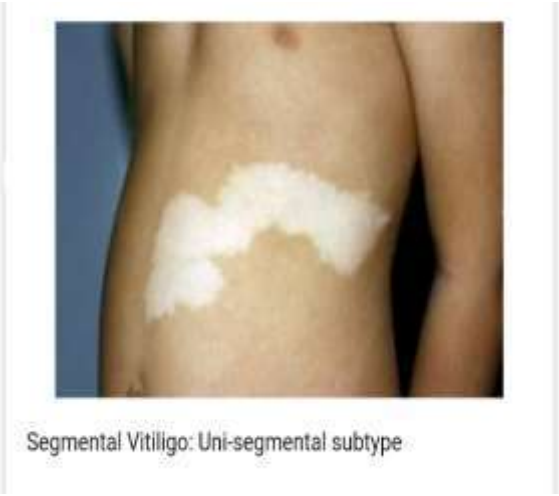
Complete or almost total skin depigmentation (affecting 80–90% of the body surface) is known as vitiligo universalis. [11]

**Mixed Vitiligo:**

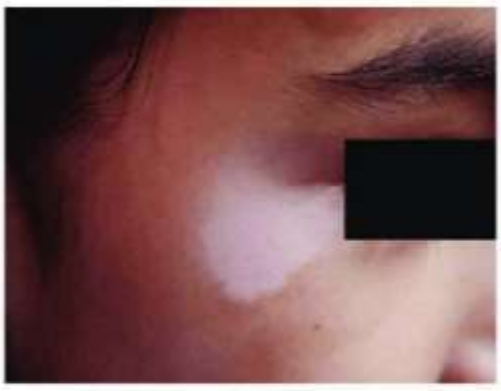
When SV and NSV occur simultaneously, it is referred to as mixed vitiligo. A segmental distribution of depigmented areas is absent at birth and during the first year of life, and a wood lamp examination rules out nevus depigmentosus, among other clinical characteristics. at least six months of delay between SV and NSV; SV affecting at least 20% of the dermatomal segment or exhibiting a distinct Blaschko linear distribution; and a difference between the response of SV (poor response) and NSV (good response) to standard narrow band ultraviolet B (NB-UVB) treatment. In SV patients, leukotrichia and halo nevi at onset may be risk factors for the development of MV [44]. Halo nevus (Sutton nevus) is the term used to describe the loss of pigmentation surrounding the pre-existing nevus that produces a halo. A high number of halo nevi indicates nested pigment-producing cell autoimmunity, which raises the risk of vitiligo [45]. Any part of the body that has strongly defined, depigmented, punctiform, 1- to 1.5-mm macules is referred to as "punctate vitiligo."[46].

**Unclassified Vitiligo:**

The two types of vitiligo that cannot be classified are mucosal, which occurs when just one mucosa is impacted, and focal, which occurs when isolated white macules without segmental dispersion [44]

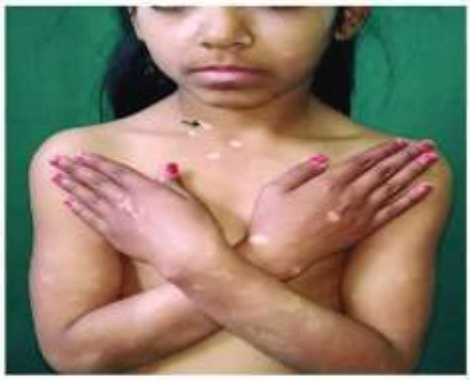


Segmental Vitiligo: Uni-segmental subtype

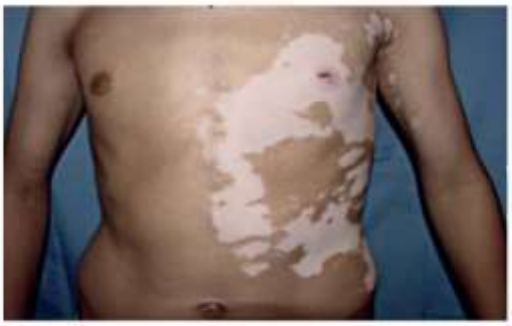


Focal vitiligo macule over the right periocular area. It did not evolve to any pattern within one year.

Mucosal vitiligo involving the upper lip.



Depigmented macules over the face, chest, and extremities in generalized vitiligo. A halo nevus is also seen (arrow).



Segmental Vitiligo. Unilateral lesions that respect, almost completely, the body midline, characterize segmental vitiligo. There are rare cases of bilateral segmental vitiligo

**Signs and Symptoms:**

One or more areas of lighter skin are the main sign of vitiligo, and for many people, this is their only physical symptom. Other symptoms and indicators could appear, including [47].

- The emergence of lighter skin spots and patches.
- The colour of the patch's changes to white.
- Lighter patches appear inside the mouth or nose.
- The patches and spots are more vulnerable to sunburn.
- The patches itch.
- Hearing loss begins.
- The colour of the eye's changes.

## DIAGNOSIS:

Vitiligo may typically be identified with certainty when mature, amelanotic, non-scaly, chalky-white macules with translucent edges are physically present in a distinctive dispersion in the mouth, lower extremity tips, genitalia, and segments and places of friction. Rarely, aside from ruling out other conditions, a skin biopsy or further testing is necessary. Skin sample and in vivo confocal imaging are non-invasive ways to assess whether a disease lacks melanocytes. Only sporadically were lymphocytes seen at the borders of the lesions as they grew. A Wood's lamp or other portable ultraviolet (UV) illumination device that produces ultraviolet A (UVA) may help with vitiligo diagnosis. Especially in people with pale skin, it helps destroy localised melanocytes and finds areas of depigmentation that might never be apparent to the naked eye. The vitiligo spots display clear edges and a vivid blue-white glow under Wood's light. Using dermoscopy, vitiligo was differentiated from other depigmenting conditions. Additionally, it might help identify the vitiligo's disease behaviour and developmental stage: Lesions that are static or repatriating exhibit perifollicular depigmentation, while those that are advancing exhibit perifollicular pigmentation. Melanoma-associated depigmentation and vitiligo may be distinguished by antibodies that target the melanoma antigen recognised by T cells 1 (MART1), even if they appear physiologically identical [48]. The vitiligo disease activity score (VIDA) and vitiligo area severity index (VASI) can be used to assess the

severity and activation of the illness. The number of hand units used to calculate the percentage of vitiligo involvement. The palm and the volar surfaces of each digit make up one hand unit, which is about equivalent to 1% of the body's total surface area [44]. Areas of depigmentation that resemble vitiligo are a common and unusual symptom of several illnesses. It's critical to distinguish vitiligo from melanoma-associated leukoderma and avoid misdiagnosing it as vitiligo, particularly since it may occur before melanoma is discovered [49]. Due to the total absence of functional melanocytes, vitiligo is characterised by the total loss of epidermal pigmentation. Electron microscopy specific to melanocytes and immunohistochemistry using markers such as Melan-A and HMB-45 can be employed for additional research. Cellular enlargement, elongated dendritic processes filled with melanin granules, and cytoplasmic vacuolization are degenerative changes seen in melanocytes.

### I. Physical Examination:

Clinical examination is usually used to diagnose vitiligo based on the following features: [50]. Macules or patches have a convex border, show no symptoms of inflammation, and have normal skin surrounding them.

- The face, neck, dorsum of hands, scalp, and trunk are frequently covered in milky white macules that range in size from a few millimetres to several centimetres.
- Additionally, trauma-prone regions like the knees and elbows may develop lesions.
- Between 20% and 60% of people with vitiligo may develop koebnerization.

### II. Medical and Family History:

• Symptom history: the origin and progression of the illness are investigated.
• Family history of vitiligo: 20% of those afflicted have a close relative who has the disorder.
• Autoimmune illness family history: find out whether there is a family history of ailments like thyroid disease, lupus, or rheumatoid arthritis (RA).
• Previous skin issues: This includes cases of severe sunburn, rashes, or other injuries that occur in areas that are light or white.
• Stress levels: Stressful circumstances that affect the body, mind, and emotions may also be a factor [51].

### III. Diagnostic Testsand Procedure:

Several diagnostic tests and procedures are performed in order to accurately identify vitiligo. The Wood's light test, for example, uses a portable UV lamp that emits UVA to reveal skin depigmentation. This test is especially useful for pale skin tones since it can detect areas of pigment loss that are invisible to the untrained eye [52]. Another diagnostic approach is a skin biopsy, which is a small sample of the affected skin tissue taken to check for pigment cells called melanocytes. In the lab, the presence or lack of these cells is next evaluated on the skin sample under a microscope. Blood tests, such as a complete blood count and an antinuclear antibody test, may occasionally be ordered in order to evaluate general health and address particular issues. Lastly, a probable eye irritation (uveitis) is evaluated or an audiologist is consulted for hearing testing if a person exhibits vision or hearing problems [51].

### IV. Differential Diagnosis of Vitiligo:

There are other conditions besides vitiligo that can result in skin depigmentation. Dermatologists therefore look into other disorders if test results or clinical indications differ from those of vitiligo. Pityriasis alba, which primarily affects children and shows up as white, scaly macules on the face and places that are exposed to the sun; Under Wood's light, whitish, scaly and places exposed to the sun, a condition that primarily affects children; Tinea (pityriasis) Versicolour is a fungal illness that appears as pale, scaly macules on the chest and back as pale, scaly macules on the chest and back that glow yellow when illuminated by a Wood's lamp; melanocytic nevus known as a "halo nevus," which is encircled by an nevus"; In young people with progressive macular hypomelanosis, the condition manifests as asymptomatic hypopigmented patches on the trunk [50].

## ASSESMENT:

Hospital therapy for vitiligo necessitates a comprehensive initial assessment. To evaluate vitiligo patients, a comprehensive history and skin examination are necessary to ascertain the severity of the disorder and any special predicting factors. An evaluation procedure that compiles the medical diagnostic queries that may be helpful for diagnosis

was created by the Vitiligo European Task Committee [53]. People need to be regularly asked about their family history of thyroid disease, vitiligo, premature hair greying, autoimmune diseases, and other skin issues. It is necessary to take into account the following factors: Skin phototype; duration of illness; extent; interaction; rate of lesions' growth or progression; Koebner's phenomenon; halo nevi; previous treatments, category, duration, and performance; past repigmentation episodes; history of work-related illnesses or exposure to toxins; and the effect of the illness on one's quality of life. Because NSV raises the risk of autoimmune thyroid disease, specifically Hashimoto's thyroiditis, thyrotropin levels need to be regularly checked, particularly in individuals who have antibodies against thyroid peroxidase during the initial test [54]. Certain body parts are particularly vulnerable to Koebner's phenomena and are associated with activities of everyday living as dressing, cleanliness, and employment [44]. The following are the clinical indicators of active, progressing illness that have been most thoroughly described: Confetti-like depigmentation, inflammatory lesions, trichrome lesions, and Koebner's phenomena [50]. Lastly, as the patient's personality and the perceived severity of their vitiligo are predictors of quality of life impairment, a comprehensive evaluation of their psychological characteristics and quality of life is necessary [55]. A quality-of-life tool tailored to vitiligo has been created and approved. Counselling and psychological help should be made available to all vitiligo patients [56].

## TREATMENT:

One of the hardest dermatological problems to cure the vitiligo. Realising that vitiligo is more than just a cosmetic condition and that there are safe and efficient therapies for it is a crucial first step in managing the condition. Phototherapy, topical and systemic immunosuppressants, and surgical procedures are some of these treatments that may help stop the disease, stabilise depigmented lesions, and promote repigmentation. along the beginning, repigmentation is seen along the edges of the lesions or in a perifollicular pattern. Treatment must be administered for a minimum of two to three months in order to assess its effectiveness. The most popular treatment for vitiligo is UV light therapy, which is linked to better results when paired with another therapy [57].

### Topical Treatment Corticosteroids

Because corticosteroids control and inhibit the inflammatory response, they have a major therapeutic effect on vitiligo. Whether they are strong (betamethasone valerate) or extremely strong (clobetasol propionate), topical corticosteroids (TCS) are the first-line treatment for vitiligo. Whereas acral zones usually yield subpar outcomes, sun-exposed parts exhibit better therapeutic effects [58].

### Calcineurin Inhibitors

Tacrolimus (0.03% or 0.1%), and pimecrolimus (1%) are topical calcineurin inhibitors (TCIs) that target the head and neck region. They have fewer side effects, especially no danger of atrophy. TCI could be taken twice daily for a minimum of six months. If there are observable benefits, the therapy can be continued. A moderate amount of sun exposure every day is recommended throughout treatment [59].

### Vitamin D3 Analogues (D3A)

Because topical vitamin D3 analogues (D3A) have immunomodulatory effects that reduce T cell function, increase melanocyte development, and trigger melanogenesis, they are ineffective as a stand-alone treatment for vitiligo. They do, however, work well as adjuncts to other therapies.100 g weekly on 30% of the body area, along with a combination of betamethasone 0.05% and calcipotriol 0.005%, is the ideal dosage for four weeks when applying the ointment and eight weeks when applying the cream .Other promising pharmacological treatments that involve the use of minocycline antibiotics include 5-fluorouracil (5-FU); methotrexate (MTX); prostaglandin F2 alpha analogues, a peptide derived from primary basic fibroblast growth factor (bFGF); inhibitors of Janus kinase (JAK); systemic therapy corticosteroids; apremilast; etc. [60].

### Physical therapy

### Narrow-Band UVB Phototherapy

UV irradiation appears to have several systemic effects, including stimulation of the central hypothalamicpituitary-adrenal axis, initiation of the

proopiomelanocortin route in the hypothalamic arcuate nucleus, immunosuppressive effects, and opioid genic outcomes. Irradiance from UVB (280–320 nm) is more noticeable than that from UVA (320–400 nm). In order to treat vitiligo, NB-UVB photodynamic therapy (wavelength of 311 nm) suppresses the immune system, stimulates melanocyte emigration from perilesional skin, enhances melanin synthesis, and produces melanocyte separation [61].

**PUVA**

The 320–340 nm wavelength of PUVA irradiation suppresses the immune system and creates an environment that is favourable for melanocyte development, which results in the generation of melanin. Psoralen is typically applied topically or consumed and then exposed to UVA light as part of this second-line treatment [62].

**Antioxidants**

Although topical antioxidants are not advised by the current consensus guidelines, they are often administered in very few trials (Leone and Paro 2015). In patients receiving phototherapy, the use of oral antioxidants in combination therapy is occasionally taken into consideration [63].

**Excimer Laser**

The effectiveness of the excimer (308 nm) laser in treating vitiligo has been investigated in a number of investigations. More than 12 weeks of treatment are required to achieve adequate repigmentation. Between 50 and 100 mJ per square cm is the starting dose. The best facial treatment outcomes were obtained with an excimer laser, just like with conventional phototherapy [64].

**Surgical Modalities**

Only cosmetically sensitive locations that have not seen any new lesions, Koebnerization, or lesion expansion in the preceding 12 months should undergo surgical procedures (level of evidence 1). Relapse was observed in 40% of patients with progressing disease compared to 10% of those with stable disease in a research by Kim and Kang34 that involved suction blister transfer. Thankfully, a number of highly effective surgical procedures are available, such as melanocyte transplants, split thickness grafts, suction blister grafts, and tiny punch grafts [65].

## CONCLUSION:

A complicated and multifaceted autoimmune condition, vitiligo is typified by the loss of skin pigmentation. People of various ages and races are affected by vitiligo, which has a 1% global prevalence. White or pale spots, discolouration, itching, redness, and low skin pigmentation are some of the signs of vitiligo. The pathophysiology of disease is now better understood because to developments in cellular and molecular genetics, opening the door for novel targeted treatments. The lack of melanocyte regeneration in vitiligo can be explained by knowledge of the causes of melanocyte degeneration and autoimmune diseases, as well as how these conditions interact with their environment. By identifying the biological mediators of disease mechanisms, novel therapy targets may be found that can improve cell regeneration and delay the progression of the disease, causing damaged areas to repigment. Patient satisfaction and compliance would increase with better diagnostic and treatment methods. Vitiligo sufferers can enhance their quality of life and manage their symptoms with early diagnosis and therapy. Because vitiligo is linked to various conditions, it may be useful to understand its pathophysiology in addition to skin issues.In addition to creating more focused and efficient treatments, further research is required to completely comprehend the causes and mechanisms of vitiligo

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