



Review on Assessment and Evaluation of Vitiligo in Primary Care

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i58B34190

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/80004>

Review Article

Received 10 October 2021

Accepted 14 December 2021

Published 15 December 2021

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ABSTRACT

Vitiligo is an acquired skin disorder characterised by the disappearance of melanocytes, resulting in well-defined white patches that are frequently symmetrically distributed. The lack of melanin pigment makes the lesional skin more sensitive to sunburn. Vitiligo can be cosmetically disfiguring, and it is a stigmatising condition that can lead to serious psychologic problems in daily life. Vitiligo is treated with a variety of topical and systemic medications, phototherapy, laser therapy, and surgical therapy. Corticosteroids, calcineurin inhibitors, and vitamin-D analogues are examples of topical treatment modalities. Phototherapy is a highly effective treatment method. It causes repigmentation in the majority of patients with early and localised disease. Because vitiligo is associated with other autoimmune disorders, a multidisciplinary approach is required. Collaboration and communication between primary care physicians and dermatologists are critical. This review aims to assess role of primary care physicians in assessment and management of vitiligo in primary care settings.

Keywords: Vitiligo; skin disorder; primary care; pigment cell.

1. INTRODUCTION

The most frequent acquired depigmenting condition is vitiligo. It has a strong societal stigma but is treated as a near-orphan disease in terms of medical care. It affects about 1–2% of the population. This condition is characterized by a restricted range of symptoms including macules or patches that are depigmented and correlate to a significant loss of epidermal function and, in some cases, hair follicle melanocytes [1-3]. Adults and children are both afflicted, and there is no gender preference [4].

Vitiligo is now clearly classified as an autoimmune disease, with hereditary and environmental variables, as well as metabolic, oxidative stress, and cell detachment abnormalities. Vitiligo should not be ignored as a cosmetic or trivial disease, as its psychological repercussions can be severe, and it can have a significant impact on everyday life [5-7]. When vitiligo appears after puberty, it usually affects the face and distal extremities, and it's more likely to be connected with other autoimmune diseases.

Vitiligo is classified into segmental or non-segmental with the second one being the more common. Multiple subtypes of non-segmental vitiligo exist, including focal vitiligo, generalized vitiligo, and acrofacial vitiligo, among others, based on the body regions where lesions appear and how they proceed. Upon examination, however, all kinds have a similar clinical appearance. Segmental vitiligo is a type of vitiligo that affects one specific part of the body. It is usually unilateral and does not reach the midline.

This type of vitiligo, which accounts for 5% to 30% of all instances, is often linear or block like in appearance and most commonly affects the face, neck, trunk, limbs, and scalp. Most cases of segmental vitiligo begin in childhood, progress fast in the affected area over the course of 6 months to 2 years, and then stabilize for the rest of the patient's life [8,9].

While Non-segmental vitiligo includes three sub-classifications which are: **focal Vitiligo**, Where lesions appear in one specific location of the body and do not spread to other parts of the body, nor do they broaden or change over the course of two years. This kind of vitiligo is most similar to other non-extensive diseases such segmental vitiligo or nevus depigmentosus. **Acrofacial vitiligo** includes sparse lesions that occur bilaterally over the face and on the distal extremities, where it might appear as amelanotic macules bilaterally, similar to localised vitiligo. Truncal lesions are rarely found in the early stages of acrofacial vitiligo, but they may emerge as the acrofacial variety progresses to generalised vitiligo [8].

Vitiligo that has spread throughout the body. Lesions in **generalized vitiligo** appear in many parts of the body and frequently begin as acrofacial or localized lesions before evolving to a widespread appearance in a bilateral, typically symmetrical pattern. The skin, body hair, and even oral/genital mucosae become nearly completely depigmented as widespread vitiligo progresses. The disorder is termed as universal vitiligo when the depigmentation reaches this level [10,11].

The prevalence of depression in a comparison group was given in eleven researches. Psoriasis patients were the most common comparator, with five trials involving 172 vitiligo patients. Only one study was able to match the control and vitiligo subjects (by sex and education) [12]. People with vitiligo had a lower overall risk of depression than those with psoriasis; the pooled relative risk was 0.66 (95 percent CI 0.48–0.90); there was no heterogeneity. Healthy controls were the second most prevalent comparator (n = 4 studies; however, only two of them revealed the prevalence of depression in the comparator groups). Depression was shown to be more common in vitiligo patients than in healthy controls in both investigations. In the study, the healthy controls and individuals with vitiligo were close in terms of age and sex, although not in the study done by Karia et al. [14].

2. EPIDEMIOLOGY AND CAUSES OF VITILIGO

In 1977, one of the biggest and greatest epidemiological surveys was conducted on the Danish island of Bornholm, where vitiligo was found to affect 0.38 percent of the population [15]. Vitiligo affects persons of all racial backgrounds and skin types equally.

However, there appear to be significant geographical disparities. For example, a study in China's Shaanxi Province found a prevalence of 0.093 percent, whereas rates in India were as high as 8.8 percent. This high figure may reflect the inclusion of cases with toxic and chemical depigmentation. Furthermore, the variation in prevalence numbers could be attributed to higher data reporting in locations where social and cultural stigma are prevalent, or where lesions are more visible in those with dark skin [16-20].

Males and females are evenly impacted, however women seek help more often than men and boys, probably due to the larger negative social impact. NSV can affect persons of all ages, however it is more common in young people between the ages of 10 and 30. Twenty-five percent of vitiligo patients get the disease before the age of ten, nearly half of vitiligo patients get the disease before the age of twenty, and about 70–80 percent of vitiligo patients develop the disease even before age of thirty [21-24].

Vitiligo is a multifactorial condition in which functioning melanocytes are lost. The elimination of melanocytes in vitiligo has been attributed to a

variety of processes. Genetics, autoimmune reactions, oxidative stress, inflammatory mediator production, and melanocyte detachment processes are among them. The immune system's innate and adaptive parts appear to be engaged. None of these proposed ideas are sufficient in themselves to explain the many vitiligo phenotypes, and the total impact of each of these processes is still up for debate, despite the fact that the autoimmune nature of vitiligo is now widely accepted. The steady loss of melanocytes could be caused by a variety of causes, including immunological attack or cell degeneration and detachment.

Multiple mechanisms may operate together in vitiligo to contribute to the loss of melanocytes, eventually leading to the same clinical result, according to the "convergence theory" or "integrated theory" [25-30].

Multiple studies have found that genetic factors have a significant role in the occurrence of vitiligo, while it is obvious that these influences are complex. Vitiligo seems to concentrate in families, according to epidemiological research, however the hereditary risk is not absolute. Around 20% of vitiligo patients have at least one first-degree family member who also has the disease, and the incidence rate of vitiligo for first-degree relatives is increased by 7-10-fold. The incidence rate of monozygotic twins is 23%, highlighting the involvement of extra stochastic or environmental variables in the development of vitiligo [31-33].

Several genes that are related to each other have now been discovered. They play a role in immunological modulation, melanogenesis, and apoptosis, and they're linked to a variety of pigmentary, autoimmune, and auto-inflammatory diseases [34-41]. Tyrosinase, that is coded by the TYR gene, is a melanin biosynthetic enzyme that catalyzes the rate-limiting stages. In widespread vitiligo, tyrosinase is a prominent auto-antigen. In European white people, a genome-wide association study found a susceptibility variation for NSV in TYR that is infrequently seen in melanoma patients. There appears to be a completely unique link between vitiligo and melanoma susceptibility, implying a genetic dysregulation of immunosurveillance against the melanocytic system [34-37].

According to studies on the pathophysiology of vitiligo, oxidative stress may be the first step in the loss of melanocytes [Moreover, melanocytes

isolated from vitiligo patients are more vulnerable to oxidative stress from those from healthy controls, and they are more difficult to cultivate *ex vivo* than melanocytes from healthy controls [38,42]. Melanocytes release reactive oxygen species (ROS) in reaction to stress. As a result, an imbalance of elevated oxidative stress markers (superoxide dismutase, malondialdehyde, ROS) and a notable reduction of antioxidative processes (glutathione peroxidase, catalase, glutathione reductase, thioredoxin reductase, superoxide dismutases, and methionine sulfoxide) It has been claimed that in vitiligo, the imbalance between pro-oxidants and antioxidants account for the increased sensitivity of melanocytes to external pro-oxidant stimulations and, over time, the induction of a presenescent state [43-47]. ROS production and accumulation can lead to DNA damage, protein oxidation and fragmentation, and lipid peroxidation, all of which impede cellular function [48,49].

In vitiligo, innate immunity crosses the barrier between oxidative stress and adaptive immunity. Early in the course of vitiligo, innate immune cells are likely to be activated by exogenously or endogenously produced stress signals emitted by melanocytes and perhaps keratinocytes there is a link between vitiligo susceptibility and genetic alterations in NALP1 (also known as CARD7, DEFCAP, and NAC), an innate immune system regulator The local microenvironment of melanocytes in vitiligo skin exhibits abnormally elevated innate immunity, notably natural killer cells, according to genomic expression analyses on the skin of patients with vitiligo .Natural killer cells have been discovered infiltrating clinically normal skin of vitiligo patients, implying that natural killer cells are early responders to melanocyte stress [50-52]. Melanocytes excrete exosomes, which appear to signal stress to the innate immune system. Exosomes are secreted by human melanocytes in exposure to chemically induced stress .Exosomes contain antigens specific to melanocytes, miRNAs, heat shock proteins, and some other proteins that operate as damage-related molecular patterns [53].

Immune disorders of the adaptive immunity, both humoral and cell-mediated, have been linked to the development of vitiligo. Antibodies to surface and cytoplasmic melanocyte antigens have previously been found in vitiligo patients' serum. By complement-mediated lysis and antibody-dependent cellular cytotoxicity, these antibodies can kill melanocytes produced in culture.

Melanocyte destruction is caused by cytotoxic CD8+ T lymphocytes that specifically target melanocytes. Histological evidence of CD8+ T-cell infiltration of the epidermis and dermis has been found. Vitiligo patients have a higher number of cytotoxic CD8+ T cells in their blood than healthy controls, and these counts correspond with vitiligo activity [54-58].

3. ASSESSMENT AND EVALUATION IN PRIMARY CARE

For the diagnosis and assessment of skin disorders, a variety of procedures are available. These techniques, we believe, can be categorized as follows:

- 1 Subjective, semi-objective, and objective; 2 Microscopic or. Macroscopic; and 3 Morphometric or Colorimetric.

Clinical assessment by a dermatologist, visual comparisons of skin tissue before and after using the treatment (using non-digital or digital images taken under visible or UV light), and a vitiligo disease activity score (VIDA) are all examples of subjective approaches . The Vitiligo Area Scoring Index (VASI) and point counting are two semi-objective methodologies. Software-based image analysis, tristimulus colorimetry, spectrophotometry, and confocal laser microscopy are some of the objective ways (CLM). photography in natural or UV light, photography with computerized image analysis, or spectrophotometry are all examples of macroscopic morphological measurement. CLM is a non-invasive micro -morphological procedure that includes CLM. It is characterized by an accurate determination of the hue and chroma of the substructures of pigmented lesions [59,60].

The majority of techniques are concerned with morphometry. The exception is the chromameter approach, which evaluates colorimetry. Furthermore, some image analysis software can evaluate both morphometry and colorimetry.

4. SUBJECTIVE METHODS

These techniques use clinical examination or the analysis of pictures taken at various intervals throughout treatment to determine the percentage of improvement. However, a consensus on a suitable scoring system is required to allow for subjective and trustworthy visual interpretation of outcomes. This standardized scoring method will allow for

reliable and suitable data gathering that can be used for direct comparisons as well as pooling treatment findings from various clinical studies. Furthermore, clinicians' interpretations of treatment results appear to differ widely, and patients should have some say in defining a therapeutic consensus [61].

Visible light photography: Serial images taken over time can reveal information about the development of the disease or the response to treatment. For medical record-keeping and instructional purposes, traditional visible light photography using standard 35-mm film has long been the preferred way of capturing photos of the skin. In exceptionally fair-skinned people, however, it can be difficult to discern between hypomelanosis and amelanosis under visible light using photography. this method has the advantages of being Quick and easy [62,63].

Ultraviolet light photography: UV photography is related to the fact that melanin in the epidermis absorbs UV rays more selectively than visible light. By focusing UV light at the patient's skin, Wood's lamp is used to diagnose skin problems. A portion of the emitted fluorescence reaches the skin's surface, but it is absorbed by haemoglobin in capillaries and epidermal melanin. This method improves the assessment of the amount of pigment disorders by enhancing epidermal pigmentation changes that are not detectable in visible light. this method has the advantages of being more clear and can give the physician more information about the activity and extent of the vitiligo [64,65].

Vitiligo disease activity score: It is a six-point scale used to evaluate the stability of vitiligo over time. It is based on the patient's report about its own disease activity. It aids in determining the efficacy of therapies in terms of stopping and halting the progression of depigmentation as Vitiligo can be active or passive. the active vitiligo includes either the emergence of new lesions or the growth of existing lesions [66].

5. SEMI-OBJECTIVE METHODS

Vitiligo area scoring index: The VASI was developed by Hamzavi et al. and is a prototype. based on the PASI score (Psoriasis Area and Severity Index) It is frequently used to evaluate psoriasis. The VASI is a sensitive, standardized method for determining the level and percentage of depigmentation. The VASI divides the patient's body into five sections. and regions that are totally exclusive: the hands, upper extremities

(With the exception of the hands), trunk, lower extremities (excluding the feet) as well as the feet. The buttocks are considered with lower extremities. the face and neck are evaluated but not included in the results The VASI is calculated for each body region as the product of the area of vitiligo in hands units (set at 1% every unit) and the extent of vitiligo depigmentation within each patch assessed in hand with values ranging between 0, 10, 25, 50, 75, 90 or 100%. this method is known for being easy and has the ability to measure the extent of depigmentation and repigmentation [67].

Point-counting method: To calculate the volumes of organs or structures, the point-counting method is employed to estimate the irregularly shaped sectional surface area. With an ordinary ballpoint pen, the lesion borders are marked, and a sheet of paper is immediately placed over the lesion. The copied bounds of the projection areas are improved for each lesion by redrawing the outlines with a pen. A translucent sheet with a point (+) written on it is randomly placed on the lesion projection region to estimate the number of points. The number of junctions that pass through the target area is counted. Each lesion's total area is calculated by multiplying the representative area of a grid point by the total number of points counted for the lesion. On the grid, each + symbol has a surface area of 0.1 cm². this method is mostly used to estimate the surface area of irregular shapes [68-70].

6. OBJECTIVE METHODS

Colorimetry-based image analysis: The tristimulus colorimeter has been demonstrated to be effective in a number of recent experiments. it is highly helpful in determining the severity of UV-induced erythema and pigmentation, disease severity, and therapy efficacy . It's perhaps the most popular way. Since this colour system, which has been approved by the International Commission, Colorimetry is defined by the Commission Internationale de l'Eclairage (CIE). A colorimeter is a device that measures colour. The tri-stimulus method is used to measure the reflecting colours of surfaces. system. A faint, continuous transition can be seen using the colorimeter. between the first erythematous response and the delayed erythematous response and darkening of skin that is not visible to the naked eye. The intensity vs. wavelength data (i.e., tristimulus analysis) is converted into three numbers that show how the data was processed [71-74].

The reflected-light colorimeter can measure five different colour schemes. Skin colour is measured using the L*a*b* system, which is stated in three dimensions: the value of L* (luminance) indicates the relative lightness of a colour, ranging from absolutely black to entirely white. The a* value reflects the colour range from entirely black (L* = 0) to completely white (L* = 100). the proportion of red (positive value) to green (negative value) The b* number shows the balance between yellow and blue. (with a positive value) and blue (with a negative value) . The device has been calibrated. Colorimetry has a wide range of clinical uses, including skin typology, race, anatomical distribution of pigment and photo-protection factors, sunscreens, and depigmentation treatments [75].

7. CONCLUSION

Vitiligo is one of the serious diseases that has been studied for long time. The process of repigmentation is sluggish and only visible after a few months of treatment. As a result, a sensitive and precise method that can detect even modest variations in depigmentation and/or repigmentation during and after vitiligo treatment is critical for the appropriate assessment of this condition in clinical studies. VASI, the rule of nine and Wood's lamp are likely to be the best techniques available for assessing the degree of pigmentary lesions and measuring the extent and progression of vitiligo in the clinic and in clinical trials.

The development of more convenient diagnostic tools is the main objectives these days especially as we learn more about the pathogenesis of the disease. Patients whose condition is difficult to diagnose, unresponsive to simple topical treatments, or causing psychological distress should be referred to a dermatology unit.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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