




## Biopsychosocial impacts faced by patients with vitiligo: A systematic review

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### ABSTRACT

**Objective:** The aim of this review was to report current knowledge about the main signs and symptoms that affect the quality of life of individuals with vitiligo. **Methodology:** The searches were carried out through searches in the PubMed Central (PMC) databases. Three descriptors were used in combination with the Boolean term "AND": vitiligo; quality of life; depression; psychosocial impact; Medical Psychology. From this search, 275 articles were found, which were subsequently submitted to the selection criteria. Of which, after applying the inclusion and exclusion criteria, 36 articles were selected from the PubMed database, and a total of 19 studies were used to compose the collection. **Discussion:** Thus, studies denote that the skin, being the largest organ in the body, is crucial for personal image and diseases that alter its pigmentation, such as vitiligo, reduce the quality of life, especially for young people. From a biological and embryonic point of view, the skin and the brain have an intimate relationship, which suggests that changes in it can be associated with mental health problems, exacerbating or triggering dermatological conditions, which culminate in nervousness, decreased self-confidence, anxiety and even depression. **Results:** It is known that there may be a biomarker for the activity or severity of vitiligo where it is related to the prevalence of psychiatric problems, creating image distortions. In summary, being a multifactorial autoimmune dermatological disease, it would generate a great impact on the lives of patients, influencing individual self-image and the way the world will perceive it, and thus resulting in a worsening of quality of life.

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## INTRODUCTION

Vitiligo is a disease characterized by the depigmentation of the skin, due to the loss of melanocytes that form white macules in all its subtypes. It can be classified according to its forms of presentation as: generalized, focal, mucous, universalis, acrofacial and mixed (BERGQVIST C.; EZZEDINE K., 2020).

Generalized vitiligo is characterized by white spots that develop symmetrically and randomly, focal is only an isolated change in the skin that does not evolve in a few years, mucosal vitiligo usually involves the mouth and genitals, universalis basically affects the entire body, and mixed vitiligo is characterized by the presence of segmental and non-segmental vitiligo concomitantly (BERGQVIST C.; EZZEDINE K., 2020).

Its global prevalence is 0.5-2%, with no higher rates in specific ethnic groups and between men and women, but with discrepant differences between distinct regions, such as China and India. It was noticed that its appearance precedes thirty years of age in 70 to 80% of cases, and its forms of presentation are more common depending on age, as in the case of segmental vitiligo (SV), which tends to start in younger people than non-segmental vitiligo (VNS) (BERGQVIST C.; EZZEDINE K., 2020).

Speaking about its pathophysiology, it is believed that genetic components, oxidative stress, and immunological alterations are involved, as well as exosomes, which alter the regulation of cells responsible for skin pigmentation through apoptosis and inhibition of melanogenesis (Yu, H. et al., 2024). Its relationship with autoimmunity shows that this pathology is also associated with other autoimmune diseases (systemic lupus erythematosus, diabetes mellitus 1, rheumatoid arthritis, etc.) (ABDELHAFEZ M.M. et al., 2021).

The diagnosis is based on the clinical characteristics of the skin changes, and it is rarely necessary to use complementary methods, such as chemical tests, biopsy or ultraviolet illumination for their confirmation. It is important that there is a preliminary investigation of several important points, such as a family history of autoimmune diseases, how long the disease progressed, how much the lesions expanded, and whether any intervention method has already been used, as the confirmation of the disease generates psychosocial impacts, which will need to be addressed later (JOGE R. R. et al., 2022).

Among the psychosocial impacts, it was seen that depression and anxiety disorder are the most prevalent in people with vitiligo, but social stigmatization, anger, sleep changes, emotional, cognitive, and behavioral changes were also reported (EZZEDINE K. et al., 2021). In this way, quality of life is consequently impacted, and can be measured by the Daily Life Quality Index (DLQI), Vitiligo Impact Scale (VIS), Vitiligo Quality of life (VitQoL) and Vitiligo Impact Patient Scale (VIPs) (SENESCHAL J., 2023).

Thus, after recognizing the psychic impact, it is known that cognitive-behavioral therapy (CBT) should be a treatment associated with drug treatments. It is directed towards changes in thoughts seen as problems and is intended to change them in conjunction with behaviors (REVANKAR R. R. et al., 2022).

CBT is also used to shape negative ideas and feelings, making individuals better cope with the challenges of future life, and is often used in various psychological disorders and dermatological changes that generate distress (REVANKAR R. R. et al., 2022).

In addition, as previously mentioned, the therapy should be included as a joint treatment with the use of pharmacological methods, which are classified as first, second, third and fourth line. Respectively, these forms of management according to their generations are topical corticosteroids and calcineurin inhibitors, phototherapy and systemic treatments with steroids, surgical techniques and grafts, and depigmenting treatments (BERGQVIST C.; EZZEDINE K., 2020).

Some other compounds such as baicalein have demonstrated antidepressant action by regulating the formation of neurons in the central nervous system, and its ability to act also in the hippocampus, with positive effects on vitiligo. On the other hand, compounds such as curcumin have demonstrated effects on mental health, such as reducing anxiety, but they do not have enough studies to know about their action on vitiligo (BARTOLOMEU L.D. et al., 2023).

Finally, the objective of this literature review was to report the current knowledge about the main signs and symptoms that affect the quality of life of individuals with vitiligo and to offer a critical analysis, since there are frequent doubts about the psychological and clinical aspect of this disease. An evidence-based review of the current literature was performed to better group more recent information and collaborate with a better understanding of vitiligo and quality of life among medical professionals.

## **METHODOLOGY**

This is a systematic review that seeks to understand the biopsychosocial impacts of vitiligo, as well as to demonstrate the main comorbidities, especially emotional comorbidities, that are correlated with the pathology, aiming to demonstrate the greatest difficulties faced in the daily lives of these patients. For the development of this research, a guiding question was elaborated through the PVO (population, variable and objective) strategy: "What are the greatest difficulties that patients with vitiligo face?".

The searches were carried out through searches in the PubMed Central (PMC) databases. Three descriptors were used in combination with the Boolean term "AND": vitiligo; quality of life; depression; psychosocial impact; Medical Psychology. The search strategy used in the PMC database was: Vitiligo AND quality of life; Vitiligo AND Depression; Vitiligo AND psychosocial impact.

From this search, 275 articles were found, which were subsequently submitted to the selection criteria. The inclusion criteria were: articles in English, Portuguese and Spanish; published in the period from 2019 to 2024 and that addressed the themes proposed for this research, in addition, review, observational and experimental studies, made available in full. The exclusion criteria were: duplicate articles, available in the form of abstracts, that did not directly address the proposal studied and that did not meet the other inclusion criteria.

After associating the descriptors used in the searched databases, a total of 275 articles were found. After applying the inclusion and exclusion criteria, 36 articles were selected from the PubMed database, and a total of 19 studies were used to compose the collection.

## DISCUSSION

The skin plays a crucial role in interacting with the world and its color is a key aspect in this interaction. Any change in skin color can have important psychological consequences (SENESCHAL J., 2023). As it is considered the largest organ in the body and is crucial for personal image, diseases, such as vitiligo, can notably reduce quality of life, especially in young patients (SALAMA A. H. et al., 2023). Vitiligo is considered a chronic condition represented by autoimmunity, in which the loss of skin pigmentation occurs, resulting in hypochromic areas. This disorder has an effect on the reduction of melanocytes, generating depigmentation (SALAMA, A. H. et al., 2023).

Unlike many other organs in the body, the human epidermis reacts immediately to mental stress, which is termed the "brain-skin connection" (MENTO C., et al., 2020). From a biological and embryological point of view, the skin and the brain have an intimate relationship, because both originate from the same germ layer during their development. This suggests that there may be a functional correspondence between them. Thus, it is plausible to speculate that significant damage to the skin may be associated with the emergence of mental health problems. On the other hand, emotional stress can exacerbate or even trigger a variety of dermatological conditions (CORTES H., et al., 2022).

Mental, physical, and emotional stresses affect the skin due to hormones that will stimulate an inflammatory response, causing a reduction in blood flow and causing irritation to the nerves present in it, and as a consequence a cascade of pro-inflammation events will occur (MENTO C., et al., 2020). The destruction of melanocytes, on the other hand, seems to be closely linked to anxiety due to dysregulated neuroendocrine mechanisms. Studies indicate that elevated levels of neurotransmitters, such as norepinephrine, are associated with the development of vitiligo. This substance has been found in high concentrations in the microenvironments where melanocytes are present, as well as in the urine and plasma of patients with vitiligo. (KUSSAINOVA A., 2020)

The effects of vitiligo can be severe, affecting careers and relationships, especially in visible areas of the body. Vitiligo not only affects physical health, but also has a profound impact on people's psychological and social well-being. Depigmented patches present on the skin can trigger a range of complex emotional reactions, including nervousness, decreased self-confidence, anxiety, and even depression. These emotional responses can significantly reduce an individual's overall quality of life by affecting not only themselves, but also their close relationships. In some cases, vitiligo can even contribute to the end of marital relationships. (SALAMA A. H. et al., 2023)

In some cultures, individuals with vitiligo may face significant social stigma, which can make it difficult to find a partner or hold stable jobs (KUSSAINOVA A., 2020). Patients with vitiligo often face difficulties in getting jobs due to their condition. On the other hand, those who develop vitiligo after getting a job usually experience a less severe impact (NIMKAR P., WANJARI A.,). This stigma can intensify psychological distress and, in extreme cases, can even lead to suicide attempts, especially when it affects visible areas of the body (KUSSAINOVA A., 2020).

Quality of life, according to the World Health Organization, reflects how well someone's reality corresponds to their goals, considering their culture and value system (SALAMA A. H. et al., 2023). In light of this, some studies have shown that adults with generalized vitiligo experience a reduction in quality of life comparable to that of patients with other skin conditions, such as atopic eczema and psoriasis (SENESCHAL J., 2023). A study conducted by Thompson et al. (2010) discusses the challenges faced by people with vitiligo and points out that the stigma associated with this disease has contributed significantly to the reduction of self-esteem and confidence in these people. This social prejudice can lead to a negative self-perception, profoundly affecting how they see themselves and position themselves in society. In addition, in specific cultures, cultural norms and ideas of beauty exert additional pressure on the individual to conform to established standards of appearance. These factors combined intensify the psychosocial challenges faced by them (SALAMA, A. H. et al., 2023).

Anxiety and depression are the main mental health problems associated with vitiligo. In addition, there is scientific evidence that indicates a possible coexistence with other disorders, such as obsessive-compulsive disorder (OCD), manic disorder, bipolar disorder, and schizophrenia. These disorders seem to have a pathogenic basis common to vitiligo, possibly related to autoimmune and inflammatory processes, demonstrated by the increase in pro-inflammatory cytokines in these groups of patients, such as IL-1, IL-6 and TNF- $\alpha$ . (BARTOLOMEU L.D. et al., 2023).

Although stress hormones are not the first pathogenetic indicators of vitiligo manifestations, cortisol and dehydroepiandrosterone (DHEAS) levels are related to the severity of the disease and appear to increase the prevalence of psychiatric problems. DHEAS is recognized as an antioxidant hormone that may play a role in the onset of vitiligo lesions, and its levels tend to increase during

oxidative stress. This suggests that DHEAS could be a future marker of vitiligo activity or severity, as well as a possible predictive factor for the development of anxiety and depression.

(BARTOLOMEU L.D. et al., 2023), (SIMONS R. E., et al., 2020).

Regarding the age group, children affected by vitiligo seem to be more likely than adolescents to develop symptoms of depression and anxiety. This can be attributed to several reasons: it is suggested that the affected areas are less easily covered by makeup in children than in adults or adolescents, which can increase self-awareness about their physical appearance. In addition, dyschromic lesions in the genital region may have a greater impact on sexual perception and development in childhood patients than in adults, indicating that both visible and invisible areas may affect self-perception (BARTOLOMEU L.D. et al., 2023).

Children affected by the disease tend to have a significant increase in the symptoms of panic disorder and depression (AUGUSTIN M., 2024). In contrast, in adolescents, the duration of the disease and the extent of the affected areas seem to be more influential factors for the emergence of psychiatric symptoms, considering that adolescence is the phase of the first sexual experiences and personal development, these aspects can intensify the emotional challenges associated with vitiligo in this age group (BARTOLOMEU L.D. et al., 2023).

As mentioned earlier, the skin is one of the ways that enables human beings to communicate with their environment. Dermatological diseases such as psoriasis, leprosy and vitiligo itself can cause image distortions in their carriers as well as create stigmas in them. By the way, since Antiquity, patients with skin diseases, especially vitiligo, suffered from cultural, social and religious marginalization. Currently, even with the demystification, there is still, although little, the perpetuation of this retrograde thinking, which favors the reduction of the quality of life of patients, contributing to negative psychological outcomes. (BERGQVIST, C. ; EZZEDINE K., 2020).

Thus, systematic reviews have made use of tools such as questionnaires, scales, and indices in order to expose the fluctuations in the quality of life of the patients in question. In this context, the Dermatology Life Quality Index (DLQI), Skindex, Vitiligo-Specific Quality of Life Instrument (VitiQOL), Vitiligo Impact Scale (VIS) and other generic instruments, such as the General Health Questionnaire (GHQ) and the Short-Form 36 (SF-36) were used. All of these had the sole objective of determining the effects of the disease on the quality of life of the patients, ranging from very little effect to the severe effect of the disease. (SIMONS R. E., et al., 2020), (BERGQVIST C. ; EZZEDINE K., 2020), (EZZEDINE K. et al., 2021), (PICARDO M. et al., 2022).

As an example, this last instrument specifically mentioned, the SF-36, exhibited variations in scores between the physical and mental components of the affected patients, demonstrating a greater mental than physical impairment. An abbreviation of this questionnaire, titled Short-Form 12 (SF-12), revealed similar results. (PICARDO M. et al., 2022).

In a comprehensive way, taking into account the scores obtained, it was possible to identify the social groups most affected by the psychosocial consequences of vitiligo, highlighting in this scenario women, individuals under 30 years of age, patients with a greater superficial area of involvement of the disease or with various lesions on the body, darker skin phenotypes and non-Caucasian race, longer duration of the disease (more than 5 years), more visible (face, neck and hands) and sensitive (genital and anogenital regions) areas of involvement, psychiatric patients and those with negative experiences about vitiligo, as well as thyroid diseases. (EZZEDINE K. et al., 2021), (PICARDO M. et al., 2022)

In addition, socioeconomic status and professional status also contributed to the results, with a worse quality of life being observed in student patients, compared to employed, unemployed and retired patients, and in patients with high socioeconomic status than in relation to medium or low status. (EZZEDINE K. et al., 2021), (PICARDO M. et al., 2022).

A plausible explanation for the higher prevalence in women was suggested by Jiani L. et al. (2021), who considered this predominance due to greater aesthetic awareness and lower self-confidence in this gender, since they have a more negative attitude of self-evaluation and greater difficulty in adapting to dermatological diseases. Also, from the biological perspective, women have a hypothalamic-pituitary-gonadal axis that is more subject to dysregulation when placed in a situation of significant stress, since this axis regulates a large part of the hormones related to anxiety, such as oxytocin, prolactin and GABA, correlating with what was previously discussed. (JIANI L., et al., 2021)

Because this dermatopathy has this psychosocial background, treatment based only on the clinical severity of this disease would not be enough to compensate for the reduction in the quality of life of patients, since psychiatric comorbidities can serve as a predisposing factor as well as a consequence of hypochromic lesions. (BERGQVIST, C. ; EZZEDINE K., 2020). Therefore, a randomized study was carried out in order to investigate the impact of cognitive-behavioral therapy (CBT) on the quality of life of these patients. Even though some limitations were present in this study, such as the retention of patients and the hesitation of some to continue treatment without medication, the results obtained were encouraging, with a considerable reduction in the scores of the questionnaires portrayed above, which indicates an attenuation of the negative effects of vitiligo on the lives of patients. (REVANKAR R. R. et al., 2022).

However, CBT should be considered as an adjuvant therapy and not just in isolation, which would facilitate the removal of the previously demonstrated bias: the hesitation not to associate other therapeutic modalities. Another study, now a meta-analysis, demonstrated the urgent need to establish more effective treatments against vitiligo, such as the improvement of repigmentation techniques, the use of cosmetic camouflage, phototherapy and photochemotherapy, homeopathic





treatment, among others. (EZZEDINE K. et al., 2021), (PICARDO M. et al., 2022), (WANG X. et al., 2024).

Finally, not only patients affected by vitiligo suffer from a decrease in quality of life, there is also a relevant emotional burden documented by caregivers. A Brazilian study that evaluated such burden in those responsible for pediatric patients recorded anxiety and depression in numbers equivalent to 42% and 26%, respectively, among its participants. Also, a new study, on this occasion Indian, revealed that the anxiety of the parents of children directly influenced the psychological condition of the children, as they developed a certain concern about the anguish of their parents. (DATTA D. et al., 2021).

Thus, there were variants of the questionnaires mentioned above to cover family issues, such as the nuance of the DLQI, named FDLQI, and the Dermatology Family Impact (FDI). These questionnaires demonstrated, in an analytical study, a significant reduction in quality of life in parents of patients with vitiligo when compared to parents of healthy controls. (PICARDO M. et al., 2022).

## CONCLUSION

In conclusion, the studies covered reveal that vitiligo is a multifactorial autoimmune dermatological disease that has a great impact on the lives of patients, since it affects the largest organ of the human body. This will influence the patient's self-image and the way the world will perceive them. In addition, several evaluations of the quality of life in patients with vitiligo have shown that these patients are more affected compared to other dermatological diseases, such as psoriasis, acne, among others. The identification of the comorbidities most frequently correlated with vitiligo is depression, anxiety, obsessive-compulsive disorder (OCD) and other mental disorders, especially in younger patients, with a greater superficial area of body involvement by the disease and in women. Therefore, there will be a worsening in the quality of life.



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