

Vitiligo Causes and Treatment: A Review

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Abstract

Vitiligo is a chronic autoimmune disorder characterized by patches of skin losing pigment due to the destruction of melanocytes, the cells responsible for producing pigment. The condition can affect people of all ages and ethnicities, with symptoms including milky-white patches on the skin, premature graying of hair, and color loss in mucous membranes like the mouth or nose. Among the main causes of vitiligo are; Autoimmune Response: Vitiligo is primarily an autoimmune disease where the immune system mistakenly attacks melanocytes, leading to depigmentation. Factors like family history, genetic predisposition, and immune system disorders contribute to its development, Triggers: Events such as sunburn, emotional distress, or exposure to certain chemicals can trigger or exacerbate vitiligo. The treatment options are; Medications: Treatments include light therapy (phototherapy), oral medications like psoralen combined with UVA light (PUVA), and depigmentation therapy using monobenzone to match skin tones Surgery: Surgical options are available for some cases of vitiligo and Psychological Support: Counseling and mental health services can help individuals cope with the emotional impact of vitiligo, in conclusion, vitiligo is a multifaceted skin condition lacking a conclusive remedy, many types of vitiligo, but the most common one is Non-segmental Vitiligo (NSV), hormonal and genetic are the most important causes of vitiligo. Important symptoms of vitiligo are; depigmented patches, hair discoloration, sensitivity to sunlight, treatment of vitiligo have many approach, among them are; topical Corticosteroids, phototherapy and Cosmetic Camouflage.

Keywords: Vitiligo, Etiology, Mixed Vitiligo, Hormones, Genetic.

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INTRODUCTION

Vitiligo is a skin condition that causes loss of skin color in patches. It occurs when the cells that produce melanin, the pigment that determines the color of the skin, die or stop functioning. Vitiligo is an autoimmune disease, and its exact cause is not fully understood, but it is believed to involve a combination of genetic, autoimmune, and environmental factors. It can affect people of all skin types, but it may be more noticeable in people with brown or Black skin [1].

The histopathological diagnosis of vitiligo traditionally relies on the observation of the absence of melanocytes and melanin in the skin biopsy. However, confirming the absolute absence of these elements can pose challenges for pathologists. Therefore, when contemplating the prospect of biopsy for a vitiligo lesion, it is imperative to consider a range of factors and variables. This condition is typically linked with several autoimmune disorders, with thyroid abnormalities being the most prevalent [2].

What Are the Different Types of Vitiligo?

Vitiligo is a skin condition characterized by the loss of pigment, resulting in irregular white patches on the skin. There are several types of vitiligo, classified based on various factors such as the distribution and progression of the depigmentation [3-5]

Non-Segmental Vitiligo (NSV)

This is the most common type of vitiligo, accounting for about 90% of cases. It typically presents with symmetrical depigmented patches on both sides of the body, often affecting areas such as the mouth, face, hands, arms, eyes, fingers, armpits, wrists, groin, genitals and feet. Non-segmental vitiligo usually progresses slowly over time. It is also known as bilateral or generalized vitiligo, the symptoms typically appear on both sides of the body symmetrically [6].

Non-segmental vitiligo affects people of all ethnicities and ages, although it often begins before the age of 30 [7]. It affects both males and females equally.

The prevalence varies between populations, with estimates ranging from 0.5% to 2% worldwide [8, 9].

Segmental Vitiligo (SV)

Segmental vitiligo is less common and tends to occur at a younger age (children) compared to non-segmental vitiligo. It manifests as depigmented patches that are localized to one side or segment of the body. Unlike non-segmental vitiligo, segmental vitiligo often stabilizes after a period of progression. White patches only affect one area of the body; however segmental vitiligo tends to stabilize after 6 to 12 months, with color loss stopping and limited development of new patches [10].

Mixed Vitiligo

Mixed vitiligo refers to a form of the condition where features of both non-segmental (NSV) and segmental (SV) vitiligo are present in an individual. This combination can manifest as depigmented patches that are both symmetrical and localized to one side or segment of the body. Mixed vitiligo presents with a combination of depigmented patches characteristic of both NSV and SV. This may include symmetrical patches on one side of the body along with localized patches on the other side [11, 12].

Universal Vitiligo

This is an advanced form of vitiligo where depigmentation affects most or the body's entire skin surface. Universal vitiligo presents with widespread depigmented patches covering most or all of the body, including the face, trunk, extremities, and even areas such as the scalp and genitals. The patches may coalesce, resulting in near-total loss of pigmentation [13, 14].

Acral Vitiligo

Acral vitiligo is a subtype of vitiligo, a condition characterized by the loss of pigment-producing cells (melanocytes) in the skin, leading to patches of depigmentation. Acral vitiligo specifically affects the extremities of the body, including the hands, feet, and face. Acral vitiligo often manifests as depigmented patches on the fingers, toes, palms, and soles of the feet. These patches may initially appear as small, well-defined areas of lighter skin that gradually enlarge over time. The borders of the patches may be irregular, and the affected skin may lack pigmentation entirely, appearing white or very pale [15, 16].

Mucosal Vitiligo

Mucosal vitiligo refers to the presence of depigmented patches or lesions on mucous membranes, such as those lining the inside of the mouth, nose, genitalia, and rectum. It is a subtype of vitiligo, a condition characterized by the loss of melanocytes, the pigment-producing cells, in the skin and mucous membranes. Mucosal vitiligo typically presents as depigmented patches or lesions on the mucous membranes. These patches may appear as white or

lighter-colored areas on the lips, gums, tongue, inner cheeks, genitalia, or anus. The borders of the lesions may be irregular, and they may gradually enlarge over time [17, 18].

Focal Vitiligo

Focal vitiligo is a subtype of vitiligo characterized by the presence of depigmented patches or lesions that are limited to specific areas of the body. Unlike generalized vitiligo, which can affect large areas of the skin, focal vitiligo typically involves only a few isolated patches. Focal vitiligo presents as well-defined, depigmented patches or lesions on the skin. These patches may appear anywhere on the body but are usually localized to one or a few areas. The borders of the patches may be irregular, and they may gradually enlarge over time [19, 20].

Etiology of Vitiligo

The exact etiology of vitiligo, including its various subtypes such as acral, mucosal, and focal vitiligo, remains incompletely understood. However, several factors have been implicated in its development, the main causes are [2]:

Autoimmune Factors

Autoimmune mechanisms are thought to play a significant role in the pathogenesis of vitiligo, particularly in generalized and segmental forms. In these cases, the body's immune system targets and destroys melanocytes, leading to depigmentation. Autoimmune factors may involve T lymphocytes, cytokines, and autoantibodies targeting melanocyte antigens [21, 22].

Genetic Predisposition

Vitiligo has a genetic component, with evidence suggesting that multiple genes contribute to its susceptibility. Several genetic loci have been identified as associated with vitiligo, including genes involved in immune regulation, melanocyte function, and oxidative stress response [23].

Oxidative Stress

In 2022 Xuan and his coworkers [24], reported that the onset of vitiligo, characterized by damage to melanocytes, is primarily initiated by oxidative stress. This stress disrupts redox homeostasis, leading to an imbalance caused by the excessive generation of reactive oxygen species (ROS) and insufficient scavenging mechanisms [24]. However, the imbalance in oxidative stress and antioxidant defense mechanisms within the skin has been implicated in vitiligo pathogenesis. Increased oxidative stress can lead to melanocyte damage and apoptosis, contributing to depigmentation [25].

Neurochemical Factors

Neurochemical mediators, such as neuropeptides and neurotransmitters, may influence melanocyte function and contribute to the development

of vitiligo. Stress, which can affect neurochemical signaling, has been implicated as a trigger or exacerbating factor in some cases [26]. On the other hand, a study carried out by Henning *et al.*, 2020 [27], reported that there is no significant correlation emerged between perceived stress and the stage or extent of disease, indicating that increased stress might not solely result from pigment loss. These findings further bolster the notion that stress plays a role as a triggering factor in the development of vitiligo [27].

Environmental Triggers

Various environmental factors, including trauma, sun exposure, chemicals, infections, and certain medications, have been proposed as triggers for vitiligo development or exacerbation, particularly in predisposed individuals [8]. The findings of Rmadi *et al.*, 2023 indicate that chemical factors significantly contribute to the onset of vitiligo. Consequently, preventing this skin condition entails identifying exposure to the implicated chemicals in all patients undergoing vitiligo treatment. Early detection of "chemical" or chemically exacerbated vitiligo leads to better prognoses for the disease [28].

Figure 1 shows the main causes of vitiligo [29].

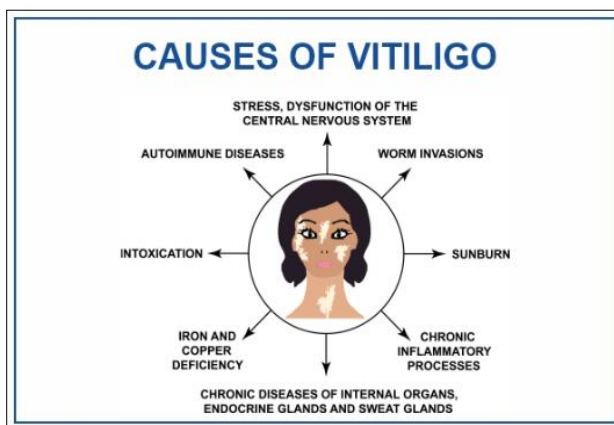


Figure 1: Etiology of vitiligo [29]

Vitiligo Symptoms

Vitiligo is a skin condition characterized by patches of depigmentation. These patches occur when melanocytes, the cells responsible for producing skin pigment, are destroyed or stop functioning. The symptoms of vitiligo can vary from person to person but commonly include [2-30].

Depigmented Patches

The primary symptom of vitiligo is the appearance of white or light-colored patches on the skin. These patches can vary in size and shape and may appear on any part of the body [31].

Symmetrical Distribution

In many cases, vitiligo patches occur symmetrically on both sides of the body. For example, if

a patch develops on one elbow, a similar patch may appear on the other elbow [2].

Progressive Spreading

Vitiligo patches may gradually enlarge or spread over time. New patches may also develop, leading to further depigmentation [32].

Hair Discoloration

In addition to affecting the skin, vitiligo can also cause hair in the affected areas to turn white or lose pigment [31].

Sensitivity to Sunlight

Some individuals with vitiligo may experience increased sensitivity to sunlight in depigmented areas. Sun exposure can cause these areas to burn more easily or become more noticeable [33].

Changes in Pigmentation of Mucous Membranes

In rare cases, vitiligo may also affect the pigmentation of mucous membranes, such as the tissues inside the mouth or nose [33].

It's very important to note and mention that vitiligo symptoms can vary widely among individuals, and not all affected individuals will experience all of these symptoms. Additionally, the progression and severity of vitiligo can vary, with some individuals experiencing only minor depigmentation while others may have extensive patches covering large areas of the body.

The Risk Factors for Developing Vitiligo

Vitiligo is a complex condition influenced by various factors, although its precise cause remains elusive. Identified risk factors contributing to its onset encompass genetic predisposition, autoimmune components, environmental influences, and specific medical conditions. Here's an overview of these contributing factors:

Genetic Predisposition

Family history of vitiligo is a significant risk factor. Studies have shown a higher prevalence of vitiligo among relatives of affected individuals [34]. In 2013 Dwivedi and his coworkers [35], indicate that NLRP1 rs6502867 and rs2670660 variations could serve as genetic predispositions for vulnerability to and advancement of generalized vitiligo (GV). The elevated expression of NLRP1 mRNA among individuals with susceptible genotypes underscores the pivotal involvement of NLRP1 in GV [35].

Autoimmune Factors

Vitiligo is often associated with autoimmune diseases such as thyroid disorders (like Hashimoto's thyroiditis or Graves' disease), autoimmune adrenal insufficiency (Addison's disease), and autoimmune polyendocrine syndrome [36].

In 2023, Hu and Wang [37], concluded in their review article that research literature establishes a link between vitiligo and ocular and auditory irregularities, autoimmune ailments, additional dermatological conditions, metabolic syndrome and associated disorders, as well as psychological illnesses. These connections underscore the significance of employing a multidisciplinary strategy in the treatment of vitiligo patients [37].

Environmental Triggers

Environmental factors like sunburn, exposure to certain chemicals, and emotional stress have been implicated in triggering or exacerbating vitiligo [38].

Vitiligo affecting the hands and feet has been linked to frequent exposure to irritating substances, excessive sunlight exposure, and repeated trauma to these areas, all significant risk factors for the condition. Early identification of these aggravating factors may

potentially help in managing the development of vitiligo [39].

Medical Conditions

Certain medical conditions, such as inflammatory skin diseases, may increase the risk of developing vitiligo [40].

Hormonal Changes

Hormonal changes, such as those occurring during pregnancy, may trigger or exacerbate vitiligo in susceptible individuals [41].

Skin Damage

Skin damage, including injuries like cuts or burns, can also contribute to the development of vitiligo [42].

Figure 2 shows Conditions coexisting with vitiligo [37].

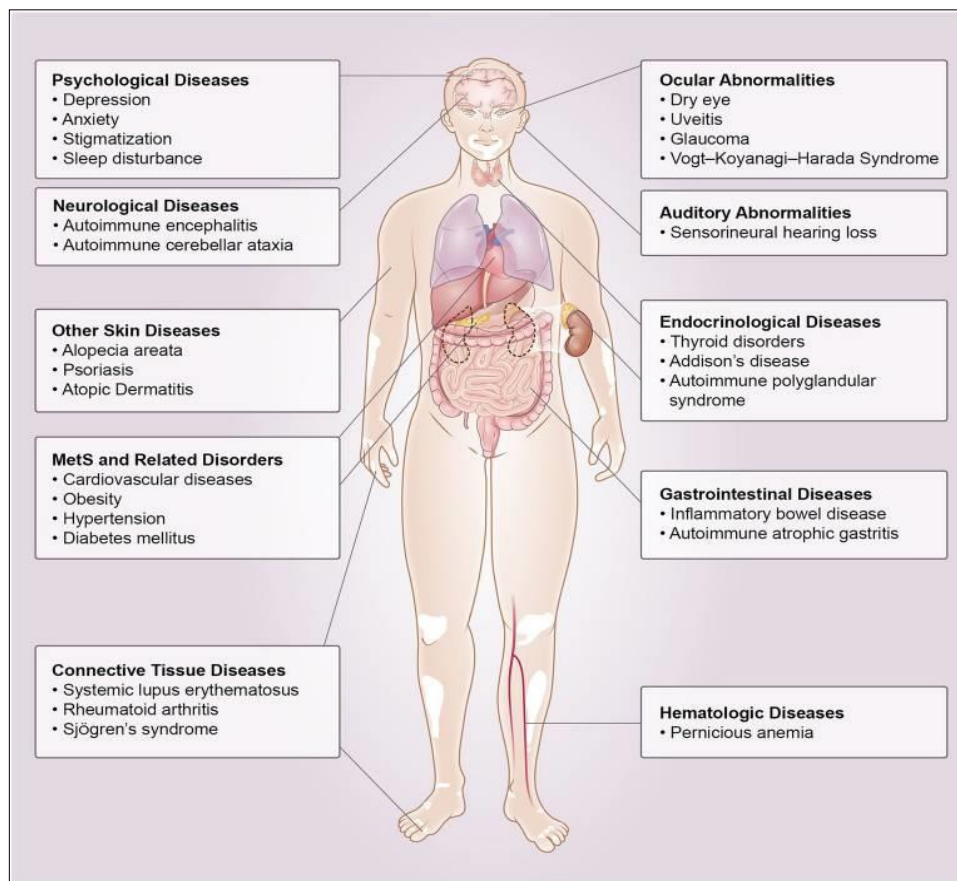


Figure 2: Associated comorbidities with vitiligo include MetS, which stands for metabolic syndrome [37]

It's crucial to acknowledge that although these risk factors are linked to vitiligo, not all individuals with these factors will develop the condition. Moreover, vitiligo can manifest in individuals without identifiable risk factors. Furthermore, it is recommended that additional studies may offer further insights into the development of vitiligo.

Vitiligo; Pathogenesis and Treatment

Vitiligo is an acquired skin disorder characterized by the disappearance of pigment cells from the epidermis, resulting in well-defined white patches symmetrically distributed on the skin. The exact cause of vitiligo is unknown but may involve genetic factors, autoimmunity, neurologic factors, toxic metabolites, and lack of melanocyte growth factors [43].

Vitiligo is a chronic skin condition marked by the loss of melanocytes, the cells responsible for producing melanin, the pigment that gives skin its color. While the exact cause is not fully understood, it's believed to result from a combination of genetic predisposition, autoimmune factors, and environmental triggers.

Pathogenesis

Autoimmune Hypothesis

One leading theory suggests that vitiligo is an autoimmune disorder, where the body's immune system mistakenly attacks and destroys melanocytes. This is supported by the observation of immune cells, particularly T lymphocytes, infiltrating the affected skin areas in individuals with vitiligo [44].

Genetic Factors

There is evidence to suggest that genetic factors play a role in predisposing individuals to vitiligo. Certain genes have been implicated in the susceptibility to the condition, although the inheritance pattern is complex and multifactorial [45].

Neurochemical Theory

Some researchers propose that neurochemicals released by nerve endings in the skin may be involved in

triggering the destruction of melanocytes. Stress and trauma have been suggested as potential triggers that disrupt the normal functioning of melanocytes [46].

Oxidative Stress

Another theory implicates oxidative stress, which refers to an imbalance between the production of reactive oxygen species (ROS) and the body's ability to neutralize them with antioxidants. Oxidative stress can damage melanocytes and contribute to their destruction in vitiligo [44].

Białczyk *et al.*, 2023 [47], mentioned that While newer forms of cell death such as necroptosis, pyroptosis, ferroptosis, and oxeiptosis are emerging as potential contributors to the pathophysiology of vitiligo, apoptosis remains the most extensively researched cell death mechanism in this condition. Studies indicate that vitamin E aids in addressing skin lipid peroxidation induced by psoralen ultraviolet A treatment. Furthermore, Polypodium leucotomos enhances the effectiveness of psoralen ultraviolet A or narrow-band ultraviolet B therapy [47].

Figure 3 representing pathogenesis between vitiligo and associated comorbidities

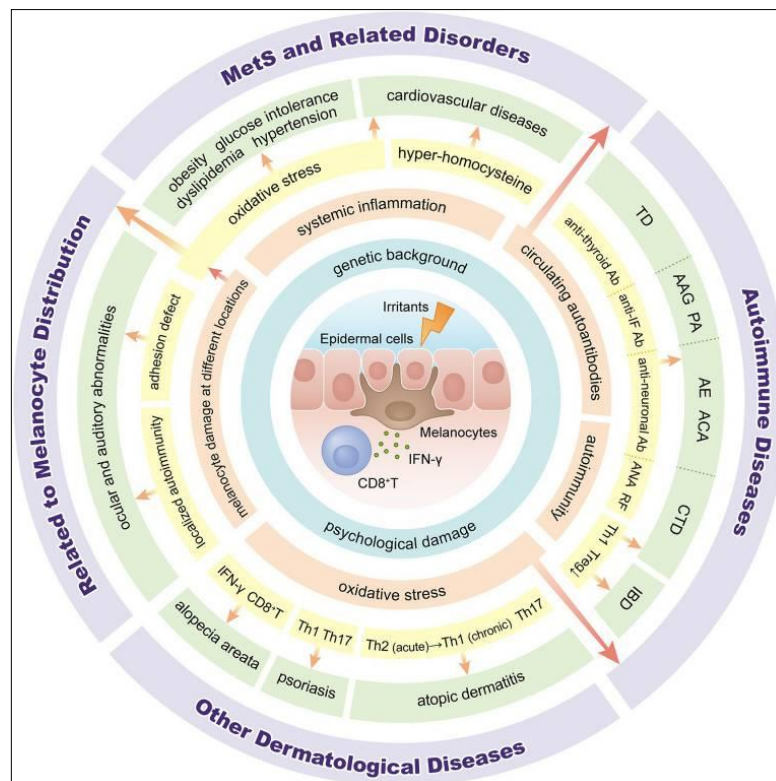


Figure 3: Pathogenesis amid vitiligo and related comorbidities [37]

IFN: interferon; *Ab*: antibody; *IF*: intrinsic factor; *ANA*: anti-nuclear antibody; *RF*: rheumatoid factor; *Th*: T-helper; *Tregs*: regulatory T cells; *TD*: thyroid disease; *AAG*: autoimmune atrophic gastritis;

PA: pernicious anemia; *AE*: autoimmune encephalitis; *ACA*: autoimmune cerebellar ataxia; *CTD*: connective tissue diseases; *IBD*: inflammatory bowel disease; *MetS*: metabolic syndrome.

Treatment

There is currently no cure for vitiligo, but various treatment options are available to help manage the condition and improve the appearance of affected skin. Treatment approaches may vary depending on the extent and severity of the condition, as well as individual factors such as age and overall health. Some common treatment modalities include [32].

Topical Corticosteroids

These anti-inflammatory medications are often prescribed to suppress the immune response in the affected skin areas and reduce inflammation. They can help to repigment the skin and may be used alone or in combination with other treatments [48].

Topical Calcineurin Inhibitors

These medications, such as tacrolimus and pimecrolimus, work by suppressing the immune system and may be used as an alternative to corticosteroids, particularly in sensitive areas such as the face and genital area [49].

Phototherapy

Phototherapy involves exposing the skin to ultraviolet (UV) light, either in the form of narrowband UVB (NB-UVB) or psoralen plus ultraviolet A (PUVA) therapy. Phototherapy can stimulate melanocyte activity and promote repigmentation of the skin [50].

Depigmentation

In cases where vitiligo affects a large portion of the body, depigmentation therapy may be considered to even out the skin tone. This involves using topical medications to bleach the remaining pigmented skin, making it match the depigmented areas [51, 52].

Surgical Treatments

Surgical options such as autologous melanocyte transplantation, blister grafting, and punch grafting may be considered for localized vitiligo that has not responded to other treatments. These procedures involve transplanting melanocytes from unaffected areas of the body to the depigmented skin areas [53].

Cosmetic Camouflage

Makeup and self-tanning products can be used to camouflage the depigmented areas and improve the appearance of the skin, particularly for individuals who prefer non-invasive options or are not candidates for other treatments [54, 55].

Collaborating closely with a dermatologist is crucial for individuals with vitiligo to craft a treatment strategy aligned with their unique needs and objectives. Moreover, prioritizing overall skin health, safeguarding the skin from sunlight, and effectively managing stress levels can aid in mitigating the advancement of vitiligo and enhancing treatment effectiveness.

Complications of Vitiligo

Vitiligo is a skin condition characterized by the loss of pigment-producing cells (melanocytes), leading to white patches on the skin. While vitiligo itself is not typically harmful or painful, it can have various complications, both physical and psychological. Here are some of the common complications associated with vitiligo [56-58].

Sunburn and Skin Cancer Risk

Skin affected by vitiligo lacks the protective pigment melanin, making it more vulnerable to sunburn and potentially increasing the risk of developing skin cancer, particularly melanoma. Individuals with vitiligo should use sunscreen with a high SPF and protective clothing when exposed to sunlight [59].

Social and Psychological Impact

Vitiligo can significantly impact an individual's self-esteem, confidence, and quality of life. The noticeable changes in appearance may lead to feelings of self-consciousness, social stigma, and even depression or anxiety. Counseling and support groups may be beneficial for managing the emotional impact of vitiligo [8].

Cosmetic Concerns

White patches caused by vitiligo can be cosmetically bothersome, particularly if they appear on visible areas of the body such as the face, hands, or feet. Makeup or self-tanning products may help conceal the patches, but these are temporary solutions and may not be practical for everyone [54].

Depigmentation

In some cases, vitiligo may progress to the point where a significant portion of the skin loses pigment. This condition, known as vitiligo universalis, can result in nearly complete depigmentation of the skin, leaving the individual with very pale or white skin all over their body completely [52].

Autoimmune Disorders

Vitiligo is believed to be an autoimmune condition, meaning the body's immune system mistakenly attacks its own melanocytes. Individuals with vitiligo may have an increased risk of developing other autoimmune disorders such as thyroid disorders, rheumatoid arthritis, or type 1 diabetes [22].

Hair Loss

Vitiligo can affect not only the skin but also the hair follicles, leading to depigmentation of the hair. This may result in patches of white or gray hair, particularly in areas affected by vitiligo particularly in head [60].

Ocular Complications

In rare cases, vitiligo may also affect the eyes, leading to conditions such as uveitis (inflammation of the uvea, the middle layer of the eye) or retinal detachment.

These complications require prompt medical attention from an ophthalmologist [61].

It is essential to recognize that the severity and consequences of these complications can differ significantly among people with vitiligo. While treatments like topical corticosteroids, phototherapy, or surgical interventions can assist in symptom management and decreasing complication risks, their effectiveness may vary. Consequently, some individuals might need continuous care to tackle both the physical and psychological dimensions of vitiligo.

CONCLUSIONS

- Vitiligo presents as a multifaceted skin condition lacking a conclusive remedy,
- Different types of vitiligo, however the most common one is Non-segmental Vitiligo (NSV).
- Autoimmune Factors, oxidative stress, environmental and genetic are the most important causes of vitiligo.
- The most important symptoms of vitiligo are; depigmented patches, Symmetrical distribution, progressive spreading, hair discoloration, sensitivity to sunlight
- Treatment of vitiligo have many pathways, among them are; topical Corticosteroids, topical Calcineurin Inhibitors, phototherapy, surgical Treatments and Cosmetic Camouflage

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