INTERNATIONAL JOURNAL IN PHARMACEUTICAL SCIENCES

Journal Homepage: https://www.ijpsjournal.com

OPEN ACCESS

Review Article

A study of challenges and quality of life (QoL) issues related to Vitiligo disease's current treatments

Yash Srivastav[1], Akhandnath Prajapati[2], Adityanath Prajapati[3], Madhaw Kumar[4], Mohammad Aqil Siddiqui[5]

[1245]Goel Institute of Pharmacy & Sciences (GIPS), Lucknow, Uttar Pradesh, India
[3]BBDNIIT, Lucknow, Uttar Pradesh, India.

ARTICLE INFO

Received: 18 Aug 2023
Accepted: 19 Aug 2023
Published: 03 Sept 2023

Keywords:
Vitiligo disease, Pathophysiology, Treatments, Nanotechnology, Quality of life (QoL), Challenges

DOI:
10.5281/zenodo.8312051

ABSTRACT

The appearance of white patches is a sign of the skin disorder vitiligo. Segmental vitiligo usually becomes dormant after two years of stabilization of the condition. Non-segmental vitiligo can reactivate even after extended periods of stability. Vitiligo is the most common depigmenting skin disorder, affecting 0.5–2% of people worldwide, including both adults and children. the hands, face, and areas close to bodily openings and the genitalia are frequent starting points. premature whitening or greying of your beard, eyebrows, or scalp hair. The mucous membranes, which line the inside of the mouth and nose, have turned grey. The aetiology of vitiligo starts in melanocytes that have been altered and exhibit an enhanced cellular stress response. This triggers an immunological response that eliminates melanocytes and results in localized depigmentation. During repigmentation, melanocytes, which typically come from hair follicles, must grow and migrate. The main histological finding in vitiligo is the absence of any functioning melanocytes in the lesions, and the inflammatory cells that are most frequently found at the edges of the lesions are CD4+ and CD8+ T lymphocytes. Currently, topical, oral, surgical, phototherapy, and other treatments are used to treat vitiligo. One may claim that the best nano-lipid carrier systems for vitiligo treatments use nanotechnology. The quality of life (QoL) of vitiligo sufferers is negatively impacted, according to subsequent studies carried out globally. Vitiligo causes social isolation, shame, low self-esteem, depressed symptoms, and self-consciousness.

INTRODUCTION

Skin areas that have vitiligo become discoloured or lose their pigment since it is a chronic (long-lasting) condition. The skin becomes milky white as a result of melanocytes, the skin cells that produce pigment, being attacked and destroyed [(1)]. The main problem is a lack or decrease of

***Corresponding Author:** Yash Srivastav
Address: *Goel Institute of Pharmacy & Sciences (GIPS), Lucknow, Uttar Pradesh, India*
Email : neelashsrv76@gmail.com

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.

melanocytes in the epidermis. The objectives of vitiligo treatment are to stabilize the depigmentation process and repigment the lesions. Repigmentation improves the skin's appearance and resistance to sunburns [2]. Vitiligo is now definitively recognized as an autoimmune illness impacted by genetic and environmental factors as well as issues with metabolism, oxidative stress, and cell detachment as a result of substantial recent improvements in our understanding of its aetiology. Vitiligo shouldn't be dismissed as a cosmetic condition or a minor illness because its symptoms can be mentally distressing and frequently have a considerable detrimental influence on daily life [3]. According to a global agreement issued in 2011, the two primary kinds of disease are nonsegmental vitiligo (NSV) and segmental vitiligo (SV). Acrofacial, mucosal, generalized, universal, mixed, and rare types of NSV are all referred to as vitiligo. One of the consensus's most important conclusions was how to distinguish SV from other types of vitiligo, primarily because of its implications for prognosis. The frequency ranges from 0.5% to 2%, and nearly half of those affected receive their diagnosis before the age of 20. The rates of recurrence appear to be the same for both men and women, and they are not influenced by race or skin tone [4]. Vitiligo may be a psychologically distressing condition, especially in people with darker skin because it is more evident on them. It seems to be genetically passed down in a polygenic/multifactorial way. The exact pathophysiology is still being debated, but it has been linked to sympathetic neurogenic disruption, oxidative stress, and/or autoimmune (AI) reasons [5]. A psychologically damaging condition is vitiligo. The fact that it often affects exposed parts (the hands and face) has a significant effect on one's self-esteem and sense of self. Vitiligo is a condition that is poorly understood and sometimes misdiagnosed as leprosy or a sexually transmitted infection. Women with vitiligo find it difficult to get married in these societies, as well as to find employment and educational prospects [6–8]. The colour difference between the healthy pigmented skin and the depigmented vitiligo patches, which gives the patients' skin the well-known leopard-like appearance, significantly lowers the quality of life for those who are affected by vitiligo. There are both nonsurgical and surgical options. Narrow-band UVB irradiation, psoralen plus ultraviolet A (UVA), broad-band UVB, topically, orally, and intralesionally delivered corticosteroids, as well as other less well-known and/or successful treatments, are well-established nonsurgical repigmentation therapy. Only when medical remedies have failed are surgical procedures recommended [9]. The depigmenting skin disorder vitiligo has a negative impact on the patient's quality of life. Despite the availability of numerous treatment options, including medicinal, physical, and surgical alternatives, none is curative. Each modality has disadvantages and adverse effects of its own. To achieve a fair risk-benefit ratio, the treatment modality must be customized for each patient, taking into account the features of the disease as well as its efficacy and safety. As a result, there is a great need for treatment. There are many medical and surgical treatment options for vitiligo, but none of them is curative. The patient's characteristics, demographics, and systemic comorbidities must be taken into consideration while developing the treatment plan because prolonged treatment is frequently required, increasing the risk of serious side effects [10]. Skin conditions can also cause negative feelings like guilt, shame, concern, insecurity, and even psychiatric symptoms like depression. The affected individuals may be dealing with severe depression symptoms and low self-esteem. They could feel uncomfortable in social settings, feel inferior, and become the target of prejudice [11]. Prevalence rates vary geographically and are

usually higher in Africa and India. The Indian subcontinent has the highest incidence of vitiligo (9.98%), followed by Nigeria (2.8%), and Romania (2.28%). Vitiligo prevalence among dermatological outpatients in India varies between 0.25 and 4%, with the states of Gujarat and Rajasthan having the highest frequency of 8.8%, according to a number of studies [12].

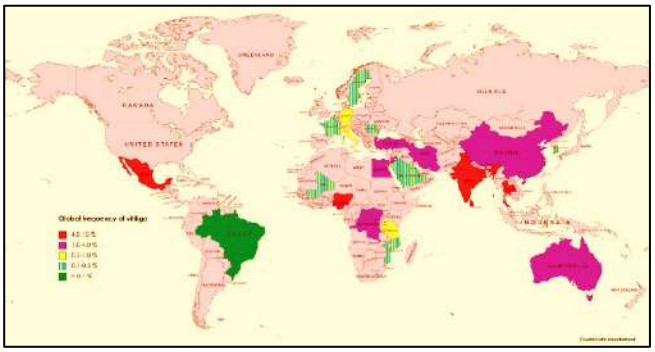

Fig.1: Worldwide prevalence of vitiligo. Estimated prevalence rates at all ages were obtained from studies conducted globally. The pink area denotes regions with unavailable vitiligo data (Novel immunological and genetic factors associated with vitiligo: A review, 2021). The map was created with the help of mapchart.net

CLASSIFICATION OF VITILIGO

Segmental, acrofacial, universal, and mucosal vitiligo types are separated from focal, mixed, and mucosal kinds of vitiligo based on the pattern of involvement.

- ***Segmental vitiligo***

Unilateral macules with a dermatomal or quasi-dermatomal distribution are the hallmark of segmental vitiligo. This kind typically manifests at a young age and, in contrast to the other forms, is not linked to thyroid disease or other autoimmune diseases. The pathogenesis has been linked to altered neuronal peptides. Polio is present in more than half of people with segmental vitiligo.

- ***Focal vitiligo***

The trigeminal nerve distribution is most frequently affected by focal vitiligo, which typically manifests as a single macule or several scattered macules in a single location. However, the neck and trunk are also frequently affected. This condition more frequently affects children.

- ***Acrofacial vitiligo***

Depigmentation of the distal fingers and periorificial regions characterises acrofacial vitiligo.

- ***Mucosal vitiligo***

Only the mucous membranes are involved in mucosal vitiligo.

- ***Universal vitiligo***

The majority of the body is covered in depigmented patches and macules in universal vitiligo, which is connected to multiple endocrinopathies syndrome.

- ***Generalized vitiligo***

Another name for generalized vitiligo is vitiligo vulgaris. The predominant pattern is this one. There are many, symmetrically distributed depigmented patches [13].

PATHOPHYSIOLOGY OF VITILIGO

According to current theories, a trigger event that eventually targets the melanocytes predisposes people to developing vitiligo and triggers stress responses in the skin that activate an autoimmune response in those who are genetically predisposed to it. The mechanisms generating vitiligo remain unexplained, as does the etiopathogenesis of the disorder, despite the fact that recent research has started to spotlight these issues [14]. However, a variety of ideas have connected it to the emergence of vitiligo. Numerous studies on the frequently occurring correlation between vitiligo and autoimmune disorders have backed the autoimmune theory, which is generally regarded and acknowledged as the dominant explanation globally. Additionally, the association between vitiligo and halo naevus—a disease characterized by a strong immune cell infiltrate and a depigmented halo-like area encircling a mole—supports the role of immune systems in the development of vitiligo [15]. The aetiology of

vitiligo starts in melanocytes that have been altered and exhibit an enhanced cellular stress response. This triggers an immunological response that eliminates melanocytes and results in localized depigmentation. During repigmentation, melanocytes, which typically come from hair follicles, must grow and migrate [16].

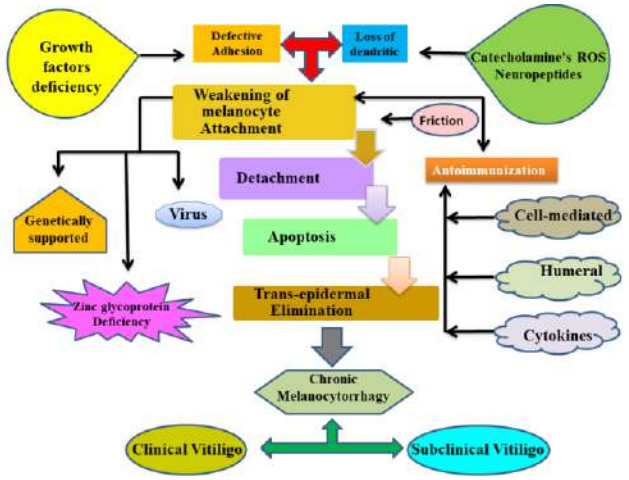

Fig.2: Vitiligo's pathophysiology (17).

CURRENT THERAPIES AND TREATMENTS FOR VITILIGO

❖ Allopathic medicine

The investigation was divided into two parts. In Part 1, 15 healthy volunteers participated in a prospective experiment using three different Dihydroxyacetone (DHA) creams with concentrations of 3.5%, 4.2%, and 5%. Retrospective investigation was done on 20 patients who got 6% DHA treatment for vitiligo that affected their hands, feet, or faces. The information was gathered using direct observation, phone interviews, in-person interviews, and pictures. We discovered that healthy individuals who had darker skin were able to match colours by using a higher proportion of DHA. Most vitiligo patients (88.9%) reported moderate to high satisfaction with the cosmetic effects of 6% DHA cream [18].

By inhibiting NFAT, a transcription factor necessary for the transcription of the genes that code for interleukin 2, Cyclosporine Drug, an oral calcineurin inhibitor, reduces the production of interleukin 2 in the body. Patients with vitiligo may benefit from treatment by inhibiting IL 2, as this essential cytokine is involved in mediating lymphocyte entry. Taneja et al.'s recent study revealed a statistically significant decrease in Vitiligo Area Scoring Index (VASI) score after treating 18 patients with oral cyclosporine (3 mg/kg/day), in two divided dosages for 3 months. Because of its direct effect on melanogenesis, cyclosporine was therefore able to produce repigmentation in addition to slowing the progression of the disease. It is linked to adverse effects include hypertension, gingival hyperplasia, and renal impairment while generally being well tolerated [19].

Oral tofacitinib citrate (Xeljanz) at a dose of 5 mg every other day was the initial course of treatment. After three weeks, the dosage was raised to 5 mg/d (arthritis patients typically receive 5 mg twice daily, which is half the recommended dosage for rheumatoid). After two months of therapy, the face and upper extremities had partially repigmented. After five months, the other damaged parts had only half recovered, but the hands and forehead had nearly totally recovered. The body's overall surface area was still about 5% depigmented. The patient tolerated tofacitinib well, and laboratory tests conducted during the course of treatment showed no changes in the patient's cholesterol, serum creatinine, hepatic function, or complete blood count [20].

The 18 examples that are reviewed here have results that are comparable to those that other observers have recorded. Ammi majus extracts were administered to 201 individuals with vitiligo, and 10% of them obtained total remission. The remaining 18% showed improvement of more than 50%, the remaining 18% showed improvement of less than 50%, the remaining 32% showed minor improvement, and the remaining 22% showed no

change. Even though the results are not particularly promising—a 10% cure rate and a 28% cure rate if the group with more than a 50% improvement is included—they are nevertheless better than the nearly total lack of cures by all other therapy techniques [21].

The mean rate of repigmentation was 58.4% after 4 months when PUVA and the 6 mercaptopurine derivative azathioprine were combined, as opposed to 24.8% with PUVA alone. The same findings were obtained with 50 mg azathioprine given every day for 6 months. similar time frame as the betamethasone pulse therapy, despite the azathioprine group's pigmentation developing more quickly [22].

The patient did not like receiving systemic immunosuppressive medications such systemic steroids. We discussed possible effects on a topical formulation of a different immunosuppressive therapy without the use of steroids. After full discussion, personal consent from the patient, and agreement to regular follow-up, we decided to try topical methotrexate 1% in gel formulation (TREXJOY 1% 20 g gel; Methotrexate 1%W/W) [23].

The study's conclusions indicate that ruxolitinib cream is a secure and effective therapy option for people with vitiligo. Due to systemic exposure to topical ruxolitinib when applied to more than 10% of body surface area or 375 gm in total, black people with vitiligo may have an increased risk of thrombosis [24].

Minocycline 100 mg treatment stopped the disease's progression in 29 patients; only three patients showed the emergence of new lesions or the expansion of pre-existing lesions. Ten individuals indicated a stop to additional depigmentation after four weeks of therapy. Seven people exhibited repigmentation that ranged from slight to obvious [25].

Our data show that oral dexamethasone pulse (10 mg) therapy is successful in halting vitiligo progression, however the majority of our patient group does not achieve satisfactory repigmentation. The pulse regimen does not cause a lasting reduction in endogenous cortisol production, despite the fact that this treatment method typically has mild to severe side effects [26].

Analogue of prostaglandin, Patients were instructed to apply a transparent gel containing 0.5 mg/3 g (166.6 g/g) PGE2 every evening to depigmented skin. The majority of lesions had hyperpigmented borders and marginal repigmentation. Our results are encouraging and offer a fresh, perhaps successful treatment for this pigmentation disorder [27].

Bimatoprost 0.03% solution looks to be a viable therapy option for stable facial vitiligo lesions, but large-scale trials are required to confirm its efficacy. A word of caution: Treating larger regions may lead to hypertrichosis, which is a limiting factor in its use. A larger-scale investigation is necessary due to the study's sample size restriction [28].

Pimecrolimus cream 1% produces repigmentation in vitiligo to variable degrees depending on where the lesion is; nonetheless, double-blind placebo-controlled studies are necessary to prove its effectiveness as a monotherapy or in conjunction with other available treatment modalities. [29].

Simvastatin may be an effective treatment for vitiligo. Repigmentation is treated with ointment and tablets of simvastatin. Repigmentation is treated with an ointment containing simvastatin at a dosage of 1.0 mmol/l [30].

The topical drug calcipotriene, commonly known as calcipotriol, has been licenced by the U.S. Food and Drug Administration (FDA) for the treatment of psoriasis. Off-label, calcipotriene is frequently applied to treat vitiligo. Calcipotriene, a vitamin D byproduct, is hypothesised to work by limiting the growth of the skin cells in vitiligo patients. When used in conjunction with phototherapy or topical

corticosteroids, calcipotriene can be more effective. For repigmentation, calcipotriol 0.005% ointment is utilised [31].

Vitiligo is treated topically with tacrolimus cream. There is 0.1% of tacrolimus present. To repigment, it is used twice daily. The vitiligo patches on his face and scalp started to repigment after two months of treatment. Each subsequent check-up revealed progressively improved results, and after 18 months of treatment, 90% of these areas had repigmented [32].

❖ **Therapeutic Methods**

The inability to fully comprehend the dynamics and physics of vitiligo has made it challenging to develop an effective treatment. Treatment for vitiligo focuses on promoting repigmentation, reducing psychological discomfort, and halting the expansion of existing white spots on the skin. The two main treatments for vitiligo at the time are drug therapy and phototherapy. Historically, corticosteroids such mometasone furoate, betamethasone dipropionate, and clobetasol propionate have been the first-line therapy for vitiligo because of their anti-inflammatory and immunosuppressive qualities. In newly updated treatment guidelines, calcineurin inhibitors like tacrolimus and pimecrolimus were also recommended as first-line treatments for the management of vitiligo [33]. According to clinical research, calcineurin inhibitors, particularly those used to treat facial leukomas, have a comparable effect on glucocorticoids. Additionally, melanocyte dysfunction is significantly impacted by the accumulation of oxidative chemicals in the skin. To restore the oxidation-antioxidant system of the skin, various antioxidants have been used. These anti-oxidants cleanse the epidermis of vitiliginous skin of excess ROS and hydrogen peroxide. Oral antioxidants such polypodium leucotomos, vitamin E, vitamin C, and minocycline are used as part of the antioxidation therapy strategy against vitiligo. Physical therapies such as phototherapy employing psoralen ultraviolet A (PUVA) and narrow-band ultraviolet A (NB-UVA), which are distinct from pharmaceutical therapy, are typically safe. 38-40 Since phototherapy, both by alone and in combination with the medicines listed, is extremely effective at causing repigmentation, these strategies have been frequently utilised in clinical practise [34].

- ***Surgical therapies***

Surgical therapies for vitiligo patients have improved repigmentation rates. Candidates for these procedures include patients who have had non-progressing vitiligo for a year and are not responding to medical therapy. Numerous surgical techniques have been tried to treat vitiligo, and the most of them don't necessitate very sophisticated tools. Tissue grafting and cellular suspensions are the two main melanocyte transplantation techniques now available for stable vitiligo [35].

- ***Laser Therapy***

This method can swiftly and precisely remove melanocytes from a specific area. For this, Q-switch Ruby and Q-switch Alexandrite lasers have been used. The use of laser therapy, which is effective on larger areas, is beneficial for all skin types. However, pain and easy access to lasers are the biggest downsides. Psoriasis, vitiligo, and mycosis fungoides are among the conditions that the monochromatic excimer laser (MEL) at 308 nm is frequently used to treat. It is very near the 311 nm wavelength of narrowband UVB (Leone, Iacovelli, Paro Violin, & Picardo, 2003). The US FDA has approved MEL for the treatment of vitiligo, however there are no specific dosage recommendations. MEL works by stimulating perifollicular amelanotic melanocytes and inducing T-cell apoptosis. Because of the reduced power density, there is less chance of overexposure, the ability to treat greater regions at once, and a shorter treatment period. Blistering, erythema, and hyperpigmentation are some of the

negative symptoms that could e surrounding normal skin. According to Leone et al. (2003), prolonged exposure to UV radiation may eventually result in skin aging and malignancies [36].

- ***Phototherapy***

Phototherapy uses either artificial or natural light to treat medical conditions. Treatment options include fluorescent lighting, halogen bulbs, natural light, and light-emitting diodes (LEDs). Light therapy and heliotherapy are two other names for phototherapy. Your type of therapy and how the light is utilised may vary depending on whether phototherapy is being used to treat eczema, psoriasis, or other medical conditions. Phototherapy is usually used as the first line of treatment for severe cases of vitiligo. It can be used as UVB, UVA, or UVA combined with psoralen phototherapy. Narrow-band UVB (NBUVB) therapy has taken the place of more traditional forms of phototherapy for vitiligo due to its enhanced efficacy and outstanding safety profile, even in pregnant women and children [37]. Lamps, fluorescent upright booths, home NBUVB phototherapy equipment, an excimer laser, or light sources are all used to deliver targeted phototherapy. NBUVB causes local immunosuppression and stimulates melanocytes in the epidermis and the outer root sheath of hair follicles to produce its desired effects [38]. Usually, the initial dose of phototherapy is 150 mJ/cm2 and is increased by 10–15% at each visit, with a maximum dose of 1 J/cm2 for the face and 3 J/cm2 for the body in a single session. Usually, two to three times a week are provided. Numerous topical medicines, including as corticosteroids, calcineurin inhibitors, vitamin D analogues, and pseudo catalase, have been successfully used with NBUVB. One-time adverse effects include xerosis, erythema, itching, and burning. A long-term drawback is photoaging and photodamage. There are no long-term data on the development of carcinogenicity in vitiligo patients following NBUVB phototherapy [39].

- **Vitiligo Drug Delivery System Using Nanotechnology**

Vitiligo is a depigmentation condition that significantly impairs a patient's physical, mental, and quality of life. Reducing oxidative stress and controlling the immunological response are the two main objectives of treatment. Sadly, the cuticle barrier's function and the lack of specific accumulation lead to unfavourable therapeutic effects and side effects [40]. The development and application of nanotechnology offer suggestions and ideas for new vitiligo treatment programs. Potential treatments for vitiligo based on nanotechnology are noted as being possible with liposomes, niosomes, nano hydrogel, and nanoparticles. Topical nano-drug delivery techniques for vitiligo treatment that promote melanin regeneration, boost transdermal penetration, and enhance drug retention [41]. Rapid developments in nano-drug delivery techniques have led to new viewpoints and treatment recommendations for vitiligo. These innovative methods assist in giving newly developed drugs a sustained or controlled release behaviour, which raises therapeutic efficacy and reduces side effects. Despite their immense potential, the present nano-drug delivery methods have some limitations. In contrast to the ideal approach to completely eradicate the problem, the majority of studies on innovative medicine delivery systems for the treatment of vitiligo choose a minimal level of symptom control. It is inevitable that researchers will carry out and complete the work necessary to significantly increase the efficacy of nano-drug delivery devices despite these challenges. Numerous receptors, including granulocyte colony-stimulating factor (G-CSFR) and melanocortin receptors 1–5 (MC1R–MC5R), are located on the surfaces of melanocytes or neighbouring keratinocytes, increasing the

possibility of developing targeted treatments. Excellent promise exists for the safe treatment of vitiligo with their endogenous ligands or analogues. One team proposed making hydrogels on their own using ultra-short cysteine-containing peptides. According to in vivo studies, one of the formulations has great biocompatibility and a limited potential for allergies. Researchers studied the self-assembly behaviour, nanostructure growth, hyhydrogenation, and phase change of two specific tripeptides using X-ray crystalline diffraction and scanning electron microscopy. The hydrophobic backbone that promotes self-assembly is made up of acetylated Leu-Ile-Val-Ala-Gly, and the C-terminal residue certainly influences how quickly and effectively the peptide fibril bonds with an SMD. As the mechanisms of crosslink and polymerization of small molecule peptide medications are understood, various peptide-based topical drug delivery techniques for the treatment of vitiligo may become more prevalent. Using existing and potential future nano-drug delivery techniques for the treatment of vitiligo [(42)]. Nano-lipid carrier systems are currently significantly gaining relevance due to their remarkable effectiveness when applied topically to the target location, despite the fact that there are numerous alternative treatment options available for the ailment. One may argue that the best nano-lipid carrier systems for treating vitiligo or a variety of other tropical diseases include liposomes, ethosomes, transethosomes, and transferosomes [(43)].

THE IMPACT OF VITILIGO ON QUALITY OF LIFE

Vitiligo has a substantial influence on quality of life, affecting routine tasks and social interactions. Regardless of how bad the condition is, vitiligo management requires psychological support and counselling. Because the impact on QoL is not inversely connected with the severity of the illness, patients frequently worry that the condition may get worse. More than 50% of vitiligo patients feel depression, which is more common in women and those who receive their first diagnosis. Low self-esteem, altered self-perception, ineffective coping methods, and a lack of social support all contribute to the psychological impacts of the condition. Dermatologists might, however, be able to acknowledge the psychological implications of the illness due to time constraints by referring patients to a psychologist or therapist who can address both the subjective and objective components of the issue. It is crucial to consider how various therapeutic regimens may impact a patient's quality of life (QoL) while choosing the best course of action. Patient support groups are an essential tool for patients to gain knowledge about their condition and make connections with people who have similar symptoms [(44)].

CHALLENGES

Research has unequivocally shown that vitiligo can have a major psychological and emotional impact. One is that you no longer feel in control of your appearance, especially the way your skin looks. Because to vitiligo, the colour of your skin may change, and white patches may form anywhere on your body, including on your face. ([(45)]. This problem has key features related to marriage and socialisation, which is a significant challenge in life. Socialisation and being an active part of society are linked to both a successful marriage and deepening a couple's understanding of one another. People with vitiligo may have problems getting married and maintaining their relationships in the long run because to their socialisation issues. Vitiligo patients who have had symptoms since infancy worry a lot about getting married. Because they would want to prevent frustration by choosing to remain single forever, women take it more seriously. Contrarily, men take marriage more seriously and look for a partner who will put their needs before their own. They decide on it because they think they can handle it

better and have a better chance of having a successful marriage with a relative. If it is thought that inheritance also plays a role in illness, the risk of a disease emerging in the next generation after a relative marries rises. Persons with vitiligo must also think about how they will raise their children both before and after getting married. During their children's formative years, parents' main worry is the chance that they would contract an illness, and they react to even the smallest skin symptoms. This sensitivity is greater when it comes to female offspring because marriage and societal integration are the key concerns of families [46].

INDIAN PATIENTS' EXPERIENCES WITH THE PSYCHOSOCIAL EFFECTS OF VITILIGO

Due to the obvious depigmentation on dark skin and, more importantly, the condition's severe stigma, patients in our country place a special emphasis on vitiligo. Studies using instruments to measure health-related quality of life (QOL), such as the dermatological life quality index (DLQI), have shown that vitiligo has an effect on QOL. For instance, a study of Indian patients showed that a significant proportion of patients have psychological morbidity, which shows up as anxiety, depression, and sleep disturbance [47]. Numerous studies have shown the importance of appearance when it comes to psychological adjustment and the impact of the physical deformities caused by depigmentation. Vitiligo sufferers have lower self-esteem than those without the illness. Women are more badly impacted by vitiligo than males are. Children with vitiligo experience psychosocial effects as well. According to research using QOL and psychiatric morbidity questionnaires, 25% of vitiligo patients had psychological morbidity (depressive episodes, difficulty adjusting, and anxiety) [48]. Indian vitiligo patients bear a particular hardship as a result of a combination of interpersonal, familial, and social responses to the condition. While many of these side effects are brought on by other disfiguring skin disorders and many patients' worries are universal, vitiligo patients in India encounter a particular set of difficulties [49]. Depression and anxiety were the two psychosocial comorbidities that were most frequently mentioned. There has been evidence of depression or depressive disorders in 41 studies involving vitiligo patients, with incidence rates ranging from 0.1% to 62.3%. These illnesses include major depressive disorder, bipolar disorder, and dysthymic disorder. The prevalence of anxiety or anxiety-related disorders, such as generalized anxiety disorder, agoraphobia, social phobia [not social avoidance], and panic disorder, was shown to range from 1.9 to 67.9% in 20 investigations [50].

ACKNOWLEDGEMENT

Authors would like to thank, Goel Institute of Pharmacy & Sciences (GIPS), Lucknow, Uttar Pradesh, India for extending their facilities.

CONCLUSION AND FUTURE DIRECTION

Our review articles begin with an overview of the vitiligo disease, its classification, pathophysiology, current therapies and treatments, including Allopathic medicine, surgical therapies, laser therapy, phototherapy, and drug delivery systems using nanotechnology, as well as its challenges and quality of life. Our review's conclusion is that while non-pharmacological treatment yields positive results but requires time and does not harm the human body, medicine does not totally cure and has negative side effects like cancer. There should be more randomized controlled studies on the management of vitiligo. We intend to carry out a preliminary analysis of vitiligo disease in the future. We are doing a counseling-based study project in our nation and its states to evaluate patient mental health and provide better statistics on vitiligo condition and its treatment.

Table.1: Current status of clinical trials on vitiligo disease.

Drug	Mode of administration	Disease	Enrollment	Allocation/Intervention model/Masking	Official Title of the study	Status	Clinical trial #
Botulinum toxin A	Injected	Vitiligo disease	10	Non-Randomized/ Single Group Assignment/ None (Open Label	Botulinum Toxin Treatment for Localized Vitiligo	Phase 4	NCT01051687
Apremilast	orally		23	N/A/ Single Group Assignment/ None (Open Label)	A Split Body Study of the Effects of Combined Therapy With Narrow-Band Ultraviolet B Phototherapy and Apremilast for the Treatment of Vitiligo	Phase 2	NCT03123016
Ruxolitinib and Vehicle	Topically		157	Randomized/Sequential Assignment/Double (Participant, Investigator)	A Randomized, Double-Blind, Dose-Ranging Study of INCB018424 Phosphate Cream in Subjects With Vitiligo	Phase 2	NCT03099304
Triamcinolone Acetonide	Injected		18	Randomized/ Single Group Assignment/ Double (Participant, Outcomes Assessor)	Efficacy and Safety of Intralesional Triamcinolone Acetonide in Vitiligo: A Prospective, Double-Blind Randomized Controlled Trial	Phase 2	NCT01766609
Total Glucosides of Paeony(TGP)	orally		200	Randomized/Parallel Assignment/Double (Participant, Investigator	Efficacy and Safety of Total Glucosides of Paeony Combined With NB-UVB in the Treatment of Sporadic Vitiligo in Proceeding: a Double-blind, Randomized, Placebo-controlled Trial	Not Applicable	NCT03608917
Tacrolimus and Placebo	Topical		42	Randomized/ Parallel Assignment/ Triple (Participant, Care Provider, Investigator	Efficacy of Tacrolimus Ointment 0.1% Versus Placebo in Adults With Facial Non-segmental Vitiligo: a Randomized Double-blind Controlled Study	Phase 3	NCT02466997
Methotrexate and Placebos	orally		44	Randomized/ Parallel Assignment/ Triple (Participant, Care Provider, Investigator)	Efficacy and Tolerance of the Combination of Methotrexate and Phototherapy Versus Phototherapy in Adults With Progressive Vitiligo: a Randomized Double-blind Prospective Study	Phase 2	NCT04237103
Diphenylcyclopropenone (DPCP)	Topically		20	N/A/ Single Group Assignment/ None (Open Label)	Efficacy and Safety of Diphenylcyclopropenone (DPCP) as a Depigmenting Therapy in Extensive Vitiligo	Phase 4	NCT04775979
Tretinoin 0.05% cream and Placebo cream	Topically		25	Randomized/ Parallel Assignment/ Single (Outcomes Assessor)	PHNA, Efficacy of Tretinoin Cream on Post-phototherapy Hyperpigmentation	Not Applicable	NCT03933774
Baricitinib Oral Product and Placebo	orally		48	Randomized/ Parallel Assignment/ Double (Participant, Investigator)	Evaluation of Effect and Tolerance of the Association of Baricitinib (4 mg) and Phototherapy Versus Phototherapy in Adults With Progressive Vitiligo: a Randomized, Double-blind, Prospective, Non-comparative Phase II Study	Phase 2	NCT04822584
Tofacitinib	Orally		47	N/A/ Single Group Assignment/ None (Open Label	Safety and Efficacy of Tofacitinib for Immune Skin Conditions in Down Syndrome	Phase 2	NCT04246372
Protopic and PlacebDiprobase	Topically	Vitiligo disease	35	Randomized/ Parallel Assignment/ Double (Participant, Investigator)	Maintenance Treatment of Non-Segmental Vitiligo With Tacrolimus Ointment 0.1% Versus Control, Randomized and Double Blind Study	Phase 2 Phase 3	NCT01841008
Crisaborole 2 % Topical Ointment And PF-07038124	Topically		64	Randomized/Factorial Assignment/Quadruple (Participant, Care Provider,	Study of Efficacy, Safety and Tolerability of Crisaborole and PF-07038124 With and Without NBUVB in Vitiligo: A Phase 2A	Phase 2	NCT05298033

0.01% topical ointment				Investigator, Outcomes Assessor)	Randomized, Double-Blind, Vehicle-Controlled Clinical Trial		
Simvastatin and Placebo	Orally		15	Randomized/ Parallel Assignmen/ Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	A Phase-II, Randomized, Placebo-controlled Trial of Simvastatin in Generalized Vitiligo	Phase 2	NCT01517893
Rapamycin and Placebo	Topically		20	Randomized/ Parallel Assignment/ Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor)	Daily Topical Rapamycin Therapy for the Treatment of Vitiligo	Phase 2	NCT05342519
Oral dexamethasone minipulse and Placebo oral tablet	Orally		100	Randomized/ Parallel Assignment/ Single (Care Provider	The Reflection of Skin Color on the Efficacy of Narrow Band UVB in Stabilization of Active Cases of Vitiligo	Phase 1	NCT04030988
Latanoprost 0.005% Ophthalmic Solution and 5Fluorouracil	Topically		40	Randomized/ Parallel Assignment/ Single (Participant)	Efficacy of Topical 5-fluorouracil Versus Topical Latanoprost With Microneedling in Localized Stable Vitiligo: A Randomised Clinical Trial	Phase 2 Phase 3	NCT05513924

REFERENCES

1. Shared decision-making for vitiligo. Br J Dermatol. 2021 Oct;185(4):e158–78.
2. Lucy Y. Liu, James P. Strassner,Maggi A. Refat, MD,John E. Harris, MD, PhD, and Brett A. King, MD P. Repigmentation in vitiligo using the janus kinase inhibitor, tofacitinib, may require concomitant light exposure. Physiol Behav. 2017;176(1):675–82.
3. Jacobsen KH, Hay MC, Manske J, Waggett CE. Curricular models and learning objectives for undergraduate minors in global health. Ann Glob Heal. 2020;86(1):1–9.
4. Alikhan A, Felsten LM, Daly M, Petronic-Rosic V. Vitiligo: A comprehensive overview: Part I. Introduction, epidemiology, quality of life, diagnosis, differential diagnosis, associations, histopathology, etiology, and work-up. J Am Acad Dermatol [Internet]. 2011;65(3):473–91. Available from: http://dx.doi.org/10.1016/j.jaad.2010.11.061
5. Boza JC, Fabbrin A, Cestari TF. Translation, cross-cultural adaptation and validation of the vitiligo-speci fi c health-related quality of life instrument. :358–62.
6. Dolatshahi M, Ghazi P, Feizy V, Hemami M. Life quality assessment among patients with vitiligo: Comparison of married and single patients in Iran. Indian J Dermatol Venereol Leprol. 2008;74(6):700.
7. Gawkrodger DJ, Ormerod AD, Shaw L, Mauri-Sole I, Whitton ME, Watts MJ, et al. Guideline for the diagnosis and management of vitiligo. Br J Dermatol. 2008;159(5):1051–76.
8. Borimnejad L, Parsa Yekta Z, Nikbakht-Nasrabadi A, Firooz A. Quality of life with vitiligo: Comparison of male and female muslim patients in Iran. Gend Med. 2006;3(2):124–30.
9. Lotti T, Buggiani G, Troiano M, Assad GB, Delescluse J, De Giorgi V, et al. Targeted and combination treatments for vitiligo: Comparative evaluation of different current modalities in 458 subjects. Dermatol Ther. 2008;21(SUPPL. 1):20–6.
10. Lotti T, Agarwal K, Podder I, Satolli F, Kassir M, Schwartz RA, et al. Safety of the current drug treatments for vitiligo. Expert Opin Drug Saf [Internet]. 2020;19(4):499–511. Available from:

https://doi.org/10.1080/14740338.2020.1729737

11. Jowett S, Ryan T. Skin disease and handicap: An analysis of the impact of skin conditions. Soc Sci Med. 1985;20(4):425–9.
12. AL-smadi K, Imran M, Leite-Silva VR, Mohammed Y. Vitiligo: A Review of Aetiology, Pathogenesis, Treatment, and Psychosocial Impact. Cosmetics. 2023;10(3):84.
13. Halder RM, Chappell JL. Vitiligo Update. Semin Cutan Med Surg [Internet]. 2009;28(2):86–92. Available from: http://dx.doi.org/10.1016/j.sder.2009.04.008
14. Henning SW, Jaishankar D, Barse LW, Dellacecca ER, Lancki N, Webb K, et al. The relationship between stress and vitiligo: Evaluating perceived stress and electronic medical record data. PLoS One [Internet]. 2020;15(1):1–14. Available from: http://dx.doi.org/10.1371/journal.pone.0227909
15. Rahman R, Hasija Y. Exploring vitiligo susceptibility and management : a brief review. 2018;1–13.
16. Mehdi Rashighi, MD and John E. Harris, MD P. Vitiligo pathogenesis and emerging treatments. Physiol Behav. 2016;257–65.
17. Rashighi M, Harris JE. Vitiligo Pathogenesis and Emerging Treatments. Dermatol Clin [Internet]. 2017;35(2):257–65. Available from: http://dx.doi.org/10.1016/j.det.2016.11.014
18. Rajatanavin N, Suwanachote S, Kulkollakarn S. Dihydroxyacetone: A safe camouflaging option in vitiligo. Int J Dermatol. 2008;47(4):402–6.
19. Mehta H, Kumar S, Parsad D, Bishnoi A, Vinay K, Kumaran MS. Oral cyclosporine is effective in stabilizing active vitiligo: Results of a randomized controlled trial. Dermatol Ther. 2021;34(5).
20. Craiglow BG, King BA. Tofacitinib citrate for the treatment of Vitiligo a pathogenesis-directed therapy. JAMA Dermatology. 2015;151(10):1110–2.
21. ALI ESMAIL AL-SNAFI. Chemical Constituents and Pharmacological Activities of Lantana Camara – a Review. Asian J Pharm Clin Res. 2019;10–20.
22. Radmanesh M, Saedi K. The efficacy of combined PUVA and low-dose azathioprine for early and enhanced repigmentation in vitiligo patients. J Dermatolog Treat. 2006;17(3):151–3.
23. Abdelmaksoud A, Dave DD, Lotti T, Vestita M. Topical methotrexate 1% gel for treatment of vitiligo: A case report and review of the literature. Dermatol Ther. 2019;32(5):2–5.
24. Uppal SK, Kearns DG, Chat VS, Wu JJ. Ruxolitinib cream for the treatment of vitiligo. Lancet [Internet]. 2020;396(10264):1735–6. Available from: http://dx.doi.org/10.1016/S0140-6736(20)32469-7
25. Parsad D, Kanwar A. Oral minocycline in the treatment of vitiligo - A preliminary study. Dermatol Ther. 2010;23(3):305–7.
26. Radakovic-Fijan S, Fürnsinn-Friedl AM, Hönigsmann H, Tanew A. Oral dexamethasone pulse treatment for vitiligo. J Am Acad Dermatol. 2001;44(5):814–7.
27. Davinder Parsad, Roma Pandhi, Sunil Dogra and BK. Topical prostaglandin analog (PGE 2) in vitiligo – a preliminary study. Int J Dermatol. 2002;41:942–5.
28. Aleksandra Vojvodic, Priyanka Karagaiah, Yan Valle, Julia Sigova, Nicola Zerbinati, Petar Vojvodic, Davinder Parsad, Robert A. Schwaertz, Stephan Grabbe MG& TL. Emerging drugs for the treatment of vitiligo. Expert Opin Emerg Drugs [Internet]. 2020;25(1):7–24. Available from:

https://doi.org/10.1080/14728214.2020.1712358

29. Şendur N, Karaman G, Saniç N, Şavk E. Topical pimecrolimus: A new horizon for vitiligo treatment? J Dermatolog Treat. 2006 Dec;17(6):338–42.
30. Hasan R, Agarwal K, Podder I, Misitzis A, Schwartz RA, Wollina U, et al. Simvastatin in vitiligo: an update with recent review of the literature. Int J Dermatol. 2021;60(10):e390–6.
31. Chiavérini C, Passeron T, Ortonne JP. Treatment of vitiligo by topical calcipotriol. 2002.
32. Sisti A, Sisti G, Oranges CM. Effectiveness and safety of topical tacrolimus monotherapy for repigmentation in vitiligo: A comprehensive literature review. An Bras Dermatol. 2016;91(2):187–95.
33. Rashighi M, Harris JE. Vitiligo Pathogenesis and Emerging Treatments. Dermatol Clin. 2017 Apr;35(2):257–65.
34. Manga P, Elbuluk N, Orlow SJ. Recent advances in understanding vitiligo [version 1; referees: 3 approved]. F1000Research. 2016;5(0):1–9.
35. Alicja Fr ˛aczek, Marta Kasprowicz-Furma ´nczyk WP and AOS. Surgical treatment of vitiligo. Dermatologic Surg. 1999;25(8):669.
36. Agarwal K, Podder I, Kassir M, Vojvodic A, Schwartz RA, Wollina U, et al. Therapeutic options in vitiligo with special emphasis on immunomodulators: A comprehensive update with review of literature. Dermatol Ther. 2020;33(2):1–14.
37. Cichorek M, Wachulska M, Stasiewicz A, Tymińska A. Skin melanocytes: Biology and development. Postep Dermatologii i Alergol. 2013;30(1):30–41.
38. Slominski A, Wortsman J, Plonka PM, Schallreuter KU, Paus R, Tobin DJ. Hair follicle pigmentation. J Invest Dermatol. 2005;124(1):13–21.
39. Bae JM, Jung HM, Hong BY, Lee JH, Choi WJ, Lee JH, et al. Phototherapy for Vitiligo: A Systematic Review and Meta-analysis. JAMA dermatology. 2017 Jul;153(7):666–74.
40. Palmer BC, DeLouise LA. Nanoparticle-Enabled Transdermal Drug Delivery Systems for Enhanced Dose Control and Tissue Targeting. Molecules. 2016 Dec;21(12).
41. Marwah H, Garg T, Goyal AK, Rath G. Permeation enhancer strategies in transdermal drug delivery. Drug Deliv. 2016;23(2):564–78.
42. Sun MC, Xu XL, Lou XF, Du YZ. Recent Progress and Future Directions: The Nano-Drug Delivery System for the Treatment of Vitiligo. Int J Nanomedicine. 2020;15:3267–79.
43. Das S, Kaur S. Nano-Lipid-Carriers for the Treatment of Vitiligo: A Recent Update, Pathophysiology and Mechanism of Drug Delivery. Curr Mol Pharmacol. 2021;14(3):306–20.
44. Baidya S, Dey P, Mohanty R. Assessment of quality of life in vitiligo patients attending a tertiary care hospital - A cross sectional study. Ind Psychiatry J. 2021;30(1):62–6.
45. Grimes PE, Miller MM. Vitiligo: Patient stories, self-esteem, and the psychological burden of disease. Int J Women's Dermatology [Internet]. 2018;4(1):32–7. Available from: https://doi.org/10.1016/j.ijwd.2017.11.005
46. Saeedinezhad F, Firouzkouhi M, Abdollahimohammad A, Rahnama M. The challenges facing with vitiligo: a phenomenological research. Int J Pharm Res Allied Sci. 2016;5(3):356–64.
47. Mishra N, Rastogi MK, Gahalaut P, Agrawal S. Dermatology specific quality of life in vitiligo patients and its relation with various variables: A hospital based crosssectional study. J Clin Diagnostic Res. 2014;8(6):18–20.

48. Mattoo SK, Handa S, Kaur I, Gupta N, Malhotra R. Psychiatric morbidity in vitiligo: Prevalence and correlates in India. J Eur Acad Dermatology Venereol. 2002;16(6):573–8.
49. Pahwa P, Mehta M, Khaitan BK, Sharma VK, Ramam M. The psychosocial impact of vitiligo in Indian patients. Indian J Dermatol Venereol Leprol. 2013;79(5):679–85.
50. Ezzedine K, Eleftheriadou V, Jones H, Bibeau K, Kuo FI, Sturm D, et al. Psychosocial Effects of Vitiligo: A Systematic Literature Review. Am J Clin Dermatol [Internet]. 2021;22(6):757–74. Available from: https://doi.org/10.1007/s40257-021-00631-6.

HOW TO CITE: Yash Srivastav, Akhandnath Prajapati, Adityanath Prajapati, Madhaw Kumar, Mohammad Aqil Siddiqui, A study of challenges and quality of life (QoL) issues related to Vitiligo disease's current treatments, Int. J. in Pharm. Sci., 2023, Vol 1, Issue 9, 17-30. https://doi.org/10.5281/zenodo.8312051