ASSESSMENT OF DRUG PRESCRIBING PATTERN, QUALITY OF LIFE AND DEPRESSION IN GENERALIZED AND LOCALIZED VITILIGO PATIENTS OF ANDHRA PRADESH

Thesis Submitted for the Award of the Degree of

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in
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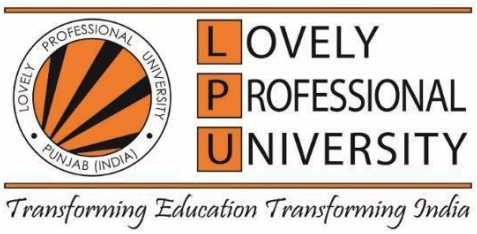

LOVELY PROFESSIONAL UNIVERSITY, PUNJAB

2024

DECLARATION

I, hereby declare that the presented work in the thesis entitled "Assessment of drug prescribing pattern, quality of life and depression in generalized and localized vitiligo patients of Andhra Pradesh" in fulfillment of the degree of **Doctor of Philosophy (Ph.D.)** is the outcome of research work carried out by me under the supervision Dr. Biplab Pal, working as Assistant Professor, in the School of Pharmaceutical Sciences of Lovely Professional University, Punjab, India. In keeping with the general practice of reporting scientific observations, due acknowledgments have been made whenever the work described here has been based on the findings of other investigators. This work has not been submitted in part or full to any other University or Institute for the award of any degree.

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CERTIFICATE

This is to certify that the work reported in the Ph.D. thesis entitled "Assessment of drug prescribing pattern, quality of life and depression in generalized and localized vitiligo patients of Andhra Pradesh" submitted in fulfillment of the requirement for the reward of degree of **Doctor of Philosophy (Ph.D.)** in Pharmacology, is a research work carried out by Somanaboina Padmakar (Reg. no.11813077), is bonafide record of his/her original work carried out under my supervision and that no part of thesis has been submitted for any other degree, diploma or equivalent course.

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ABSTRACT

Vitiligo is a dermatological condition characterized by white spots or patches on the skin due to the loss of skin pigment called melanocytes. The estimated prevalence of vitiligo is about 0.5 to 2% of the world population, but in India, the prevalence rate varies from 2 to 8%, depending on the region. This study aimed to evaluate the drug prescribing pattern, compare the difference in the quality of life (QoL) and depression between generalized and localized vitiligo and compare the efficacy and safety of synthetic drugs with herbal drugs. A total of 464 drugs were prescribed to 200 patients. All the drugs were prescribed by generic names. Almost all prescriptions mentioned the strength, the quantity of the drug to be used, the frequency, and application site. The most commonly prescribed class of drugs was corticosteroids (42.9%), followed by calcineurin inhibitors (13.4%), vitamins (14.6%), basic fibroblast growth factor (9.5%), moisturizers (6.9%), antihistamines (6.5%), and minerals (6.2%). Topical corticosteroids were prescribed more often than orally. Betamethasone was the most commonly prescribed drug among corticosteroids, followed by clobetasol propionate. Tacrolimus was secondary to steroids, followed by decapeptide, vitamins A and D, glycerin, chlorpheniramine maleate, B- complex, and calcium. Generalized vitiligo had significantly ($p < 0.05$) lower QoL than localized vitiligo. Apart from item 4 of the DLQI questionnaire, all other domains of QoL showed significantly higher ($p<0.05$) DLQI scores in generalized vitiligo compared to localized type. Among various domains of QoL, the treatment domain (Item 10) had the highest impact on QoL in both types of vitiligo. In generalized vitiligo, 51.1% of patients experienced an extremely large effect, and 15.5% had a very large effect on the QoL. Whereas in localized vitiligo, the proportion of an extremely large effect and a very large effect was experienced by 29.3% and 13.8% of patients, respectively. The prevalence of depression was 89.5% ($n = 179$) in vitiligo patients. Severe and very severe depression was observed among 27.4% and 36.9 % of generalized vitiligo patients, respectively. Whereas, the proportion of severe and very severe depression among localized vitiligo patients was 18.1 % and 2.6 %, respectively. Complete repigmentation (Grade 5) was not achieved in 39 patients. Two patients (one from

each group) showed 90% repigmentation (Grade 4) at the end of the study period. Thus, overall, a good response (75–100% repigmentation) was seen only in the tacrolimus group, with 13.6% in the first follow-up and 23.5% in the second follow-up. In the aloe vera group, the better response (50–74%) was achieved in 18% and 11.7% of patients during follow-up I and II, respectively. In the tacrolimus group, better responses were noticed in 18.1% and 41.1% of patients during follow-up I and II. The quality of life is significantly impaired in patients with vitiligo, and depression was also prevalent in this population. In order to improve patient conditions, a holistic approach that incorporates psychological interventions, counseling, and effective therapy is recommended. The findings of this study also suggest that using topical aloe vera gel and topical tacrolimus as monotherapy was safe and appeared to be very effective in stable forms of vitiligo. Aloe vera was beneficial in enhancing or improving repigmentation in most of the patients in the study, which suggests that it could be used as an alternative treatment for vitiligo.

Keywords: Vitiligo, Prescribing pattern, corticosteroids, Depression, Quality of life, Tacrolimus, Aloe vera

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LIST OF ABBREVIATIONS

BDI: Beck’s Depression Inventory

Bfgf: Basic fibroblast growth factor

BID: Twice a day

BSA: Body Surface Area

CDI: Child Depression Inventory

CES: Cultured epidermal cell suspension

CES-D: Center for Epidemiologic Studies Depression Scale

DASS: Depression Anxiety Stress Scale

DLQI: Dermatology Life Quality Index

ER: Excellent repigmentation

ES-Q: Emotional State Questionnaire

GHQ: General Health Questionnaire

GR: Good repigmentation

HADS: Hospital Anxiety and Depression Scale

HADS: Hospital Anxiety Depression Scale

HAM-D: Hamilton Depression Rating Scale

HDRS: Hamilton Depression Rating Scale

HLA-DR: Human Leukocyte Antigen – DR isotype

ICD: International Classification of Diseases

IgG: Immunoglobulin G

IgM: Immunoglobulin M

KUVA: khellin plus UVA

MADRS: Montgomery–Asberg Depression Rating Scale

MCHR1: Melanin-concentrating hormone receptor 1

MEL: Monochromatic Excimer Light

MR: Moderate repigmentation

NB-UVB: Narrowband ultraviolet B

NCES: Non-cultured epidermal cell suspension

NCFS: Non-cultured follicular cell suspension

NF-Kb: Nuclear Factor Kappa B

NIPD: Netherlands Institute for Pigment Disorders

PAS: Psychiatric Assessment Schedule

PA-UVA: phenylalanine and ultraviolet A

PGA: Physician Global Assessment

PHQ-9: Patient Health Questionnaire

PR: Poor repigmentation

PUVA: Psoralen plus UV-A

QIDS-SR-16: Quick Inventory of Depressive Symptomatology

QoL: Quality of Life

RCT: Randomized Controlled Trial

RIA: Radioimmunoassay

ROS: Reactive Oxygen Species

SDS: Self-rating Depression Scale

SF-36: Short Form 36

Th1: T helper cell-1

TID: Three times a day

TNB-UVB: Targeted narrowband UVB phototherapy

TNF: Tumor necrosis factor

UV: Ultraviolet

UVA: Ultraviolet A

UVB: Ultraviolet B

UVR: Ultraviolet radiation

VASI: Vitiligo Area Scoring Index

VETF: Vitiligo European Task Force

VNS: Vitiligo Noticeability Scale

WPG: water/2-propanol/propylene glycol

1. INTRODUCTION

Vitiligo is a dermatological condition characterized by pigment loss on the skin in the form of white macules and patches. The degree of involvement can range from limited to widespread, and the onset can be sudden or gradual (1). It can appear at any age and affects both genders equally. In India, vitiligo prevalence typically ranges between 0.9 and 8% (2). Vitiligo can be categorized into two primary forms, namely generalized and localized, which are determined by the extent and distribution of skin lesions. The localized form, in turn, can be divided into focal, segmental, unilateral, and mucosal subtypes, while the generalized type includes acrofacial, vulgaris, and universal subcategories (**Figure 1**) (3). The term "mixed form" refers to an overlap of different.

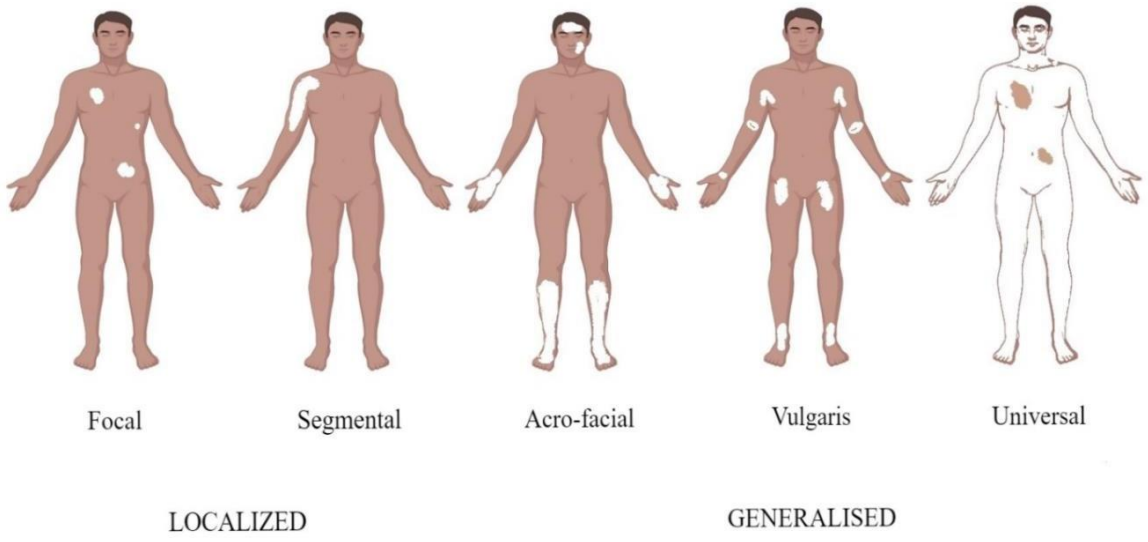

Figure 1: Classification of vitiligo

Focal vitiligo is characterized by a few isolated white patches in a single area. For example, a small patch might appear on the hand or knee (4). Segmental Vitiligo usually affects one side of the body and follows a dermatomal distribution. An example is a patch that appears along a nerve pathway, such as on one side of the face or torso (5). Similar to the segmental form, unilateral vitiligo may not strictly follow a dermatomal pattern and affects one side of the body. For instance, patches might appear on one leg or one arm (4). The mucosal type affects the mucous membranes of the mouth or genitals. An example is depigmentation of the lips or inside the mouth (6).

Acrofacial type affects the distal parts of the body such as fingers, toes, and facial orifices (eyes, nose, mouth). An example is depigmentation around the mouth or fingertips (4). Vulgaris form is characterized by scattered patches over various parts of the body. For instance, patches may appear on the trunk, limbs, and face (6). Universal Vitiligo is the most extensive form, where more than 80% of the body's skin loses pigment. An example is a person having almost entirely depigmented skin (4).

Numerous research studies have sought to elucidate the underlying causes of vitiligo, including genetic factors, oxidative stress, degenerative theory, and autoimmune hypothesis. These theories don't explain the different vitiligo phenotypes, and their contribution to vitiligo as a whole is still debated, although there is no consensus on its autoimmune nature (7,8). Cytotoxic CD8+ T lymphocytes mainly target melanocytes, destroying melanocytes. Histological evidence shows that CD8+ T lymphocytes penetrate deep into the skin in the epidermis and dermis. For example, studies have shown that Patients with vitiligo have been shown to have high levels of cytotoxic CD8+ T lymphocytes in their blood compared to a control group (8,9).Oxidative stress is a widely accepted model that plays a significant role in losing melanocytes. The lesional areas of vitiligo are characterized by raised levels of free radicals, which lead to chemotactic signals that promote the activities of innate and adaptive immune cells (10). For instance, an increase in hydrogen peroxide levels in the epidermis of vitiligo patients has been documented, leading to the impairment of melanogenesis and contributing to melanocyte destruction (11).

At present, there is no cure for vitiligo; however, several treatment alternatives are available that have proven to be effective. These therapies aim to lessen the disease's severity and accelerate the re-pigmentation rate on vitiligo patches, thereby enhancing patients' quality of life (QoL). The three main methods currently used in the treatment are 1. Phototherapy (UVB in particular) and transplantation of melanin cells can activate melanocyte regeneration. 2. Topical and systemic immunomodulatory agents can regulate the autoimmune response, and 3. Oxidative stress in melanocytes can be reduced using topical and systemic antioxidants (12)

Smaller lesions may benefit from topical therapy with corticosteroids or calcineurin inhibitors, but better outcomes are seen when these treatments are combined with phototherapy or natural sunlight (13,14). Narrowband ultraviolet B (NB-UVB) phototherapy has proven to be the most successful treatment option. It has been largely replaced with Ultraviolet A phototherapy with the photosensitizer psoralen (PUVA) due to its superior efficacy and lower risk of side effects (15). Because of its immunomodulatory effect, NB-UVB is thought to reduce disease activity and enhance melanocyte migration and proliferation (16). It has been reported that xenon chloride (308 nm) excimer laser is more advantageous than NB-UVB therapy (17) Stable vitiligo patches with a small reservoir of melanocytes may be suitable for surgical therapies when non-surgical options have failed. Melanocytes can be transplanted using various methods, such as punch grafting, split-thickness skin grafting, melanocyte cell suspension, and suction blister grafting. Surgical treatment with autologous punch grafting is standard practice for vitiligo. This approach is easy to implement and has successfully treated localized and generalized vitiligo (18).

Skin color is part of a person's body image and can lower self-esteem if pathological changes occur (19). Vitiligo patients frequently face substantial stigma as a result of their disfigured appearance. Stigma is more prevalent among young unmarried females, who also experience problems planning their marriages. Women who develop vitiligo after getting married often face marital difficulties that can ultimately result in divorce. Vitiligo has a profound impact on the lives of those affected, often causing feelings of shame, humiliation, low self-esteem, and social withdrawal (20–23). This eventually affects patients' relationships with friends and family, and patients may go into hiding. Lesions on prominent body parts, particularly the face, may cause more embarrassment and frustration than others (24). In many regions of the world, especially India, vitiligo is regarded as a punishment from GOD for mistakes. As per reports, around 75% of vitiligo people have psychiatric morbidities (25). A meta-analysis study found that individuals with vitiligo were nearly five times more prone to develop depression compared to the control group (26). Moreover, people with vitiligo commonly grapple with psychological concerns such as anxiety, depression, obsessive-compulsive disorder, and thoughts of self-harm (27).

Quality of life (QoL) is a term that refers to the physical, social, and psychological aspects of a person's well-being. The visible depigmented patches associated with vitiligo can cause social stigma, discrimination, and psychological distress, which can impair the QoL of the patients (24). In vitiligo patients, general and dermatology-specific health-related quality of life (HRQoL) questionnaires can evaluate the QoL. Unfortunately, vitiligo does not yet have disease-specific HRQoL instruments. These questionnaires provide an overall description of the QoL rather than focusing on any aspect of a particular disease. The Short Form 36 (SF-36) General Health Survey, developed as part of the Medical Outcomes Study, is an excellent example of a generic HRQoL questionnaire (28). Dermatology-specific HRQoL questionnaires are created to assess the impact of skin diseases on individuals' daily lives. HRQoL of different skin diseases can be compared using these questionnaires. Some standard dermatology-specific HRQoL questionnaires include the Skindex-29 (29) and the Dermatology Life Quality Index (DLQI) (30).

In vitiligo, the chronic and unpredictable course of the condition, coupled with concerns about societal acceptance and altered appearance, contributes to psychological distress and an increased risk of depression (22). Depression can be assessed through a range of methods, offering a comprehensive evaluation of individuals' mental well-being. One approach involves clinical diagnosis, which relies on the established criteria provided in the Diagnostic and Statistical Manual (DSM) for mental disorders. In addition, professionals utilize various validated assessment tools specifically designed to measure the severity of depressive symptoms. These scales play a crucial role in providing a standardized and quantifiable measure of depressive symptoms, allowing for a more comprehensive understanding of an individual's mental health (31).

2. REVIEW OF LITERATURE

2.1. Vitiligo

2.1.1. History

Ancient Indian scriptures, such as the Vinay Pitak (a Buddhist text from 224–526 B.C.) and the Atharva Veda (from 1400 B.C.), recorded about vitiligo. Vitiligo and numerous other achromic and hypochromic maladies are referred to in the Atharva Veda by a variety of names, including "Sveta Khista," "Charak," and "Kilasa." "kilas" is derived from the Sanskrit term kil, which means "white." Therefore, "kilas" means "that throws away color"(32). Sveta Khista refers to white leprosy, and vitiligo is most likely confused with macular leprosy. The term charak is used by villagers to describe something that spreads or is concealed. The Buddhist text Vinay Pitak also refers to white spots on the epidermis as "kilas" (33). Other ancient Indian texts, such as Charaka Samhita (800 B.C.), Amorkasha (600 A.C.), and Manusmriti (200 B.C.), describe vitiligo and other leukodermas. "Makataminoharai," an ancient Shinto collection of prayers extending back to around 1200 B.C., mentions a malady called "shirabito," which means "white man." This could be vitiligo. The ancients were aware of vitiligo, the disease characterized by white blotches, but mistook it for leprosy. Similarly, Hippocrates (460–355 BC) did not distinguish vitiligo from leprosy and classified it alongside psoriasis, lichen, leprosy, and vitiligo (32).

Vitiligo was categorized as pigmentary dystrophy in dermatological textbooks published in the late 19th century. The absence of pigment in vitiligo lesions is accompanied by a rise in pigmentation around the lesion’s margin. Louis Brocq (1856–1928) described this characteristic as "dyschromy" (34).

2.1.2. Prevalence of vitiligo

The prevalence of vitiligo diverges widely across different regions of the world, ranging from 0.5 - 2% of the total population (35). In India, the vitiligo prevalence among dermatology outpatients ranges from 0.25- 4%. Notably, specific regions such as Gujarat and Rajasthan have reported elevated rates, reaching up to 8.8% (36).

According to a large-scale study conducted across 30 medical colleges in 21 states in India, vitiligo prevalence among patients in these institutions was 0.89%. The study further observed a slightly higher prevalence in females (0.93%) compared to males (0.86%) (37).

According to a web-based survey of 30,000 adults, the prevalence of vitiligo among US adults aged 18 to 85 years was 0.76%, which corresponds to an estimated 1.9 million cases in 2020 (38). A study from Europe, Japan, and the USA found that the prevalence of vitiligo among adults ranged from 0.1% to 0.8%, and that vitiligo had a negative impact on the QoL of the affected individuals (39). The prevalence of vitiligo in South Asian, Mexican, and American populations has been as high as 4% (40). According to a multicontinental study, hospital-based vitiligo prevalence was 1.6% in Asia, 2.5% in Africa, and 1.5% in the United States (41).

In Japan, a retrospective study analyzed the clinical data of 67,448 patients who visited dermatology clinics and found that the prevalence of vitiligo was 1.68%, with higher rates in older age groups and women (42). According to the yearly reports of different research groups, the proportion of people with vitiligo in Korea rose by 0.12%, and 0.13% from 2009 to 2011 (43). In a comprehensive study conducted by a Chinese research group, involving home visits to 42,833 individuals and examined participants for signs of vitiligo. The findings revealed that 0.093% of the surveyed population had vitiligo (44). According to a community-based study in six cities in China, the prevalence of vitiligo among adults was 0.56%, with higher rates in men (0.71%) than in women (0.45%) (45)

A one-year prospective study conducted in the French West Indies, involving 2,077 patients, identified a prevalence rate of 0.3% for vitiligo (46). In South Africa, a retrospective study of 7029 patients' medical records revealed a vitiligo prevalence of 1.2% (47). Out of 403 dermatological patients who visited the selected clinics of Mekelle City in northern Ethiopia from 2017 to 2019, 13.15% of patients had vitiligo (48). During a one-year prospective study across 12 distinct clinics in Tunisia, involving 28,244 patients, it was observed that vitiligo constituted 1.1% of various skin diseases (49).

2.1.3. Classification of Vitiligo

The grouping of vitiligo can vary depending on the criteria location and size of lesions, the disease can be classified as generalized or localized. 'Mixed type' refers to a situation in which multiple categories overlap. Vitiligo lesions can be classified as nonsegmental, segmental, or mixed based on whether or not they cross the midline The localized type and generalized type are subcategorized as follows (50):

1. Localized vitiligo

Localized vitiligo refers to a specific form of vitiligo where depigmentation occurs in distinct and limited areas of the skin. In this type of vitiligo, white or light-colored patches develop in particular regions, and the condition is characterized by its focal nature rather than widespread involvement.

A. *Focal:* This subtype refers to the presence of one or more patches in a single location on the body but without a segmented pattern.

B. *Segmental:* In this subtype, one or more maculae (flat, distinct areas of discoloration) appear in a dermatomal distribution. The lesions are usually unilateral (affecting one side of the body) and even affect the face.

2. Generalized vitiligo

Generalized vitiligo also called non-segmental vitiligo, is characterized by symmetrical lesions that affect various parts of the body. It is further subdivided into the following forms:

A. *Acrofacial:* This subtype affects the face and distal extremities, such as the hands and feet.

B. *Vulgaris:* It is characterized by a symmetrical distribution of lesions throughout the body and is the most prevalent form among generalized vitiligo subtypes.

C. *Mixed:* This subtype refers to a combination of segmental vitiligo (lesions following a dermatomal distribution) with vulgaris or acrofacial varieties.

3. Universal Vitiligo

Universal vitiligo is an advanced and extensive form of vitiligo characterized by widespread depigmentation across the majority of the body's surface. This form of vitiligo is distinguished by its extensive involvement, affecting more than 80% of the body (51).

Koga Classification

The Koga classification system further categorizes vitiligo into two main varieties:

Non-segmental (*Type A*) vitiligo is more common and can change throughout a person's life. It is linked to autoimmune conditions like Addison's disease, thyroid disorders, Sutton's nevus, pernicious anemia, and juvenile diabetes mellitus. It is also connected to Koebner's phenomenon, which is the development of newly appearing skin lesions in areas of trauma or damage.

Vitiligo Segmental (Type B): This kind has a dermatomal distribution and is less frequent. Although it develops quickly at first and stays stable over time, its course.

These classifications help dermatologists and researchers better understand the different forms and manifestations of vitiligo. This can aid in disease diagnosis, treatment planning, and monitoring (52).

2.1.4. Etiopathogenesis

The pathophysiology of vitiligo has been the subject of numerous theories. All of the clinical and experimental observations made on this disorder cannot be fully explained by any of these theories. The predominant theories are:

A. Autoimmunity theory
B. Neurological theory
C. Self-destruction/ self-slaughter theory
D. Combination of 1, 2, and 3

A. Autoimmunity theory

The autoimmunity theory in vitiligo posits that the condition's etiology and pathogenesis are primarily driven by an autoimmune response. In cases of vitiligo, particularly the 'generalized' or nonsegmental subtype, the immune system is thought to mistakenly target and attack melanocytes, leading to their destruction. This autoimmune attack on melanin cells is often related to the presence of autoimmune comorbidities, further supports the role of immune dysregulation in the development of vitiligo. Additionally, the consistent positive responses observed with immunosuppressive therapy underscore the influence of autoimmune mechanisms in the manifestation of this skin disorder (53).

The role of humoral immunity

One of the aspects of immune dysregulation in vitiligo is the role of humoral immunity, which involves the production of antibodies by B cells. Antibodies are specialized proteins that selectively attach to distinct antigens, whether they be foreign entities or self-antigens, facilitating their targeted elimination by other components of the immune system. In vitiligo, some studies have reported the presence of autoantibodies against melanocyte antigens, such as tyrosinase, tyrosinase-related protein 1, and gp100 (54). These autoantibodies may contribute to the damage of melanocytes by activating complement-mediated cytotoxicity, antibody-dependent cellular cytotoxicity, or opsonization (55).

Patients with active forms of vitiligo exhibit the presence of antibodies against melanocytes, specifically immunoglobulin G (IgG) and immunoglobulin M (IgM), in 80% of cases. Conversely, the inactive forms and control groups demonstrated low levels of immunoglobulin (56). Anti-thyroglobulin antibodies, anti-thyroid antibodies, anti-thyroperoxidase antibodies, and anti-smooth muscle antibodies are also present. These are commonly associated with thyroid disease and other autoimmune disorders (43).

The contribution of Cell-mediated immunity

An analysis using immunohistochemistry to study inflammatory infiltrates in the skin surrounding vitiligo lesions demonstrated that normal skin exhibits higher melanocyte densities than unaffected skin in vitiligo patients. This analysis involves single and double immunostaining for melanocytes, Langerhans cells, T-cells, and macrophages. These T cells have a much higher CD8 to CD4 ratio. Therefore, cytotoxic CD8 T-cells may be a factor in the death of melanocytes (53). These T cells had a much higher CD8 to CD4 ratio. Therefore, cytotoxic CD8 T-cells may be a factor in the death of melanocytes. All vitiligo patients had perilesional HLA-DR production, especially along supra-basal and basal keratinocytes, as a result of local T cell reactivity. Additionally, macrophages were more common in vitiligo than in controls, and the vitiligo-specific CD36 subset of macrophages was more common in vitiligo (58).

The contribution of cytokines in vitiligo

Cytokines are molecules that regulate the immune system and inflammation. They play a crucial role in the development of vitiligo, a skin disorder that causes depigmentation of the skin due to the loss of melanocytes. There are different types of cytokines that are involved in vitiligo, such as Innate pro-inflammatory cytokines, such as interleukin (IL), and tumor necrosis factor (TNF)-α. These cytokines are formed by various cells, such as keratinocytes, macrophages, and dendritic cells, and they activate the adaptive immune response against melanocytes. The sera and tissues of 30 vitiligo patients and 20 healthy patients were compared, and the results showed that the vitiligo patients had considerably higher levels of interleukins throughout their illness (53).

B. Neurological hypothesis

According to Lerner's "Neural Theory," an increase in the release of a certain chemical (like melatonin) from peripheral nerve endings in the skin causes depigmentation in vitiligo. This chemical lessens pigment and prevents the production of fresh melanin. As per Lerner's findings, segmental vitiligo often exhibited a distinct

dermatomal pattern, and areas affected by vitiliginous lesions were observed to display increased sweat production in resting. He also found that 30% of the 128 vitiligo patients in his study reported significant psychological stress before the onset of vitiligo, and a further 39% blamed anxiety, accidents, illnesses, surgeries, or births for the disease's onset. Overall, 69% of patients claimed that stress was the cause of their vitiligo's onset (55). To ascertain the link between stress and the start of vitiligo, Manolache and Benea conducted case-control research with 32 vitiligo patients, 45 alopecia areata patients, and controls who had skin conditions that were not related to stress (such as infections). Data from patients with vitiligo and alopecia areata were independently analyzed. The onset or worsening of vitiligo was associated with stressful events in 65% of the patients, while only 21% of the controls who were matched by age and gender had the same experience. Most vitiligo patients said that their main sources of stress were related to their personal and pecuniary matters (60).

Overall, the research offers proof that a traumatic life event could be a factor in the development or beginning of vitiligo (60). Koga & Tango described the vitiligo clinical symptoms in 480 patients and developed a set of classifications for the condition based on their results. Halo-nevi, the Koebner phenomenon, and autoimmune are associated with type A vitiligo. It can develop at any age and moves forward continually with intervals of remission and exacerbation. On the other hand, type B vitiligo appears earlier, spreads quickly for a short while, and then goes away. The neurological hypothesis is particularly relevant for Type B vitiligo, which spreads throughout the dermatomal area that is afflicted (52). An additional classification that is pertinent to the neurological theory is segmental vitiligo, in which lesions develop in the distribution or "segment" of one or more nerves, albeit they may not always impact the entire segmental region (59).

C. Self-destruction hypothesis

This hypothesis contends that melanocytes are poisoned by the antecedents and byproducts of melanogenesis. Lerner claims that melanocytes contain an internal defense mechanism that gets rid of harmful free radicals and melanin precursors such

as dopa, dopachrome, and 5.6 dihydroxy indoles (57). This pathway may be impaired in vitiligo, leading to an accumulation of free radicals and indoles that damage melanocytes (61).

This concept is supported by clinical evidence showing that hydroquinone derivatives, such as mono benzyl ether of hydroquinone, can cause chemical leukoderma. These substances most likely prevent melanin from being produced normally, which causes hazardous intermediates to be produced excessively or to seep into the cytoplasm of melanocytes, finally leading to cell death (62,63). Additionally, after UV exposure, vitiligo is more common in hyperpigmented skin regions, demonstrating a link between greater melanogenesis and a higher chance of developing vitiligo (63). Furthermore, there is proof that melatonin receptor stimulation alters melanogenesis and ultimately leads to the apoptosis of all melanocytes (64). Schallreuter's group has contributed to a more comprehensive understanding of the neural and self-destructive pathophysiology of vitiligo through their research (65). They proposed that faulty protein homeostasis is a key factor in the degeneration of melanocytes. Tetrahydrobiopterin is a crucial cofactor for phenylalanine hydroxylase's conversion of phenylalanine to tyrosine. Due to impaired tetrahydrobiopterin recycling and increased monoamine oxidase activity in the afflicted epidermis, hydrogen peroxide levels are high, which inactivates the detoxifying enzyme catalase (66). Melanocytes may be destroyed in the lesional epidermis of vitiligo patients because of an accumulation of cytotoxic breakdown products of pterin homeostasis, an increase in hydrogen peroxide concentration, and a decrease in catalase levels. In addition, chronic vitiligo patients' serum levels of glutathione peroxidase, an enzyme involved in the breakdown of hydrogen peroxide, were lower than those of healthy controls. These findings serve as the foundation for the innovative topical pseudo-catalase therapy (67). Compounds including ubiquinone, vitamin E, selenium, and methionine that raise the amount of the circulating antioxidant pool and, as a result, the epidermal antioxidant pool, may be beneficial to patients with active vitiligo. The usefulness of antioxidants is currently being researched (68).

D. Combination of A, B, and C

It has been suggested that a combined theory is more applicable in etiology than a single theory. Additionally, the fact that patients display a variety of clinical symptoms and give different illness beginning histories shows that different people may have different vitiligo aetiologies. According to the "convergence theory" proposed by Le Poole et al. in 1993, factors such as stress, the buildup of toxic substances, infections, autoimmune, mutations, changed cellular environments, and decreased melanocyte migration and/or proliferation can all aid in the vitiligo phenomena (57).

The knowledge about the pathophysiology of vitiligo is growing quickly. New questions about the mystery have also been raised by the identification of novel pathogenic processes. The depletion of melanocytes in the hair and epidermis may be caused by a variety of other endogenous and external factors, even though the autoimmune hypothesis is supported by the majority of studies. These discoveries open up new directions for the future creation of treatment plans for this condition.

2.1.5. Diagnosis

In its early stages, vitiligo can seem like many other disorders. Patients are categorized as having segmental or nonsegmental vitiligo based on the specified criteria (**Table 1**) (69). A practical clinical strategy is to categorize them according to the extent of the lesions, the pattern of the lesions, and the level of pigment loss. Additional clinical differentiation is possible due to additional morphologic indicators such as secondary epidermis and dermis. Wood's light proves valuable in distinguishing between depigmented and hypopigmented lesions (70). Wood's light is a kind of long-wave UV radiation that is released from a mercury arc lamp under high pressure after going through a compound filter made of barium silicate and 9% nickel oxide. The majority of Wood's light is reflected in depigmented lesions because epidermal melanin is unable to absorb it due to the lack of melanocytes. Furthermore, a hole is made for dermal collagen's autofluorescence, which releases a slender blue light band. Depigmented lesions appear as brilliant bluish-white areas under Wood's light (70). In

a dark environment, this tool is useful for differentiating hypopigmented disorders that do not accentuate established vitiligo (depigmented) (71). When assessing vitiligo in people with pale skin, when the lesion and its borders may be hard to see, Wood's light is very helpful (70).

Patients are classified based on criteria predetermined individuals who fulfilled all the necessary criteria and met one or more of the supplementary criteria were categorized as having segmental vitiligo, who did not meet the specified criteria were categorized as having nonsegmental vitiligo.

Table 1: The Predetermined clinical guidelines for diagnosing segmental vitiligo

Requisite criteria (major)

- Pigment loss in specific areas that develop on one side of the body without extending across the midline or with a minimal overlap onto the opposite side.
- These depigmented patches are confined to distinct body regions
- They exhibit identifiable patterns, such as blaschkoid, dermatomal, phylloid, checkerboard, linear/oblong, or other specific varieties.

Additional/Supplementary criteria (minimal)

- Onset occurring before the age of 15 years.
- More than 50 percent of white or depigmented hair within the affected area, extending beyond its boundaries.
- Existence of normal or darker pigmented areas within the affected region or segment without any treatment.
- Boundary irregularity or a straight line account for more than 50 percent of the lesion.
- Stability in disease progression attained within 1 year

2.1.6. Treatment modalities

Various therapies are available for vitiligo(68–70). Vitiligo patients have a range of treatment options available, such as topical corticosteroids, oral and topical psoralens in combination with ultraviolet A (PUVA), and narrow-band UVB radiation (74). Different treatment options have emerged, including narrow-band UV-B phototherapy, topical immunomodulators, targeted light therapy, and calcipotriol combined with UV light (75). There are advantages and disadvantages to all of these treatment methods, and not all modalities are suitable for everyone with vitiligo.

Vitiligo is a cryptogenic dermatological disorder characterized by pigment loss and with no definite therapy (72). Vitiligo treatment aims to repigment the lesions and stabilize the depigmenting process. As a result of repigmentation, the skin appears more cosmetically appealing and is more likely to tolerate sunburns (72). Due to the sluggish and slow response of melanocytes to current therapy methods, it is usually necessary to continue treatment for six to twelve months to achieve an optimal response. The treatment option is determined by the patient's age and clinical type (72).

2.1.6.1. Topical or systemic therapies

Corticosteroids

In 1959, Tsukada released the initial research paper on corticosteroid use in treating vitiligo. By administering corticosteroid injections directly into the affected areas, the researcher noticed the repigmentation of the skin (76). Topical steroids work best for lesions on the face, elbows, and knees, but they have limited effectiveness on the extremities farthest from the body. Several factors affect repigmentation rates at different anatomical sites. These factors encompass the movement of remaining melanocytes from unaffected skin, skin permeability, the potential recovery of damaged melanocytes, and, notably, the preservation and concentration of follicular reservoirs (77). In 1977, Bleehen conducted a study involving 20 vitiligo patients, where they

were treated with 0.1% betamethasone valerate or 0.05% clobetasol propionate creams in specific areas, along with placebos in similar control areas. The authors concluded that the application of topical corticosteroids for vitiligo treatment has the potential to induce skin repigmentation (78).

Systemic corticosteroids may arrest vitiligo progression and restore pigmentation. Low-dose oral prednisolone (0.3 mg/kg body weight) is a successful treatment for rapidly spreading vitiligo and does not lead to severe side effects (79). Betamethasone/dexamethasone (5 mg) oral mini-pulse therapy appears to arrest vitiligo progression and trigger spontaneous repigmentation (80). The exact mechanism of corticosteroids in vitiligo is unknown. A common belief is that corticosteroids inhibit the inflammatory processes seen in lesions that are active and developing (81). Topical corticosteroids cause hypertrichosis, skin atrophy, striae, telangiectasia, and acne-form eruption (82). On administration of oral corticosteroids in vitiligo, the following side effects have been documented: Cushing syndrome, irregular menstruation, weight gain, abdominal pain, increased appetite, dizziness, gastrointestinal distress, diarrhea, and frequent urination. These adverse effects are transient and mild (83).

Calcineurin inhibitors

Vitiligo is commonly treated with topical corticosteroids, but their side effects can become problematic if used for an extended period. Tacrolimus and pimecrolimus are topical immunomodulators. They inhibit calcineurin's activity, preventing T-cell activation and releasing inflammatory cytokines. There is promising evidence supporting the efficacy of both tacrolimus and pimecrolimus in the treatment of various inflammatory and immunologic skin conditions, including vitiligo (84). A minimum of 6 months of application twice daily on the face and neck is recommended for best results (85). Tacrolimus 0.03% ointment is advised for use on children under 16 years old due to being associated with hyperpigmentation and hypertrichosis in the targeted area. The results of tacrolimus 0.03% were similar to those of tacrolimus ointment 0.1% when used in adult patients (84). Topical calcineurin inhibitors may result in pruritus,

hyperesthesia, burning sensations, and an increased risk of infections such as herpes simplex and molluscum contagiosum (86).

Basic fibroblast growth factor-derived peptide (bFGF)

A lack of basic fibroblast growth factor (bFGF) has been linked to Melanocyte homeostasis (87). In lesional skin, bFGF mRNA levels are significantly lower, possibly related to depigmentation. bFGF provides an efficient therapeutic target by stimulating melanocytes from nearby hair follicles and functioning as a chemotactic agent to draw additional melanocytes to the lesional site (86). Using novel topical modalities like bFGF (a melanocyte mitogen) and related decapeptides has been shown to provide therapeutic benefits by re-pigmenting vitiligo lesions. The first step in managing vitiligo is stabilizing the disease process. Later, the focus switches to melanocyte stimulation to stimulate patch repigmentation (88). It's advisable to apply it before bed and spend 10 minutes in the morning sunlight. It has a mild side effect profile and is safe for children and adults (86).

Vitamin D3 analogue

Melanocytes and keratinocytes are significantly affected by vitamin D. According to in vitro studies, vitamin D3 stimulates tyrosinase activity and melanogenesis (89), which may result in the repigmentation of skin lesions in vitiligo. Vitamin D analogs like calcipotriol and tacalcitol also induce repigmentation in vitiligo patients (90,91). These compounds are applied directly to the skin and are often used alongside phototherapy. A combination of betamethasone 0.05% and calcipotriene 0.005% is safe for application on up to 30% of the body surface area, with a maximum weekly dosage of 100 grams. Creams and solutions can be used for a maximum of eight weeks, while ointments can be used for up to four weeks. Overall, topical D3 analogs are considered safe for both children and adults and the only reported side effect is typically mild skin irritation (86).

2.1.6.2. Phototherapy

UV therapy

Patients with more extensive vitiligo are usually recommended phototherapy because it exposes the entire body. When vitiligo affects over 10-20% of the skin, the recommended initial treatment includes both UVB and UVA therapies (92). In a comprehensive meta-analysis, which examined 35 studies involving 1,428 patients, it was observed that mild response to narrowband UV-B phototherapy occurred in 74% of cases at 6 months and 75% after 12 months. Furthermore, a significant response was achieved by 19% of patients at 6 months, increasing to 36% at the 12-month assessment (93). Based on Arca et al. study (94), marked/complete repigmentation rates were 41.6%, moderate repigmentation rates were 37.5%, and minimal repigmentation rates were 20.0%. In another study, it was discovered that 53% of children achieved a repigmentation of at least 75%, with 6% of them achieving complete repigmentation, following NBUVB treatment (95). Topical agents, such as corticosteroids, calcineurin inhibitors, pseudo catalase, and vitamin D analogs, have been used with NBUVB therapy (96).

Psoralen plus UV-A (PUVA)

Psoralen photochemotherapy combines the chemical compound psoralen, which makes cells more sensitive to ultraviolet light. This produces a beneficial result that would not be possible with either alone. Psoralen is a furocoumarin compound that absorbs solar energy (97). The precise way in which PUVA therapy triggers repigmentation in vitiligo lesions remains unclear. PUVA prompts melanocytes at the edges of vitiligo-affected areas and those within the outer root sheath of hair follicles to enlarge, multiply, and exhibit enzyme activity (98).

PUVA therapy can be administered either topically or systemically. Topical PUVA is suitable for patients above the age of two with localized vitiligo. However, it is not recommended for treating vitiligo that affects less than 20% of the total body

surface area (99,100). In cases of extensive vitiligo, oral PUVA therapy is used whenever topical psoralen application is not feasible (99). In the treatment of this condition, 8-methoxy psoralen is typically ingested 90 to 120 minutes before exposure to UVA light, with a dose of 0.5 mg per kilogram of body weight. Alternatively, equivalent quantities of 5-methoxy psoralen or trimethyl psoralen can be used. PUVA therapy should be suspended if patients experience excessive or intense pruritus, erythema, blisters, and edema (99). Possible adverse reactions comprise blistering, burning sensations, excessive erythema, cataract formation, itching, xerosis, fatigue, nausea, stomach discomfort, potential cancer risk, and the natural aging process (99,100).

Phenylalanine plus UVA

Vitiligo has been treated well with phenylalanine and ultraviolet A exposure (PA-UVA) since 1983. L-phenylalanine can be administered orally or topically (101). L-phenylalanine is administered at a dose of 100 mg/kg body weight 1.5–2 hours prior to exposure to UVA or sunlight. Reducing the dose to 50 mg/kg body weight is recommended if the patient experiences nausea after ingestion (102). In order to evaluate the efficacy of oral and topical treatments for vitiligo, 10 patients applied a cream containing 10% L-phenylalanine to the vitiligo patches, whereas 21 patients received oral L-phenylalanine at a dose of 100 mg/kg along with UVA radiation. The second group showed the best outcomes, and neither group experienced any negative effects (101). Combining L-phenylalanine with UVA resulted in 75% positive results, resulting in 30-60% pigmentation, whereas placebo or placebo plus UVA did not produce positive results (103).

A retrospective analysis of 25 patients who had undergone PA-UVA therapy for about five years revealed that 64 percent of the patients had permanent depigmentation and 44 percent had permanent repigmentation. No patient had documented long-term negative effects (104).

Laser Therapy

As one of the advanced light technologies utilised in dermatology (101), Using xenon and chloride (XeCl) together, monochromatic excimer light (MEL, 308 nm) is created. Excimer lasers, which target afflicted skin with coherent light, and excimer lamps, which treat a larger region of skin with nondirectional monochromatic light, are the two primary types of MEL devices. It is unknown how MEL works in vitiligo. Like NB-UVB, MEL may suppress and modify immunological responses to aid in repigmentation, stabilisation, and disease maintenance (105).

When compared to narrow-band UVB phototherapy, 308 nm MEL is a more effective therapy for vitiligo due to its quicker skin repigmentation, shorter treatment periods, and improved patient compliance. Hong et al. conducted a controlled trial on eight patients, using NB-UVB twice a week for up to 20 sessions in addition to excimer laser therapy. Between lasers and NB-UVB, there was a statistically significant difference (106,107)

2.1.6.3. Surgical Therapies

Patients with stable vitiligo who resist conventional medical approaches can benefit from surgical interventions. Vitiligo can be treated surgically with the following methods (108):

Punch grafting

Several motorized punch grafting devices have been introduced in recent years, making the procedure more convenient and cost-effective with improved outcomes. Mini grafting, or miniature punch grafting, is the most straightforward and least expensive procedure for treating vitiligo. There can be punches as small as one mm and as large as two mm, spaced 5-10 mm apart on the recipient's skin. In this procedure, circular pieces of skin tissue are transferred from the donor area into pits on the

recipient's skin that are similar in shape to those on the donor (109). This procedure has the highest risk of side effects. Cobblestone appearance, polka dot appearance, graft depigmentation, per graft halo, and graft rejection are all potential side effects (109).

Suction blister grafting

Epidermal grafts are taken from induced blisters at the donor site, typically the buttock or thigh (86). The suction creates fragile skin grafts by splitting the dermo-epidermal junction. Derm-abraded recipient skin is then covered with these thin grafts. There is very little chance of scarring at the recipient or donor site following suction blister grafting (110). Suction blister grafting works particularly well on lips and areolae. This procedure has two main disadvantages: it is time-consuming and can only treat a limited area of skin in one session (109).

Split-thickness skin grafting

This tissue-grafting technique is another option for treating vitiligo that provides sound, cosmetically acceptable repigmentation at the recipient site without leaving a significant scar behind. Furthermore, the procedure is simple and can be completed in one session for a large area. Split-thickness skin grafting's only limitation is the need for a properly trained practitioner since the quality of the grafts influences the overall results obtained (111).

Non-cultured epidermal cell suspension

A split-thickness skin graft involves separating the different components of the cells. This method applies a mixture of epidermal keratinocytes and melanocytes to a derm-abraded recipient area (112). An advantage of this procedure over tissue grafting techniques is the ability to treat a relatively large area in a single session. Typically, this is accomplished with a much smaller donor graft (109).

Cultured melanocyte transplantation

The method involves isolating and culturing melanocytes from normal human skin. The cells are then transplanted into the recipient's vitiliginous area. As a result, we can cover large vitiliginous areas using only a tiny donor skin, unlike the non-culture method, which covers a smaller area (119). One of the most prominent advantages of the procedure is its ability to treat a large area in a single session. (109). The management pathway for people with vitiligo is shown in **Figure 2.**

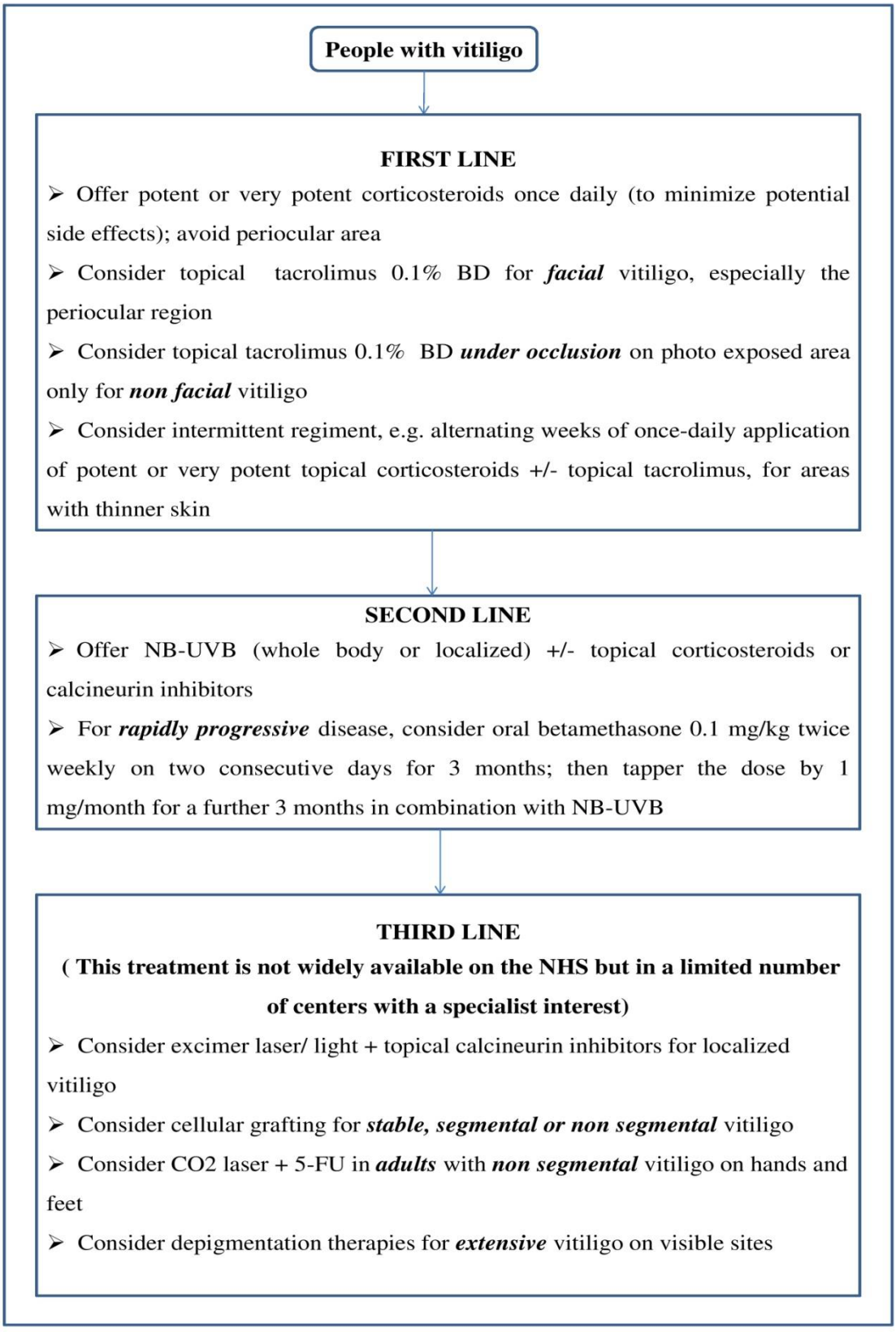

Figure 2: Management pathway for people with vitiligo.
5-FU - 5-fluorouracil; BD - twice daily; NB-UVB - narrowband ultraviolet B.

2.2. Herbal Therapy in vitiligo

Various therapeutic options for the management of vitiligo are corticosteroids, immunomodulators, phototherapy (UVB), photochemotherapy (PUVA), and surgery. These conventional therapies have several limitations in terms of success rate, cost of therapy, and ADRs. Treatment with PUVA increases the risk of skin cancer, corticosteroids induce skin atrophy, and UVB therapy is associated with skin boils (114,115). For the treatment of vitiligo, topical corticosteroids are recommended as first-line therapy (116). Tacrolimus or Pimecrolimus are excellent immunomodulators for patients with minor depigmentation, notably on the face and neck (117,118). When vitiligo is severe, rapidly spreading, or does not respond to topical treatment, phototherapy alone or in combination with it is the basis of therapy. For isolated, stable lesions that have not responded to prior treatments, surgery is an effective option. The low benefit-to-risk ratios of the current therapeutic approaches have led to the search for safe and effective alternative therapies (119).

In clinical and preclinical studies, herbal drugs have been reported to promote melanin synthesis and prevent its damage (120–123). Herbal drugs are thought to be relatively safe, reliable, easy to access, and affordable to the general public (124). For thousands of years, herbal drugs have been widely used for the management of many skin diseases such as acne, alopecia, dermatitis, herpes simplex, herpes zoster, pruritus, psoriasis, scabies, skin cancer, wounds, burns, as well as vitiligo (125). Herbal products shown to have valid therapeutic effects in the treatment of vitiligo are ginkgo biloba, khellin, Cucumis melo, green tea polyphenols, capsaicin, and picrorhizakurroa (126). Some of the herbal plants used in the treatment of vitiligo are shown in **Figure 3.**

Figure 3. Photographs of herbal plants used in the treatment of vitiligo
Ginkgo biloba L. (b) Nigella sativa L. (c) Turmeric
(d) Cucumis melo (e) Polypodium Leucotomos (f) Picrorhizakurroa
(g) Ammi visnaga (h) Psoralea corylifolia L.

2.2.1. Ginkgo biloba

Ginkgo biloba is widely used in medicine as an anti-aging, antioxidant, moisturizing, and soothing agent. It is used in the treatment of brain disorders, circulatory problems, respiratory disorders, and many other dermatological diseases such as acne, psoriasis, dermatitis, and eczema (127). It contains flavone glycosides and terpene lactones. Ginkgo biloba prevents oxidative stress and having anti-inflammatory and immunomodulatory properties. These mechanisms probably play role in the treatment of vitiligo. Its antioxidant effect is valuable in the treatment of vitiligo and other free radical-induced disorders (128). Many studies reported that this herb controls the spread of vitiligo as well as induced re-pigmentation (120,128–130).

In a clinical trial study, 12 vitiligo patients were treated with Ginkgo biloba capsule 60 mg two times daily for 3 months (130). This study reported poor treatment outcomes in which 25% of patients achieved 30% re-pigmentation. Mild watery diarrhea was experienced by one patient. Treatment response was improved (50% re-pigmentation) by prolonging the duration of therapy to 6 months (128). In this study, ginkgo was used at a dose of 40 mg thrice daily in 52 patients. Mild nausea was developed in 2 patients (128). Another study was carried out by Abu Raghif et al. by administering 75 mg of ginkgo twice daily for 2 months (131). No difference in treatment outcome over placebo was observed.

2.2.2. Nigella sativa

Nigella sativa belongs to the family of *Ranunculaceae* and can be found all over the globe. It has tapering green leaves and rosaceous white and purplish flowers. Thymoquinone is the main component of the seed that has antioxidant properties. It also strengthens the immune system (132). Nigella sativa was found to be effective in the disorders of respiratory, digestive, kidney, liver, cardiovascular, and immune systems. Nigella sativa oil is well-tolerated, safe, and efficacious in the treatment of vitiligo (133). A clinical trial study was conducted by Sarac et al., in which 33 patients received nigella sativa twice daily for 6 months. Re-pigmentation was observed in more than 50% of the area in the face, hands, and genital regions and none of the patients developed any adverse reactions (133).

2.2.3. Turmeric

Turmeric is a rhizomatous plant of the family Zingiberaceae. Turmeric has anti-inflammatory, antioxidant as well and anti-cell proliferation actions. It is effective in a wide variety of conditions such as diseases of the skin, respiratory tract, joints, and digestive system. It is also promoted as a dietary supplement (134). Turmeric can suppress the excessive production of TNF-alpha and block the TNF-dependent activation of NF-kB (135,136). Despite widespread application in many diseases, only one study is available for vitiligo. In this study, 30 vitiligo patients received treatment with turmeric cream twice daily for 4 months and showed a good result by significantly

decreasing the size of the lesions on the affected part of the body when compared to placebo (134).

2.2.4. Polypodium Leucotomos

It is also known as Calaguana. It belongs to the family of *Polypodiaceae*. It's used for the treatment of psoriasis, atopic dermatitis, and vitiligo. It is also effective in the prevention of sunburn, and squamous cell carcinoma (137,138). It also exhibits antioxidant property and thus prevents lipid peroxidation. It also inhibits the synthesis of IL-2, IFN-γ, and TNF- α, and increases the synthesis of IL-10 thus producing immunomodulatory effects (139,140). These mechanisms are probably playing role in vitiligo.

Middelkamp-Hup et al. performed a RCT to see if the antioxidative and immunomodulatory effect of Polypodium leucotomos improves NB-UVB-induced re-pigmentation in vitiligo patients (141). A total of 50 vitiligo patients randomly received 250mg oral *P. leucotomos* or placebo thrice daily, in combination with NB-UVB two times weekly for 25 – 26 weeks. Increased re-pigmentation was observed when phototherapy was administered in combination with oral *P. leucotomos*. Itching, dryness of the skin, and gastrointestinal upset were common adverse events reported in the study. In another study, a combination of PUVA + polypodium leucotomos 720 mg once daily for 3 months was administered to 19 vitiligo patients, whereas patients in the other arm were treated with PUVA + placebo in the same dose and duration. Re-pigmentation was more prominent in the Polypodium leucotomos treated group than placebo (142).

2.2.5. Picrorhizakurroa

picrorhizakurroa is also known as "kutki". Because of its efficacy in hepatic and respiratory problems, it is well-known in conventional medicine (143). It is also used to treat fever, dyspepsia, diarrhea, scorpion bite indigestion, fever, and food poisoning. Currently, this plant is in danger of extinction due to unregulated and excessive harvesting (144). Oral administration of picrorhizakurroa in combination with methoxsalen was found to be useful in vitiligo. An RCT by Bedi et al. administered

picrorhizakurroa (200 mg) capsule in combination with methoxsalen (0.75%) two times daily for 7 months in 30 vitiligo patients (144). Results revealed that 26.6% of patients were completely cured with a progress score of +4, whereas 53.3% showed a rapid and continuous reduction of patches with a progress score of +3.42 Erythema, itching, and pruritis were experienced by 16 patients. No serious toxicities were observed (144).

2.2.6. Khellin

Khellin is a furanochromone, obtained from the plant *Ammivisnaga*. It is effective in the treatment of renal stones, coronary diseases, asthma, vitiligo, and psoriasis (145). The clear mechanism of action of khellin in vitiligo is unknown. It is proposed to work by reducing the melanocyte antigens and Langerhans cells and thus inhibits the progression of antibody-dependent cell-mediated cytotoxicity against the melanocytes (146). Liver dysfunction and allergic reaction are the major drawbacks associated with this therapy. Hence, analogs of khellin with better safety and effectiveness profiles were developed in the last decade for the treatment of vitiligo. Khellin can be administered either systemically or topically (147).

A recent RCT study successfully used khellin topically in association with monochromatic excimer light 308 nm (144). Excellent response (>75%) was achieved in approximately half of the studied population. Treatment response was further improved upon the addition of antioxidant therapy (vitamin-E) to topical khellin and excimer light in which 76-100% re-pigmentation was observed in more than half of the studied patients and none of the patients developed any serious toxicities (148).

Two different studies reported good treatment response with minimal adverse effects when khellin was given with UV therapy in various doses and duration (149,150). In a retrospective study, khellin 100mg was administered orally in combination with UVA therapy in 28 vitiligo patients (149). Forty-one percent of patients reported 70% re-pigmentation after receiving 3 months of therapy. No serious toxicity was reported however, nausea was experienced by one-third of patients. No actinic damage or skin cancer was observed up to 9.2 years of follow-up (mean 3.3 years). Another similar observation was also reported by Ortel et al., in which UVA phototherapy thrice weekly in combination with oral (n = 25) or topical (n = 3) khellin

was given in 28 patients. At least 70% or higher re-pigmentation was achieved among 41% of patients after 6 months of therapy (149).

In another study, 60 patients received treatment with 100 mg of khellin or a placebo, along with natural sunlight exposure given daily for 15 minutes (147). After 4 months, 16.6% of patients had 90–100% re-pigmentation, and 23.3% showed 50–60% re-pigmentation. No re-pigmentation was reported in the control group. Khellin was also tried in combination with phenylalanine and UVA/UVB therapy for 12 months, re-pigmentation of 50-100% was observed in 72% of treated locations (150).

A clinical trial study was done using a triple combination of khellin (1%) gel + WPG + UVA thrice weekly for 6 months (117). Whereas, patients in the other arm were treated with a topical gel containing only WPG + UVA for the same frequency and duration. Excellent re-pigmentation was observed in the khellin-containing triple combination regimen.

2.2.7. Psoralea corylifolia

Psoralea corylifolia, also known as Babchi, is a well-known herb that has been used for centuries to treat leukoderma, psoriasis, and vitiligo (152). This plant's chemoprotective, antioxidant, antimicrobial, and anti-inflammatory properties actions are also being studied pharmacologically (153). A significant reduction in patch diameter was noted when Psoralea corylifolia (10% w/w) was given along with sunlight exposure for 3 months. Similarly, a complete facial re-pigmentation was observed when Psoralea corylifolia oral and topical form in combination with daily sunlight exposure was given daily for 6 months (154).

2.2.8. Other herbs

Cucumbers (*Cucumis sativus*) contain antioxidants as well as free radical scavenging properties. The presence of carotenoids, phenolic flavonoids, tannins, polyphenols, and lycopene contributes to its antioxidant activity. Cucumber juice can help to improve skin texture, and treat skin infections, and eczema (155). According to Liu Z et al., rubbing vitiligo lesion areas with sulfur powder adhered to fresh cucumber

slices provided significant benefits (156). Sonchus oleraceus is an herbal plant of the *Asteraceae* family, a natural source of antioxidants, and is rich in vitamins A, D, and E(157). An infusion of S. oleraceus causes the pigmentation of white spots in patients with vitiligo(157). Resende et al. studied 12 vitiligo patients using an oral infusion of leaves extract of *Solanum paniculatum, Jacaranda brasiliensis, and Sonchus oleraceus* (800ml) OD for 12 months and observed re-pigmentation on the left foot, knee, elbows, and lips (158). Zouhir Djerrou et al. used a new formulation on a patient suffering from facial vitiligo, containing honey bee, a decoction of dry oat stems, and red onion juice. The formulation is rich with antioxidant components and anti-inflammatory activity and observed complete re-pigmentation on the face after 11 months (159). A summary of the efficacy and safety of herbal therapies in various studies is presented in **Table 2**.

Table 2: Summary of the herbal medications and their combinations used in the treatment of vitiligo

Author, Year of publication, country	Sample Size	Study design	Drugs/Dose/Duration	Assessment tools	Treatment outcomes	Safety Outcomes
Szczurko et al. (2011), Canada (120)	12	Open-label pilot clinical trial	Ginkgo biloba (60mg) capsule, BID for 3 months	VASI and VETF	25% of participants achieved 30% re-pigmentation	Mild watery diarrhoea
Parsad et al. (2003), India (128)	52	Placebo-controlled trial	Group A: Ginkgo biloba (40mg) capsule, TID for 6 months Group B: Placebo, TID for 6 months	Comparison of paper tracings, measurement of the vitiligo patchy areas, and written descriptions	Complete re-pigmentation of the existing lesions in 50% of patients	Mild nausea
Abu-Raghif et al. (2013), Iraq (131)	50	Randomized, single-blind and placebo-	Group A: Ginkgo biloba (75mg) capsule, BID for 2 months	VASI	No difference in VASI between test and placebo group	NM

		controlled trial	Group B: Placebo (sucrose) capsule with food for 2 months			
Sarac et al. (2019), Turkey (133)	33	Clinical trial	Nigella sativa topical cream, BID for 6 months	Digital photography	Re-pigmentation ≥50% was achieved in facial, hand, and genital involvement	No adverse reactions
Ghorbanibirgani et al. (2014), Iran (132)	52	Randomized Double-blind clinical trial	Group A: Nigella sativa oil, BID for 6 months Group B: Fish oil, BID for 6 months	VASI	The average VASI score reduced from 4.98 ± 4.81 to 3.75 ± 3.91 in group A, Where 4.98 ± 4.80 to 4.62 ± 4.36 in group B	No adverse reactions
Deshmukh et al. (2020), India (122)	15	Pilot clinical trial	Vishakalpa (Shwetralepa), BID for 1 month	VETI score	Patchy size was reduced in 26.6% of patients (3mm reduction).	Mild irritation and pustules
Hussain et al. (2016), Pakistan (160)	20	Self-controlled clinical trial	Psoralea corylifolia (10% w/w) ointment, OD + exposed to sunlight for 3 months	Photographs	Reduced white patch diameter and pigmentation from the corner to the center	Mild to moderate irritation

Jalalmanesh et al. (2022), Iran (134)	30	Randomized placebo-controlled trial	Turmeric cream BID for 4 months	VASI, VNS, PGA	Compared with placebo, turmeric cream reduced the size and improved lesions	No adverse reactions
Resende et al. (2015), Brazil (158)	12	Clinical trial	Herbal oral infusion containing- Solanum paniculatum, Jacaranda brasiliensis, Sonchus oleraceus (800ml), OD for 12 months	Photography	Re-pigmentation was observed in left foot, knee, elbows, and mouth lips	No adverse reactions
Djerrou (2015), Algeria (159)	1	A case study	A topical application containing- honey bee, decoction of dry oat stems, and red onion juice, OD for 11months+ Exposure to sunlight for 15–20 min, OD for 11 months, and Citrus lemon fruit juice was used occasionally.	Photography	Complete re-pigmentation on face	No adverse effects
Hussain et al. (2019), Larkana (154)	1	Case study	Psoralea corylifolia (5grams) oral powder, OD for 6 months + Psoralea corylifolia (5%w/w) topical cream,	Photography	Re-pigmentation was started after 15 days. Full facial pigmentation was	No adverse reactions

			OD for 6 months + sun exposure for 2-3 hours, OD for 6 months		observed after 24 weeks of therapy	
Orecchia G et al. (1998), Italy (121)	36	Double blind clinical trial	Group A: Topical gel containing khellin (1%)-WPG+UVA thrice weekly for 6 months Group B: Topical gel containing WPG+UVA thrice weekly for 6 months	Photographs and following criteria: re-pigmentation, >-51% (excellent), 26-50% (good), 11-25% (moderate), <10% (poor), 0 (none)	Re-pigmentation (>l0%) of 86.1% in group A whereas 66.6% in group B	No adverse reactions
Ortel et al. (1988), Austria (149)	28	Clinical trial	Khellin (2%) topical solution+ Khellin oral (100 mg) +UVA (10–15 Joules/cm2) thrice weekly for 18 weeks.	Photographs	Re-pigmentation of >70% was achieved in 41% of patients	Nausea, and mild rise in liver transaminases
De Leeuw et al. (2003), Netherland (150)	74	Clinical trial	Group A: Khellin (0.005%) and phenylalanine topical solution, BID for 12 months+ UVA/UVB one minute daily, 5 times weekly for 12 months	Photographs	Re-pigmentation of 50% to 100% was observed in 72% of treated locations	No adverse reactions

			Group B: UVA/UVB one minute daily, 5 times weekly for 12 months			
Saracenoet al. (2009), Italy (148)	48	Open prospective, controlled study	Group A: MEL 308 nm once-weekly + oral vit. E capsule (400 IU), OD for 3 months Group B: MEL 308 nm once weekly+ khellin (4%) ointment (MEL-K) + oral vit. E capsule (400 IU), OD for 3 months Group C: oral vit. E capsule (400 IU), OD for 3 months	Re-pigmentation was categorized as No re-pigmentation, moderate (<50% lesions healed), good (51– 75% of lesions healed), and excellent (76-100%of lesions healed).	Group I- moderate re-pigmentation in 12.5%, good in 62.5%, and excellent in 25% patients Group II- moderate re-pigmentation in 12.5% patients, good in 31.25%, and excellent in 56.25%, Group III- moderate re-pigmentation in 18.75%, a good in 6.25%, 62.5% patients didn't show re-pigmentation.	Erythema, pain/ burning, perilesional hyperpigmentation, was observed in group A & B No adverse reactions in group C

Valkova et al. (2004), Bulgaria (161)	33	Pilot study	Group A: khellin (5%) topical (emulsion)+ KUVA (12 J/cm2), 3-5 times weekly for 7months Group B: PUVA (1.5 J/cm2), thrice weekly for7 months	Planimetry methods and using criteria of re-pigmentation 90-100% (significant improvement), 60–80% (moderate), 20–50% (slight), no effect (no re-pigmentation)	Significant improvement was observed in 18.7% of the patients treated KUVA and 11.8% with systemic PUVA	No adverse reactions Erythema, with moderate itch, stomach pain, vomiting or dizziness patients from group
De Leeuw et al. (2011), Netherland (162)	19	Double-blind observation study	Khellin (0.005%) BID+ UV therapy thrice weekly	Photographs	A re-pigmentation of 75–100% was achieved in 2 patients, 50–75% in 6 patients	Not mentioned
Fenniche et al. (2017), Tunisia (163)	20	Open label prospective study	Topical khellin + Excimer lamp (308 nm) therapy (250 mJ/cm2) twice weekly for 6 months	Percentage of lesions area re-pigmented grouped as ER (>75%), GR (50%–75%), MR (25%–50%), and PR (<25%)	45% of patients achieved ER, GR in 25% of patients achieved GR	Mild transitory burning and erythema

Abdel-Fattah et al. (1982), Egypt (151)	60	Double-blind clinical study	Group A: Khellin (100mg) tablet, OD for 4 months + Sunlight exposure for 15 minutes Group B: No treatment	Photography	16.6% patients' re-pigment with 90-100%, 23.3% with 50-60%, 36.6% with 25% or less	No adverse reactions
Bedi et al. (1989), India (144)	30	Randomized, placebo-controlled trial	Picrorhizakurroa (200 mg) capsule, BID+ Methoxsalen (10–20 mg) tablet, OD+ methoxsalen (0.75%) lotion, BID for 7 months	Clinical examination of lesions	26.6% of patients were completely cured, 53.3% showed rapid and continuous decreases in the number and size of lesions	Erythema, itching, and pruritus
Asawanonda et al. (2010), Thailand (164)	10	Randomized control trial	Group A: topical tetrahydrocurcuminoid (THC) cream, BD + TNB-UVB (100 mJ/cm2) twice weekly for 3 months Group B: TNB-UVB (100 mJ/cm2) followed by 50 mJ/cm2 increments	Digital photography	90% of the lesions repigmented in group A	Erythema, itching, burning sensation, and hyperpigmentation

			at each session, twice weekly for 3 months			
Middelkamp-Hup et al. (2007), Netherlands (141)	50	Randomized double-blind placebo-controlled trial	Group A: Polypodium leucotomos (250mg) TID+ NB-UVB two times a week for 25-26 weeks Group B: Placebo + NB-UVB (210 and 360 mJ/cm2) two times a week for 25-26 weeks	Photography, Physician Global Assessment (PGA)	Re-pigmentation was observed in 72% of cases in the P. leucotomos group, whereas 43% in the placebo group.	Mild to transient itching and skin dryness
Reyes et al. (2006), Spain (165)	19	Randomized controlled trial	Group A: PUVA + Polypodium leucotomos (720 mg) capsule OD for 3 months Group B: PUVA+ Placebo (720mg) OD for 3 months	Clinical examination	The percentage of subjects with a skin re-pigmentation of >50% was higher in group-A	No adverse reactions
Buggiani et al. (2012), Italy (166)	149	Open observational study	Group A: Re-Pigmenta® gel (Phenylalanine + Cucumis melo extract + acetyl cysteine) TID for 12 weeks.	Photography	Re-pigmentation (>75 %) was seen in 38.4% of Group A, 61.14% of Group B, 73.54% of	Hypertrichosis, skin atrophy, teleangiectasias, experienced by

			Group B: UVB phototherapy once weeklyfor 12 weeks Group C: Pigmenta® gel TID + UVB once weekly for 12 weeks. Group D: Clobetasol propionate (0.05%) TID for 12 weeks		Group C, and 56.24% of Group D patients.	people in group D

VASI-Vitiligo Area Scoring Index; VETF-Vitiligo European Task Force; VNS- Vitiligo Noticeability Scale*;* PGA- Physician Global Assessment; WPG-water/2-propanol/propylene glycol; ER- Excellent Repigmentation; GR-Good Repigmentation; MR- Moderate Repigmentation; PR- Poor Repigmentation; UV-ultraviolet; UVA-ultraviolet A; UVB-ultraviolet B; KUVA-Khellin and UVA; PUVA- psoralen and UVA; NM- Not mentioned; MEL- Monochromatic Excimer Light; NB-UVB-Narrow-band ultraviolet B; TNB-UVB-targeted narrowband UVB phototherapy; TID- three times a day; BID- twice a day; RCT- randomized controlled trial.

2.3. Quality of life in vitiligo

The WHO defines QoL as "individuals' perceptions of their position in life in the context of the culture and value systems in which they live and concerning their goals, expectations, standards, and concerns" (167). The QoL of a patient can be greatly impacted by chronic skin disorders. In addition, the presence of skin lesions also substantially affects the patient's self-confidence, sense of cosmetics, social relationships, and self-esteem (168,169).

The degree of a person's QoL varies greatly depending on the individual and the disorder's natural history; the subject's demographics, including age, gender, location of residence, and origin; their character, personality, and traditions; their situation in life; and those around them and their attitudes in society (170). In order to enhance the standard of care given to patients and to comprehend the impact of the disease on social and everyday life in addition to the therapy given, it is imperative to investigate the QoL in disorders requiring dermatology.

Vitiligo is typically linked to poor mental health, which significantly lowers one's QoL. Those with vitiligo often feel stigmatized as a result of their condition. Patients with vitiligo are typically anxious, despondent, and frustrated. They feel humiliated when they encounter strangers, experience disruptions in their interpersonal relationships in society, or initiate a sexual relationship (171). Although the disease isn't directly harmful to the body, it can be detrimental to the psychological well-being of the subjects. The condition has many mental health issues, including anxiety, stigmatization, depression, lack of confidence, and embarrassment. Suicide attempts have also been documented among vitiligo patients with low QoL(172). This is because they are always in a state of depression due to the disease. Families are frequently negatively impacted by a patient's deplorable condition and social outcomes (172).

2.3.1. Factors that affect QoL in vitiligo

Presence of vitiligo

The presence of vitiligo lesions on the body can significantly impact the QoL for individuals who are affected by the condition. Many people with vitiligo may experience feelings of self-consciousness, embarrassment, and lowered self-esteem due to societal perceptions of beauty (173). The impact on QoL can extend beyond the emotional aspects, as individuals with vitiligo may also face social stigma and discrimination. This could lead to difficulties in forming relationships, both personal and professional (174,175).

Visibility of lesion

Vitiligo on exposed body parts is very noticeable, especially in people with dark skin, and it has emotional and social effects on vitiligo patients (176). A case-control study using the DLQI measured the QOL of people with vitiligo and found that they had more psychological effects and lower QOL due to their visible lesions (177). Patients with lesions on visible body parts, such as the face and extremities, exhibited diminished QOL. This was especially true for patients who believed their appearance was significant (177–181).

Gender

It has been observed that the gender of vitiligo patients also affects their QoL, with females having a lower QoL than males. Females, in general, may give more importance to their physical appearance, and alterations to the skin can have a more pronounced impact on their self-esteem and emotional well-being. The visibility of vitiligo lesions may have a more pronounced impact on social interactions, relationships, and marriage prospects for females compared to males (182,183). As per a survey administered by the DLQI in Pakistan, women with vitiligo experienced negative consequences, especially when the lesions were situated in visible areas of the

body (184). In Iran, a study was conducted on 77 vitiligo patients and found that General and psychological health, social relationships, and sexual activity were more affected by female patients than male patients (185).

Sexual relations

In many studies, vitiligo has been found to negatively affect sexual relations, particularly for patients with lesions in the genital area (179,186,187). In a questionnaire-based survey of 158 people with vitiligo, 108 respondents said the condition had a negative effect on their ability to have physical relationships. These patients felt ashamed of their appearance and avoided contact with new people (178). Despite the study focusing on the effects of vitiligo on sexual relationships, no standardized instrument was used. In addition, the sample size was sufficient. This report compares with the outcomes of a study conducted in Pakistan where no sexual issues were identified among 100 surveyed patients using the DLQI. Because different instruments were utilized in these investigations, making direct comparisons is not feasible. However, the DLQI measures sexual difficulty in vitiligo with a question on sexual relationships(178).

Disease Severity

As the severity of vitiligo increases, the visibility of depigmented patches becomes more pronounced. This visible disfigurement can lead to heightened self-consciousness, social anxiety, and a negative impact on body image, thereby diminishing overall QoL (188–190). In Holland, a study involving 78 individuals with vitiligo who completed the DLQI revealed that a rise in both the severity and extent of their condition was linked to a decrease in their QoL (189). In a study of 100 patients, those with more extensive disease scored higher on the DLQI, indicating poorer QoL (190).

Childhood vitiligo

Young adults who experienced vitiligo from childhood were found to have impaired QoL (191). In a study of 232 young adults, it was found that young adults who had childhood vitiligo with negative experiences had lower QoL in comparison to those who did not undergo negative experiences. In this retrospective assessment, patients were asked about their childhood. Despite the study's focus on negative childhood experiences, there would have been a biased recall.

Duration of disease

According to the research conducted by Tabassum et al., vitiligo patients with a disease duration of five to ten years experienced a greater decline in QoL (192). A study of 119 vitiligo patients in the Netherlands utilizing the DLQI discovered no correlation between disease duration, family history, and QoL (188). A survey of 133 vitiligo patients in Korea using the Skindex-29 revealed contradictory findings (193). The study concluded that a long duration of disease and regular clinic visits have a negative impact on QoL (193).

Marital status

Vitiligo's QoL has also been linked to marital status (179,182). Single people, particularly men, had lower QoL in a study of 158 vitiligo patients (179). In this study, no standardized instruments were used. As opposed to this, an Iranian study that used the DLQI to evaluate 100 vitiligo patients found married women to have less QoL than unmarried women. A comparison was made between the QoL of vitiligo patients who were married and those who were single. Discrepancies in sample size (158 versus 100), variations in culture, and diverse methodologies might account for the differences in the findings (182).

Skin color

Vitiligo patients with darker skin types have worse QoL than those with lighter skin types (171). Study results were based on data from 248 patients who completed Skindex-29 and SF-36 forms. There needed to be more information on how many dark skin patients participated in this cross-sectional study. In addition, darker-colored patients may have suffered from impaired QoL due to more prominent vitiligo spots on their skin (171).

2.3.2. Assessment of QoL in vitiligo

QoL impairments were assessed using the DLQI, VitiQoL, and VIS22 scales. Due to population heterogeneity and assessment methods, there was a wide variation in the proportion of QoL impairment between studies. The summary of studies assessing the QoL in patients with vitiligo is given in **Table 3**.

Dermatology Life Quality Index (DLQI)

The DLQI was the first quality-of-life tool developed in 1994, targeting dermatology. Ninety languages are available for the application, widely used in over 80 countries. A total of 1000 publications have been published based on the DLQI questionnaire, with the majority being multinational studies (194,195).

DLQI has been designed for patients of age over 16 years and is related to six various domains. Listed as follows A DLQI questionnaire is designed for patients over 16. consists of six main domains, related to symptoms and feelings. As this questionnaire is self-explanatory, no detailed instructions are needed so the subject can fill it out without an exhaustive explanation. In the DLQI, there are ten questions, and each has four possible answers. Each answer can be scored from 0 to 3.

The DLQI score is derived by summing up the scores from individual questions, with a maximum score of 30 points and a minimum score of 0. A higher score indicates a greater degree of impairment in QoL (196).

Vitiligo-specific quality-of-life (VitiQoL)

The VitiQoL instrument is comprised of sixteen questions organized into three domains: participation limitations, stigma, and behavior. In the participation limitations domain, participants are asked about their capacity to participate in daily activities, social activities, and recreational activities. As part of the stigma, patients are concerned about embarrassment and what others think of them. Behavior issues include grooming practices and clothing choices affected by vitiligo (197). The item scores for VitiQoL vary between 0 (never) to 6. (all the time). It provides a total score ranging from 0 to 90. In VitiQoL questionnaire question 16, participants report their disease severity level from 0 (no skin involvement) to 6 (most severe) (198).

Vitiligo Impact Scale22 (VIS22)

The VIS-22 is a valid, reliable, responsive vitiligo-specific QoL scale designed to address patient concerns. The VIS-22 questionnaire contains 22 questions that cover a variety of domains, including social interactions (3, 12, 13), self-confidence (5, 18), anxiety (2, 11), depression (6, 9, 10, 14), treatment (7, 15, 16), attitude (questions 1, 4, 17, 19), marriage (20), family (8), school or college (22) and occupation (21). Each question is graded on a scale of 0 to 3. (3: very much, 2: a lot, 1: a little, 0: not at all). The total score ranges from 0 to 66, with higher scores indicating a more significant impact on life (199).

Table 3: Summary of studies assessing quality of life in patients with vitiligo					
Author, year of publication	**Location**	**Population/ Sample size**	**QoL instrument(s)**	**Main findings**	**Reference**
Yang et al. 2022	Taiwan	143	DLQI	About 13.3% of patients had significantly impaired QoL with a DLQI score of >10	(200)
Bassiouny et al. 2021	Egypt	100 (males-56, females-44)	DLQI	Vitiligo affected the QoL of 36% of cases, indicating a large impact.	(201)
Hooshmand et al. 2021	Afghanistan	170	DLQI	In 34.1% of cases, the DLQI score was 10-20, indicating a significant impairment of their QoL.	(202)
Anaba et al. 2020	Nigeria	29	DLQI VitiQoL	QOL was impaired in 96.6% of cases, with mild, moderate, and severe impairments in 27.6%, 24.1%, and 44.8% of cases, respectively.	(203)
Sawant et al. 2019	India	100	DLQI	48% of males and 53% of females had very large to extremely large impairments in their QoL due to vitiligo, indicating the significant impact the disease has on QoL.	(204)
Hammam et al. 2019	Egypt	203 (males-51, females-152)	DLQI	There was an extremely high effect on QoL in 3% of patients with vitiligo, a moderate effect in 32.5%, and no effect in 35% of patients.	(205)

Chen et al. 2019	China	884 (males- 413, females-471)	DLQI	It was reported that 33.3% of patients had small effects, 22.4% had moderate effects, and 18.5% had large to extremely large effects on QoL.	(206)
Kota et al. 2019	India	150 (males-67, females-83)	DLQI	Based on the DLQI, 34.7% of patients had a small effect on QoL, 26% had a moderate effect, 23.3% had a very large effect, and 1.3% had an extremely large effect.	(207)
Dabas et al.2019	India	95	DLQI	The effects on QoL were extremely large in 12%, very large in 34%, moderately large in 24%, and small in 18% of vitiligo patients.	(208)
Chahar et al. 2018	India	54	DLQI	Vitiligo patients' mean DLQI was 8.64±4.32, whereas those with acrofacial vitiligo had a mean DLQI of 11.78±5.61.	(209)
Gül et al. 2017	Turkey	64	DLQI	High QoL impairment was found in 31.2% of vitiligo patients, moderate impairment in 56.9%, and mild impairment in 9.4%.	(210)
Hedayat et al.2016	Iran	173	VitiQoL	The VitiQoL score had a mean and standard deviation of 30.5 ±14.5, indicating a moderate effect on QoL.	(211)
Sangma et al.2015	India	100	DLQI	The DLQI was elevated in 95% of the patients, with very large, moderate, and mild effects in 38%, 38%, and 19%.	(212)

Aradhya et al. 2015	India	300	DLQI	QoL impairment was found to be minimal, mild, moderate, severe, and very severe in 30%, 28%, 15.3%, 21.7%, and 4.7% of patients, respectively.	(213)
Eltahe et al.2015	Egypt	95	DLQI	A small impairment in QoL was found in 13.7% of vitiligo patients, a moderate impairment in 38.9%, a very large impairment in 42.1%, and a very large impairment in 4.2%.	(214)
Mishra et al. 2014	India	100	DLQI	A total of 37% of patients experienced a small impact on their QoL, 21% a moderate impact, and 26% a very large impact.	(215)
Chan et al. 2013	Singapore	222	DLQI	According to the DLQI scores, 35.6%, 38.7% and 25.7% of patients reported that vitiligo had no effect, a small effect and a moderate to extremely large effect on their QoL, respectively.	(216)
Kiprono et al. 2013	Tanzania	88	DLQI	Patients' QoL was moderately affected by the mean DLQI score of 7.2 (SD ± 4.8). 11% of patients had no effect on QoL, whereas 24% had a very large effect.	(217)
Radtke et al. 2009	Germany	1,023	DLQI	It was found that 24.6% of patients with vitiligo had a DLQI score of > 10, indicating significant reductions in QoL.	(183)

In many cases, vitiligo patients are concerned that their disease will worsen, which affects their physical, psychological, social, and environmental well-being (13). Vitiligo is inherently a psychologically distressing condition. Its tendency to manifest in visible areas contributes to a range of psychiatric complications. The visibility of the skin lesions, coupled with the unpredictable nature of their emergence and spread, can evoke adverse emotional responses (13). The physical appearance of people with vitiligo can result in stigmatization and embarrassment, which can lead to decreased self-esteem, depression, and social isolation. (218). Some of the psychological issues that vitiligo patients experience include anxiety, depression, obsessive-compulsive disorder, and suicidal ideation (219). It has been reported that approximately 75% of vitiligo patients have psychiatric disorders (220). According to a meta-analysis, vitiligo patients have a 4.96-fold higher risk of depression than control subjects (26).

Dermatologists often overlook the depressive burden in dermatological patients, resulting in underdiagnosis and undertreatment (221). According to Picardi et al., untreated co-morbid psychiatric disorders may impair the dermatological disorder's response to prescribed therapies. (222). Psychological interventions should be included in treatments for vitiligo patients who are experiencing emotional effects. This may result in better adaptation to the disease and improved QoL. Based on the sample size, study population, and outcome measures, depression prevalence varies significantly in vitiligo patients (223).

One of the most popular mechanisms for vitiligo's depigmentation has been implicated in neuroendocrine dysregulation, which has been linked to the development of depression. High acetylcholine and norepinephrine levels have been hypothesized to play a significant role (224). Psychological stress triggers pigment loss. Catecholamines, released by the hypothalamic-pituitary-adrenal axis in response to psychological stress, bind to and activate receptors in the arterioles of the skin, leading to vasoconstriction, hypoxia, excess production of oxygen free radicals, and finally, death of melanocytes (225). According to Namazi, vitiligo patients who experience depression may benefit from

taking an antidepressant like amitriptyline because of its potent anticholinergic effect and relatively weak norepinephrine reuptake blockade (223).

2.4. Depression in Vitiligo

Depression is a mental health condition marked by hopelessness, emotions of sadness, and diminished interest or participating in activities. It extends beyond typical mood fluctuations and can substantially disrupt an individual's daily life, impairing their social, professional, and personal functioning (226).

The pathogenesis, or the biological mechanisms underlying the development of depression in individuals with vitiligo, is not yet clear and likely involves a combination of genetic, neurobiological, and psychosocial factors. Some studies have suggested that there may be a genetic predisposition to both vitiligo and depression, as they share some common genes that are involved in immune regulation, melanin synthesis, and neurotransmitter metabolism (227). Autoimmune factors Imbalances in neurotransmitters, particularly serotonin and dopamine, are implicated in depression. Chronic stress associated with the visibility of vitiligo and societal reactions may affect these neurotransmitter systems, contributing to depressive symptoms. Chronic stress can also lead to dysregulation of stress hormones like cortisol. Continuous exposure to elevated cortisol levels is associated with mood disorders, including depression (228). There are several assessment tools available to assess or screen for depressive disorders. The explanations for the various tools used for depression are as follows:

Hamilton Depression Rating Scale (HAM-D)

The first antidepressants were evaluated using the HAM-D, which was developed by Max Hamilton, a Leeds University psychiatrist, in the late 1950s (229). The scale became the most widely used tool for measuring the efficacy of antidepressant drugs in clinical trials (230).

The scale was available in two commonly used versions, containing either 17 or 21 items, and is rated on a scale of 0 to 4 points. The initial 17 items gauge the severity of depressive symptoms, with examples including the interviewer's assessment of observed agitation or the impact of mood on an individual's work and leisure activities. The extended 21-point scale includes an additional four items designed to assess factors potentially associated with depression. Scoring is conducted using the 17-item scale, where scores ranging from 0 to 7 are considered normal, 8 to 16 indicate mild depression, 17 to 23 suggest moderate depression, and scores exceeding 24 indicate severe depression. The highest attainable score on the 17-point scale is 52 (231).

Beck Depression Inventory (BDI)

The BDI comprises 21 items that are assessed on a 4-point scale, ranging from 0 (indicating the absence of symptoms) to 3 (representing severe symptoms). While it doesn't evaluate anxiety symptoms, it does cover affective, cognitive, somatic, and vegetative symptoms, aligning with the DSM-IV criteria for major depression. To calculate the score, you sum up the highest ratings across all 21 items, resulting in a minimum score of 0 and a maximum of 63. Higher scores indicate more severe symptoms. In non-clinical populations, scores exceeding 20 suggest the presence of depression. In cases of depression diagnosis, scores in the range of 0 to 13 represent minimal depression, while scores from 14 to 19 indicate mild depression. Scores between 20 to 28 signify moderate depression, and scores falling between 29 and 63 points to severe depression (232).

Self-Rating Depression Scale (SDS)

In clinical settings, the SDS is commonly used to assess the severity of depression. The scale comprises 20 items that are added together to give a range of 20-80 points. A higher score indicates that depressive symptoms are more severe (233). The HADS was developed to evaluate anxiety and depression. The questionnaire can be completed in 2-5 minutes and contains 14 questions in total (7 related to anxiety and 7 related to depression).

Although questions about anxiety and depression are intermixed throughout the questionnaire, they must be scored separately (234).

Center for Epidemiologic Studies Depression Scale (CES-D)

The CES-D scale was created to assess depression experienced in the week preceding the evaluation. It comprises 20 items, with each item scored on a scale from 0 (infrequent or absent) to 3 (most or all of the time). The overall interpretation is that a higher total score suggests an increased likelihood of experiencing depression. The overall score ranges between 0 to 60 (235).

Depression Anxiety Stress Scale (DASS)

The DASS is a popular tool for measuring anxiety, depression, and stress. The scoring system is given 0 to 3 points, where 0 represents non-conformity and three means consistency. The greater the score, the stronger the negative emotions (236). The PHQ is a self-administered diagnostic tool to evaluate mental disorders. The PHQ-9 consists of nine questions with scores ranging from 0 to 27. A threshold of 15 was used to identify probable cases of major depressive disorder (237).

Quick Inventory of Depressive Symptomatology–Self-report (QIDS-SR16)

The QIDS-SR16 was designed to assess depressive Symptoms. The QIDS-SR16 evaluates symptom domains over the previous week. Each item is assigned a score between 0 and 3 points. The range of total scores is 0 to 27(238). Skindex-16 is a questionnaire that has 16 items on a single page. The questionnaire consists of 16 items that measure the impact of anxiety on various aspects of life. There are three categories of items: symptoms (items 1–4), emotions (items 5–11), and functioning (items 12–16). Each item is rated on a seven-point Likert scale ranging from 0 to 6, There are three categories of items: symptoms (items 1–4), emotions (items 5–11), and functioning (items 12–16), with a

seven-point Likert scale ranging from 0 to 6,-where 0 means never bothered and 6 means always bothered (239). Depending on the symptom's severity, type, number, and functional impairment, ICD–10 categorizes clinically significant depression episodes as mild (score 4), moderate (score 5-7), and severe (7+) (237).

General Health Questionnaire (GHQ)

A self-administered screening questionnaire, GHQ, was designed for use in consultation settings to identify individuals with diagnosable mental disorders (Q9 for depression). The GHQ-12 comprises 12 items, each of which rates the intensity of mental illnesses in the last one week on a 4-point scale ranging from 0 to 3. Scores ranged from 0 to 36, with higher scores indicating worsening health conditions (240).

Children's Depression Inventory (CDI)

CDI is a popular tool which contains 27 items used to determine the severity and extent of depressive symptoms in children and adolescents (ages 7-17 years). When the depression scores are added together, the total depression score ranges from 0 to 54. A higher CDI score indicates a more depressive state (241).

Emotional State Questionnaires (ES-Q)

The ES-Q, a validated Estonian version, assessed depression and anxiety symptoms. The ES-Q has 28 items and is graded on a 5-point scale (0–4). Two eight items related to inferiority are hopelessness about the future, self-accusation, loss of interest, sadness, loneliness, inability to be joyful and suicidal thoughts, with a depression cut-off score of 12 (242). The prevalence and assessment tools for depression used in different studies was presented in **Table 4.**

Table 4: Summary of studies assessing prevalence of depression in patients with vitiligo						
Author, year publication	**Location**	**Study design**	**Population/Sample size**	**Depression instrument(s)**	**Main findings**	**Reference**
Abhilasha et al. 2022	India	Case-control	110 (case-55, control-55)	HAM-D	Among vitiligo patients, 76.4% had mild depression, with 16.4% having moderate depression	(243)
Ning et al. 2022	China	Cross-sectional	170 (vitiligo patients)	SDS	Patients had a mean SDS score of 44.05 ± 6.76, which is greater than the Chinese norms of 41.88 ± 10.57	(244)
Nasser et al. 2021	Egypt	Case-control	100 (case-50, control-50)	DASS	Depression was found in 80% of the case group and 10% of the control group.	(227)
Alharbi et al. 2020	Saudi Arabia	Cross-sectional	308 (vitiligo patients)	BDI	Depressive symptoms were reported by 54.5% of patients.	(245)
Hamidizadeh et al. 2020	Iran	Case control	200 (case-100, control-100)	BDI	Moderate and severe depression was observed in 16% and 12% of patients respectively.	(246)
Baidya et al. 2020	India	Case-control	160 (case-80, control-80)	HAM-D	Depression was found to be more prevalent in the vitiligo group (23.75%) than in the control group (6.25%).	(247)

Silpa-archa et al. 2020	Thailand	Cross-sectional	104 (vitiligo patients)	PHQ-9	The prevalence of depression in vitiligo patients was 13.5%.	(248)
Sawant et al. 2019	India	Cross-sectional	100 (vitiligo patients)	BDI	The overall prevalence of depression in vitiligo was 52%	(204)
Kota et al. 2019	India	Cross-sectional	150 (vitiligo patients)	QIDS-SR-16	It was found that 44.7% of all vitiligo patients had depression.	(207)
Sarkar et al. 2018	India	Case-control	122 (case -61, control- 61)	skindex	As compared to a control group (6.65%), vitiligo patients were more likely to suffer from depression (62.29%).	(249)
Vernwal 2017	India	Case-control	200 (case-100, control-100)	HADS	The prevalence of depression among vitiligo patients is 18%	(250)
Karia et al. 2015	India	Case-control	100(case-50, control-50)	HAM-D	The presence of depression was found in 20% of patients.	(251)
Saleki et al. 2015	Iran	Case-control	110 (vitiligo patients)	HDRS	The prevalence of depression was observed in 52.7% of vitiligo patients	(252)
Mufaddel et al. 2014	Sudan	Cross-sectional	210 (case- 105, control-105)	HADS-D & ICD-10 criteria	50% of vitiligo patients had HADS-D scores of 8 or higher, while 8.3% had	(253)

			(case: vitiligo-24, psoriasis-19, Eczema- 16, Acne-20, Other -26)		symptoms that met the ICD-10 criteria for depression.	
Ramakrishna et al. 2014	India	Cross-sectional	53 (vitiligo patients)	HDRS	Major depressive disorder accounted for 56% in vitiligo patients	(254)
Karelson et al. 2013	Estonia (Europe)	Case-control	168 (Case-111, control-57) (case: vitiligo- 54, psoriasis- 57)	ES-Q	According to the scores, 20% of the subjects were depressed.	(242)
Chan et al. 2012	Singapore	Cross-sectional	145 (vitiligo patients)	CES-D	Depressive symptoms were present in 17.2% (n = 25).	(255)
Bilgicet al. 2011	Turkey	Case-control	87 (case-41, control-46)	CDI	The CDI scores of children with vitiligo were higher (23.14 ±12.35) compared to non-vitiligo children (19.24 ±10.77).	(256)
Yamamoto et al. 2011	Japan	Cross-sectional	54 (vitiligo patients)	CES-D	The CES-D revealed that 15 (27.8%) of 54 patients had depressive symptoms.	(257)
Layegh et al. 2010	Iran	Cross-sectional	300 (vitiligo-87, Psoriasis-62, Acne-	BDI	The prevalence of clinical depression was 70.1% among vitiligo patients	(258)

			78, Alopecia Areata-73)			
Zaki et al. 2009	Egypt	Cross-sectional	30 (vitiligo patients)	HAM-D	About 56.67 % of vitiligo patients experienced depression.	(259)
Saleh et al. 2008	Egypt	Cross-sectional	150 (vitiligo-50, psoriasis-50, Alopecia area-50)	SDS	Depression was found in 24% of the vitiligo patients.	(260)
Ahmed et al. 2007	Pakistan	Cross-sectional	100 (vitiligo patients)	PAS	Major depressive illness was found in 15% of vitiligo patients.	(261)
Esfandiar Pour et al. 2003	Iran	Cross-sectional	120 (vitiligo patients)	HAM-D	Depressed mood was present in 38.34% and major depressive disorder was present in 30.83% of patients.	(262)
Sharma et al., 2001	India	Cross-sectional	60 (vitiligo-30, psoriasis- 30)	GHQ	Depression was found in 10% of vitiligo patients.	(263)

HAM-D - Hamilton Depression Rating Scale; **SDS**–Self-rating Depression Scale; **DASS** - Depression Anxiety Stress Scale; **BDI** - Beck's Depression Inventory; **PHQ-9** - Patient Health Questionnaire**; QIDS-SR$_{16}$**-16-item Quick Inventory of Depressive Symptomatology–Self-report; **HADS** - Hospital Anxiety Depression Scale**; ICD-10** -International Classification of Diseases; **CES - D** - Centre for Epidemiologic Studies Depression Scale; **GHQ** - General Health Questionnaire; **CDI** - Child Depression Inventory; **PAS** - Psychiatric Assessment Schedule; **ES-Q** - Emotional State Questionnaires; **Ref.**-Reference

3. HYPOTHESIS, AIM AND OBJECTIVES

3.1. Hypothesis of research

3.1.1. Hypothesis for conducting study on drug prescribing pattern

Globally, dermatological disorders are a significant issue, with approximately one-fourth of all cases in everyday medical practice related to dermatology (264). Analyzing prescribing patterns is crucial in monitoring, evaluating, and potentially suggesting modifications to healthcare practitioners' prescribing behavior to ensure rational and cost-effective medical care (265).

It is imperative to note that drug prescribing practices can vary between countries and even within different regions of the same country. These variations are influenced by various factors, including regulatory agencies, healthcare systems, cultural differences, and available resources (266). Consequently, examining drug utilization patterns in specific settings is necessary to understand prescribing practices better.

Numerous studies have been conducted in India on drug utilization in dermatology clinics. However, disease-specific drug prescribing patterns remain limited. Researchers and healthcare professionals can gain insights into dermatological treatment preferences and trends by studying disease-specific drug prescribing practices in India. This information can be valuable for optimizing therapeutic approaches, promoting evidence-based medicine, reducing costs, and improving patient outcomes.

3.1.2. Hypothesis for conducting a study on Quality of Life (QoL)

Hypothesis

Comparison of QoL between generalized and localized vitiligo

a. *Null Hypothesis (H0):* The QoL is not significantly different between patients with generalized and localized vitiligo.

b. *Alternative Hypothesis (H1):* The QoL is a significant difference between patients with generalized and localized vitiligo.

Rationale

Vitiligo can have significant psychosocial consequences due to its impact on appearance, which may lead to stigmatization, anxiety, and diminished self-esteem. While various studies have explored the psychosocial aspects of vitiligo, limited research has directly compared the QoL of patients with generalized and localized forms of the condition. This study aims to address this gap in the literature and provide valuable insights for clinicians and researchers. Understanding such differences can help to make an interventions and support services for these specific patient populations.

3.1.3. Hypothesis for conducting a study on Depression

Hypothesis

Comparison of QoL between generalized and localized vitiligo

a. *Null Hypothesis (H0):* There is no significant variation in the prevalence of depression between generalized and localized vitiligo.
b. *Alternative Hypothesis (H1):* The prevalence of depression differs significantly between generalized and localized vitiligo.

Rationale

Depression is an important factor to consider when evaluating the overall health and well-being of vitiligo patients. Understanding, if there is a significant difference in the prevalence of depression between those with generalized and localized vitiligo, can aid healthcare providers in tailoring treatment plans, psychological support, and counseling to the specific needs of each group.

3.1.4. Hypothesis for comparing the synthetic and herbal drugs prescribed for vitiligo

The treatment of vitiligo is multifaceted and relies on factors such as the extent and location of the affected areas, as well as whether the condition is in a more stable or active phase (267). Traditional treatment approaches for vitiligo include topical or systemic therapies and phototherapies. However, over the past few years, there has been a growing fascination with natural herbal medicine because of its antioxidative and anti-inflammatory characteristics, which are believed to be relevant in addressing oxidative stress and inflammation associated with vitiligo. Herbal medicines are often considered alternatives to conventional therapies. However, no studies have been conducted to directly compare the efficacy and safety of herbal and synthetic drugs for vitiligo treatment.

3.2. Aim

To assess the drug prescribing pattern, quality of life, and depression in generalized and localized vitiligo patients of Andhra Pradesh

3.3. Objectives

- To evaluate the drug prescription pattern in vitiligo patients.
- To compare the synthetic and herbal drugs prescribed in vitiligo patients.
- To assess and compare the QoL in generalized and localized vitiligo
- To assess the severity of depression by using the Hamilton depression rating scale

4. SUBJECTS AND METHODS

4. MATERIALS AND METHODS

4.1. Methodology for Objective 1:

- **To evaluate the drug prescription pattern in vitiligo patients**

Study design and settings

This cross-sectional study was carried out in the dermatology department of Rajiv Gandhi Institute of Medical Science, a tertiary care teaching hospital located in Andhra Pradesh, India from December 2019 to December 2020.

Study Population

A total of 200 patients' prescriptions were reviewed. All patients aged ≥18 years, of either sex, diagnosed with any type of vitiligo, and receiving treatment were included in the study. Patients with other medical co-morbidities and incomplete prescriptions were excluded from the study. We also excluded participants who did not consent to participate in the study.

Ethical statement

The study was conducted after getting approval from the Institute Ethics Committee of Rajiv Gandhi Institute of Medical Science (RIMS) [Ref no: RIMS/IEC/2019/12/19]. All subjects provided written consent after a thorough explanation of the research's objectives, significance, and potential benefits, along with the assurance that their participation was voluntary. They were also guaranteed that any data collected would be treated confidentially, used exclusively for research purposes, and would not impact their treatment.

Sample size

The number of patients required for this study was calculated with the formula,

$$\text{Sample size (n)} = Z^2 \times p\,(1-p) / d^2$$

Where Z-score is 1.96 associated with a confidence level of 95%, the sample proportion (p) is 8 (268) (expressed as a decimal, 0.08), and the margin of error (d) was 4% (expressed as a decimal, 0.04).

$z = 1.96, p = 0.08, e = 0.04$

$n = 1.96^2 * 0.08 * (1 - 0.08) / 0.04^2$

$n = 0.2827 / 0.0016 = 176.714$

$n \approx 177$

The calculated sample size was 177. But to increase the power of the study, a total of 200 patients were recruited in the study.

Data collection

Patient data were collected from both the outpatient and inpatient departments of dermatology. A data collection form was designed incorporating all necessary variables including age, gender, type of vitiligo, duration since vitiligo developed, current medical conditions, diagnosis, medications prescribed, treatment duration, dosage form, frequency, and route of administration. Patients were evaluated by an experienced dermatologist at the Department of Dermatology. In addition to the distinct loss of pigmentation on the skin, Wood's lamp examinations were used to confirm the diagnosis of vitiligo. All the relevant data were collected from the patient's file.

Data analysis

To analyze the data, a statistical package for social sciences (SPSS® version 18.0) was used. A descriptive analysis of the data was performed using frequencies, percentages, means, and standard deviations.

4.2. Methodology for objective 2 & 3:

- **To assess and compare the QoL in generalized and localized vitiligo**
- **To assess the severity of depression by using Hamilton depression rating scale**

Study Setting and study design

A cross-sectional study was performed in the dermatology outpatient department of Rajiv Gandhi Institute of Medical Science (RIMS), a tertiary care hospital in Andhra Pradesh, India, from November 2020 to December 2021.

Study participants

The study included patients of both sexes, aged ≥ 18 years, and diagnosed with vitiligo. Patients with diabetes, thyroid problems, rheumatoid arthritis, psoriasis, pityriasis, leprosy, or other co-morbidities were excluded. We used a convenience sampling technique to recruit patients for the study. All participants were instructed to complete the questionnaires by themselves. A face-to-face interview was conducted with illiterate patients.

Data collection

Three different questionnaires were used to collect data. The first questionnaire includes questions related to clinic-demographic parameters. The second questionnaire was the Dermatology Life Quality Index (DLQI) for measuring QoL, and the third was the Hamilton Depression Rating Scale (HAM-D) for assessing depression.

DLQI

DLQI consists of six domains:

- Items 1& 2 - "symptoms and feelings"
- Items 3 & 4 - "daily activities"
- Items 5 & 6 - "leisure", and
- Items 8 & 9 - "personal relationships"

Each with a maximum score of 6

- Item 7 - "work or study" and
- Item 10 - "treatment",

All with highest scores of 3

The DLQI is calculated by summing the scores of each item, yielding a minimum of 0 and a maximum of 30. The higher the score, the poorer the QoL(265).

HAM-D

We also used a self-administered, 17-item version of the HAM-D for measuring depression. The total score of HAM-D is obtained by summing each item.

- Scores of 0-7: These scores indicate a normal range, suggesting the absence of significant depressive symptoms.
- Scores of 8-16: This range is considered mild depression, indicating the presence of some depressive symptoms, but they are generally not severe and do not greatly impair daily functioning.
- Scores of 17-23: Falling within this range suggests moderate depression. It indicates a higher level of depressive symptoms, potentially interfering with various aspects of a person's life.

Scores equal to or greater than 24: Scores in this range indicate severe depression. This suggests the presence of significant and debilitating depressive symptoms that may require immediate attention and intervention (225).

Ethical statement

The Institute Ethics Committee of RIMS approved the study protocol [Ref no: RIMS/IEC/2019/12/19]. All patients provided their written informed consent before participating in the study.

Sample size

The number of patients required for this study was calculated with the formula, n = z2 p (1-p) / d2 where z= 1.96 for a confidence level of 95%, p= proportion (8%), taken from the previous study (258), d = margin of error. The required sample size was 177. To increase the power of the study, a total of 200 patients were included.

Data Analysis

Microsoft Excel and Statistical Package for Social Sciences (SPSS version 21) software were used to analyze the data. For numerical data, frequency, and percentages, and for qualitative data, mean and standard deviation were used. Student's t-test was used to compare the mean between the continuous variables. A P-value less than 0.05 was considered statistically significant.

4.3. Methodology for objective 4:

- **To compare the synthetic and herbal drugs prescribed in vitiligo patients**

Study setting and study design

A retrospective review of medical records was carried out on vitiligo patients recommended natural Aloe Vera leaf pulp and tacrolimus (0.1%) ointment as a monotherapy at the Government General Hospital in Andhra Pradesh, India, during the period between July 2021 to August 2022.

Ethical statement

The study was conducted after getting approval from the Institute Ethics Committee of Rajiv Gandhi Institute of Medical Science (RIMS), Andhra Pradesh. Because the study entailed a retrospective examination of patient charts, obtaining informed consent from the patients was not feasible. To maintain confidentiality, medical records were identified using patients' medical registration numbers. Personal details of individual subjects, such as names, addresses, and phone numbers, were not collected during the data extraction process.

Study Population

A total of 39 patients' medical records were enrolled in the study. The study included all patients aged 18 years and above, of either gender, who had been diagnosed with vitiligo of any type. Patients who had active lesions were not included in the study due to concerns about the potential spread of new lesions. Other exclusion criteria include underlying any other skin diseases (atopic dermatitis, psoriasis, and/or eczema) and a history of using other topical medications.

Treatment protocol

About 22 patients were treated with topical Aloe Vera 95% gel three times daily for 24 weeks. Patients were advised to collect fresh Aloe Vera leaves and clean them with water. A knife was then used to remove the leaf's spines and outer green rind so that the aqueous whole-leaf pulp (inner parenchyma) could be collected. The patients were then instructed to massage a small amount of pulp onto the lesions thrice daily for 6 months. The patients were also advised to gradually increase their exposure to natural sunlight from 5–10 minutes at the start of the study to a maximum of 30 minutes after 3 months. Patients were also instructed to return to the treatment center for outcome assessments three and six months after treatment initiation. Wood's Lamp method, or photographic evaluation, was used to assess treatment outcomes. The remaining 17 patient who were prescribed tacrolimus 0.1% topical ointment was advised to apply a fingertip unit (FTUs) of ointment on lesions twice daily in the morning and the same amount in the evening, every day, for 24 weeks.

Efficacy and safety

The primary efficacy endpoint was the proportion of patients achieving at least ≥75% in re-pigmentation of the target lesion at the end of 24 weeks, which constituted a "good response," while 50% or higher re-pigmentation constituted a "better response" (260). The extent of re-pigmentation was assessed as per the protocol and graded from Grade 0 to Grade 5. Grade 0 indicates "no re-pigmentation," Grade 1 indicates "1-25% re-pigmentation," Grade 2 indicates "25-50% re-pigmentation," Grade 3 indicates "50-75% re-pigmentation," Grade 4 indicates "75-99% re-pigmentation," and Grade 5 indicates "100% re-pigmentation (270). The primary endpoint for the safety assessment was the proportion of patients who experienced at least one adverse event during the 24-week treatment period. A secondary safety outcome was the proportion of patients who stopped treatment before 24 weeks due to side effects.

Data analysis

The data were collected and exported to Microsoft Excel software version 2019 for statistical analysis. The descriptive analyses for numerical data were shown as frequency (n) and percentage, for categorical data, mean and standard deviation (SD) were used. All data analyses were conducted using SPSS version 21 statistical software.

5. RESULTS

5.1. Drug Prescribing Pattern in vitiligo

5.1.1. Age and gender

In the present study, 200 patients were recruited and their prescriptions were evaluated, of which 54% (n=108) were females, and 46% (n=92) were males. The mean (±SD) age of the patients was 48.5 ± 13.5 years (age range 26–75 years) and the mean (±SD) duration of vitiligo was 7.8 ± 3.8 years for all the patients. The majority of patients 51 (25.5%) were under the age group of 45–55 years, followed by the age group of 25-35 years (n=46). The least number of patients 30 (15%) were observed in the age group of 65-75 years (**Table 5**). Gender and Age-wise distribution of vitiligo patients is shown in **Figure 4**.

Table 5: Distribution based on patients' demographics

Parameter	Number of patients (n=200)	Percentage (%)
Gender		
Male	92	46
Female	108	54
Age (in years)		
25 - 35	46	23
36 - 45	33	16.5
46 - 55	51	25.5
56 - 65	40	20
66 - 75	30	15

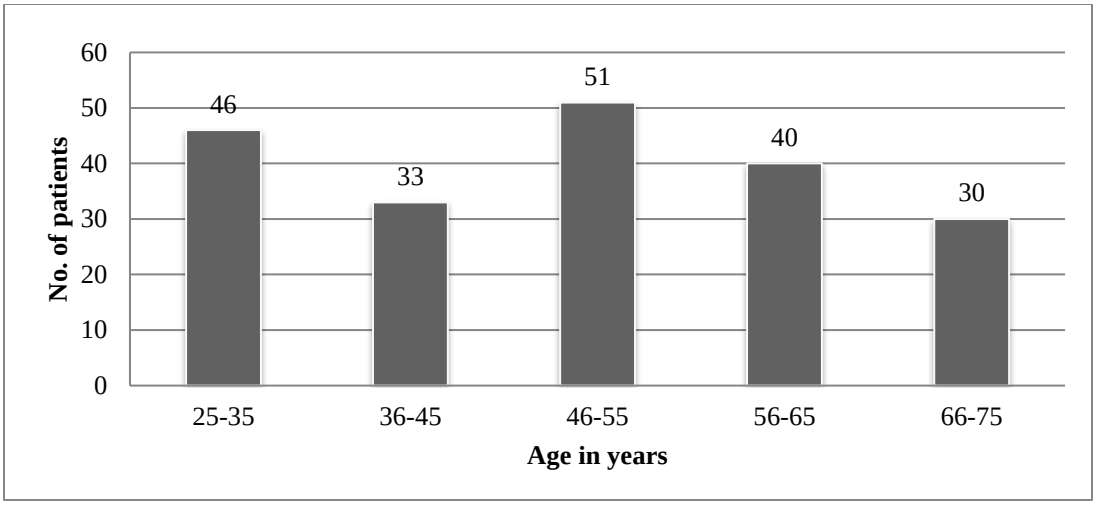

Figure 4: Distribution of patients based on Age groups

5.1.2. Clinical subtypes

The most prevalent clinical type was acrofacial, noted in 78 cases, accounting for 39% of the cases, followed by focal, vulgaris, segmental, and universal vitiligo (**Table 6**). The photographs of each type are shown in **Figures 5 to 9**. A total of 29 subjects developed vitiligo vulgaris as the initial clinical subtype, and 3 of them developed universal vitiligo. It is observed that 7 cases of focal vitiligo and 3 cases of acrofacial vitiligo have changed into vitiligo vulgaris. None of the segmental vitiligo changed into another subtype.

Table 6: Distribution based on patients' clinical subtype

Clinical subtype	Number	Percentages
Acrofacial	78	39
Focal	42	21
Vitiligo vulgaris	36	18
Segmental	74	37
Universal	11	5.5
Total	200	100

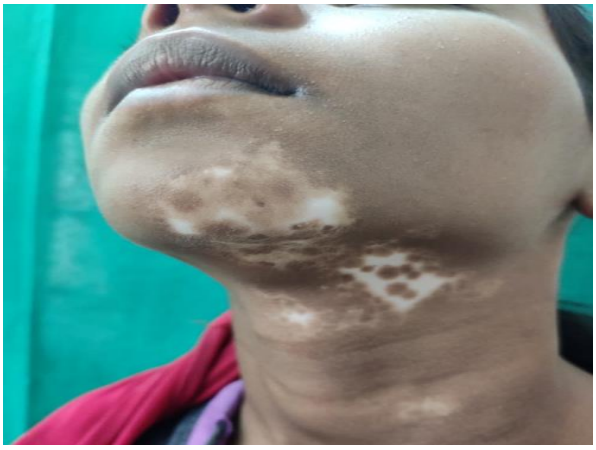

Figure 5: Segmental vitiligo

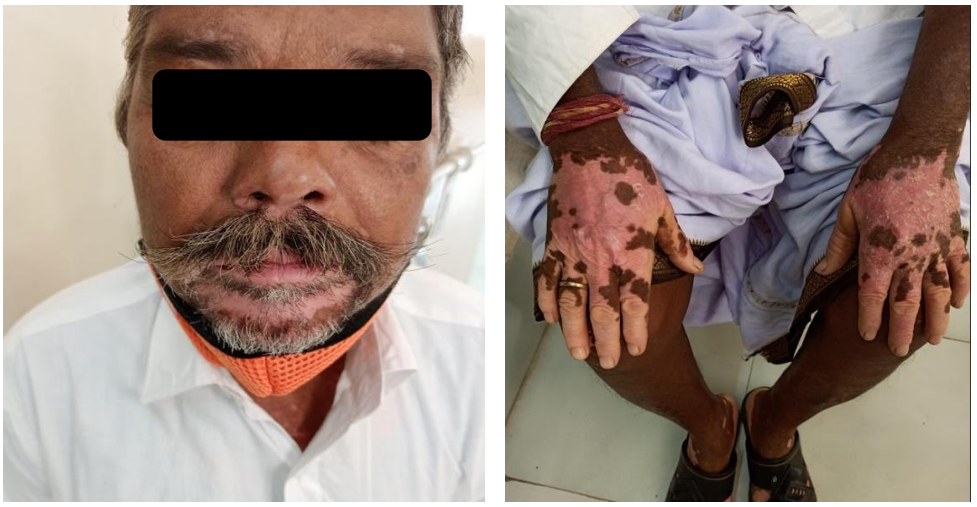

Figure 6: Acrofacial vitiligo

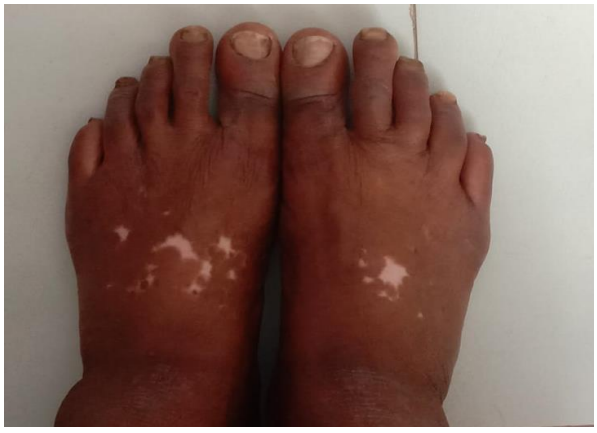

Figure 7: Focal vitiligo

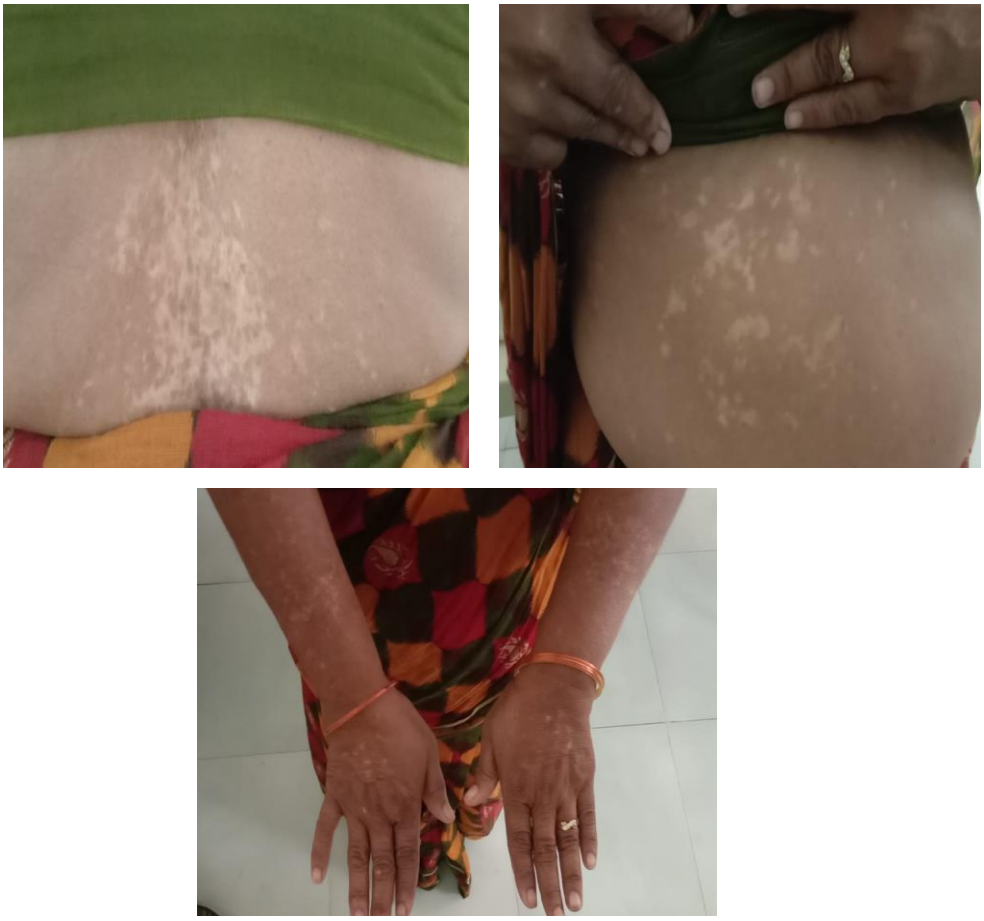

Figure 8: Vitiligo vulgaris

Figure 9: Universal vitiligo

5.1.3 Distribution based on sites of onset of vitiligo

In a total of 200 patients, 283 different affected regions of the body were identified. The most commonly affected sites were, lower and upper limbs 92 (32.5%) were the most commonly affected, followed by the head, and neck 88 (31%), the trunk 49 (17.3%), the chest 36 (12.8%), the mucous membranes 13 (4.6%), and genital area 5 (1.8%) (**Figure 10**).

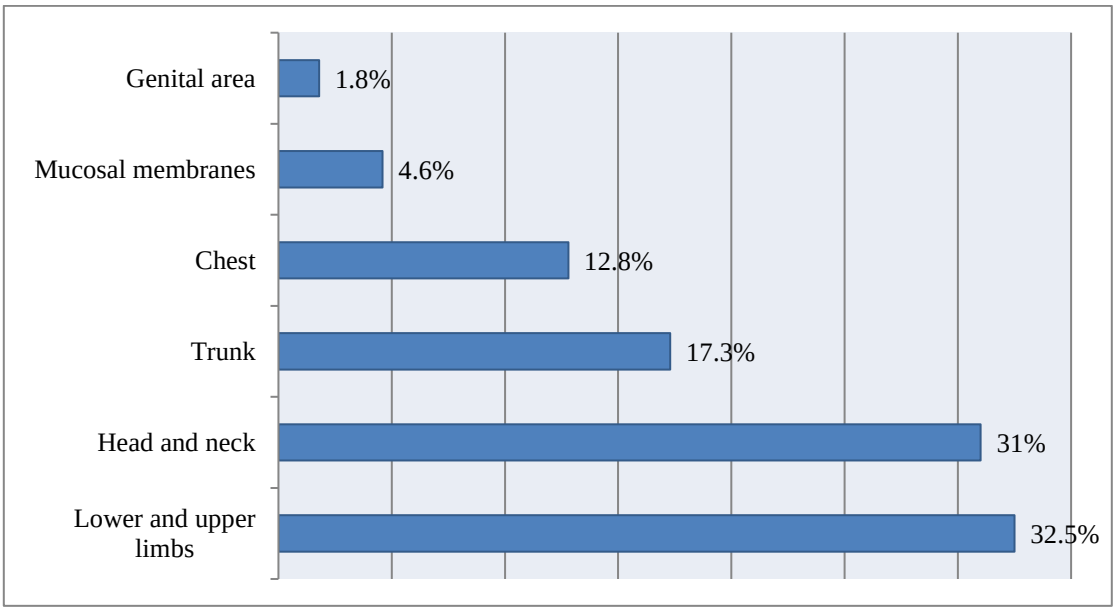

Figure 10: Distribution based on sites of onset of vitiligo

5.1.4 Prescription patterns based on therapy

Out of 200, 142 (71%) patients who were treated with combination therapy. Only 58 patients (29%) with a very small amount of depigmentation received monotherapy (**Figure 11**).

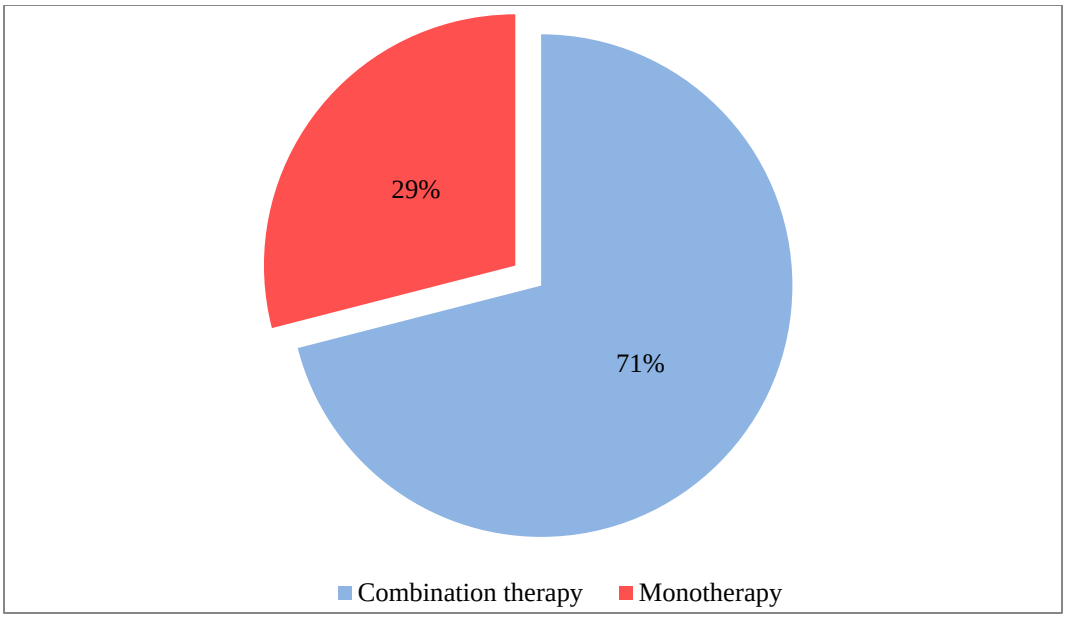

Figure 11: Prescription patterns based on therapy

5.1.5 Prescription pattern based on dosage forms

Out of 464 prescribed drugs, the majority of drugs were prescribed as ointments (40.8%) followed by tablets, lotions and capsules as shown in **Figure 12**.

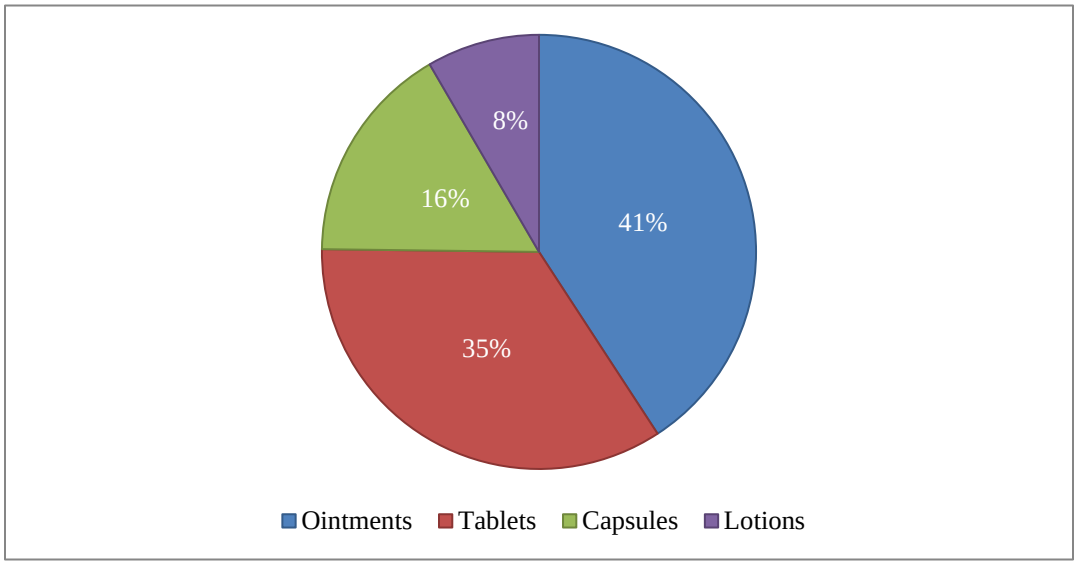

Figure 12: Distribution based on prescribed dosage forms

5.1.6 Distribution based on symptoms

Out of 200 patients, 122 experienced disease symptoms. Among these 122 patients with disease symptoms, 52 (26%) had itchy sunburns in their lesions. Additionally, 46 patients (23%) had only itchy symptoms and 24 patients (12% of the total patients) had only sunburn-like symptoms as shown in **Figure 13**.

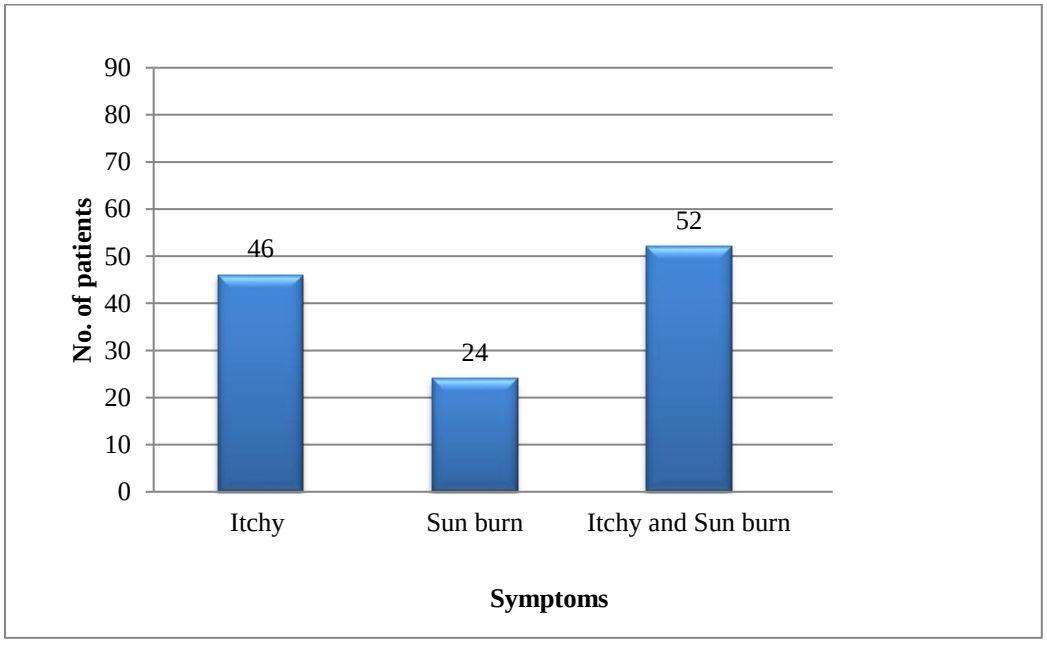

Figure 13: Distribution of patients based on symptoms

5.1.7. Distribution based on drugs prescribed

A total of 464 drugs were prescribed to 200 patients. Almost all prescriptions mentioned the strength, the quantity of the drug to be used, the frequency, and the site of application. The most commonly prescribed class of drugs was corticosteroids (42.9%), followed by calcineurin inhibitors (13.4%), vitamins (14.6%), basic fibroblast growth factor (9.5%), moisturizers (6.9%), antihistamines (6.5%), and minerals (6.2%) (**Figure 14**).

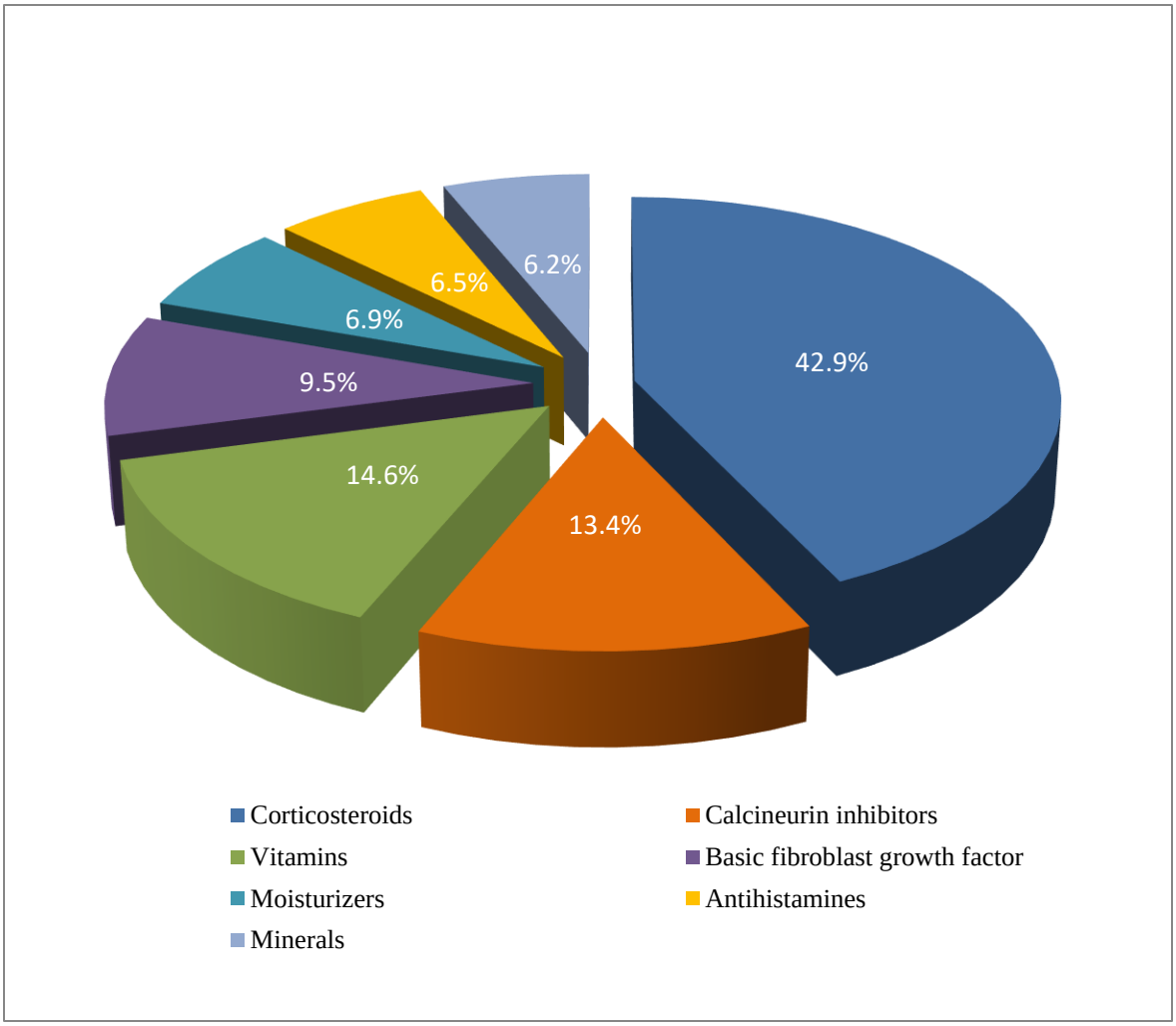

Figure 14: Distribution based on prescribed class of drugs for vitiligo

Topical corticosteroids are prescribed more often than orally. Betamethasone was the most commonly prescribed corticosteroid, followed by clobetasol propionate. Tacrolimus was secondary to steroids, followed by decapeptide, vitamins (A and D), glycerin, chlorpheniramine maleate, B-complex, and calcium (**Table 7**). However, phototherapy and surgical therapy were not performed in any patients.

Table 7: The most commonly prescribed drugs for vitiligo in (n=464)

Drugs prescribed	Value (%)
1. Corticosteroids	
Tab. Betamethasone	72 (15.5)
Oint. Betamethasone	68 (14.7)
Oint. Clobetasol propionate	59 (12.7)
2. Calcineurin inhibitor	
Oint. Tacrolimus	62 (13.4)
3. Vitamins	
Cap. Vit. A &D	39 (8.4)
Tab. Vit. B-complex	29 (6.2)
4. Basic fibroblast growth factor	
Lot. Decapepide	44 (9.5)
5. Moisturizers	
Lot. Glycerin	32 (6.9)
6. Antihistamines	
Tab. Chlorpheniramine maleate	30 (6.5)
7. Minerals	
Tab. Calcium	29 (6.2)

Note: Tab: Tablet**; Oint:** Ointment**; Cap:** Capsule**; Lot:** Lotion.

5.2. Quality of Life (QoL) in vitiligo

A total of 200 patients were included in the study, of which 84 had generalized vitiligo and 116 had localized vitiligo. Generalized vitiligo had 36 males and 48 females, and localized vitiligo comprised 56 males and 60 females. The mean (±SD) age of the generalized and localized vitiligo patients was 49.53±13.1 years and 47.83±13.8 years, respectively. The mean (±SD) duration of the disease for generalized and localized vitiligo was 8.21±2.9 and 7.50±4.3 years, respectively (**Table 8**).

Table 8: Mean ages and duration of vitiligo in the patients with different clinical types

Types	Number (M/F)	(%)	Mean (±SD) age in years	Mean (±SD) duration of disease
Generalized	84 (36/48)	42	49.5 ±13.1	8.2 ±2.9
Localized	116 (56/60)	58	47.8 ±13.8	7.5 ±4.3

Generalized vitiligo had significantly ($p < 0.05$) lower QoL [mean (±SD) DLQI scores 12.2 (±1.3)] than localized vitiligo [mean (±SD) DLQI scores 7.9±1.6]. In our study, a statistically significant difference was observed concerning different marital groups ($p = 0.04$), education ($p = 0.02$), and residential location ($p = 0.04$) of lesions with respective to DLQI scores. In generalized vitiligo, the mean DLQI score was the highest (13.2) in the age group of >60 years, whereas it was the highest (12.5) in the age group of 26–35 years in localized vitiligo. The socio-demographic details associated with generalized and localized vitiligo was shown in **Table 9**.

Table 9: Socio-demographic details of generalized and localized vitiligo

Variables	Class	Generalized vitiligo (n=84) N (%)	Localized vitiligo (n=116) N (%)
Gender	Male	36 (18)	56 (28)
	Female	48 (24)	60 (30)
Age (in year)	26-35	17 (8.5)	29 (14.5)
	36-45	14 (7)	19 (9.5)
	46-55	15 (7.5)	33 (16.5)
	56-65	26 (13)	14 (7)
	>60	9 (4.5)	21 (10.5)
Marital status	Single	25(12.5)	42(21)
	Married	59(29.5)	74(37)
Disease duration (in year)	<5	29 (14.5)	40 (20)
	5-10	51 (25.5)	23 (11.5)
	>10	21 (10.5)	36 (18)
Education	Illiterate	62 (31)	78 (39)
	Educated	26 (13)	34 (17)
Occupation	Employed	38 (19)	46 (23)
	Unemployed	74 (37)	42 (21)
Stabilization of disease	Stable	34 (17)	57 (28.5)
	Progressive	50 (25)	59 (29.5)
Residential location	Urban	66 (33)	72 (36)
	Rural	18 (9)	44 (22)

Based on the interpretation of the DLQI scale results, 9(7.7%) patients of localized vitiligo and 4(4.8%) patients of generalized vitiligo did not show any impairment in QoL. In generalized vitiligo, 51.1% of patients experienced an extremely large effect, and 15.5% had a very large effect on the QoL. Whereas in localized vitiligo, the proportion of an

extremely large effect and a very large effect was experienced by 29.3% and 13.8% of patients, respectively (**Figure 15**).

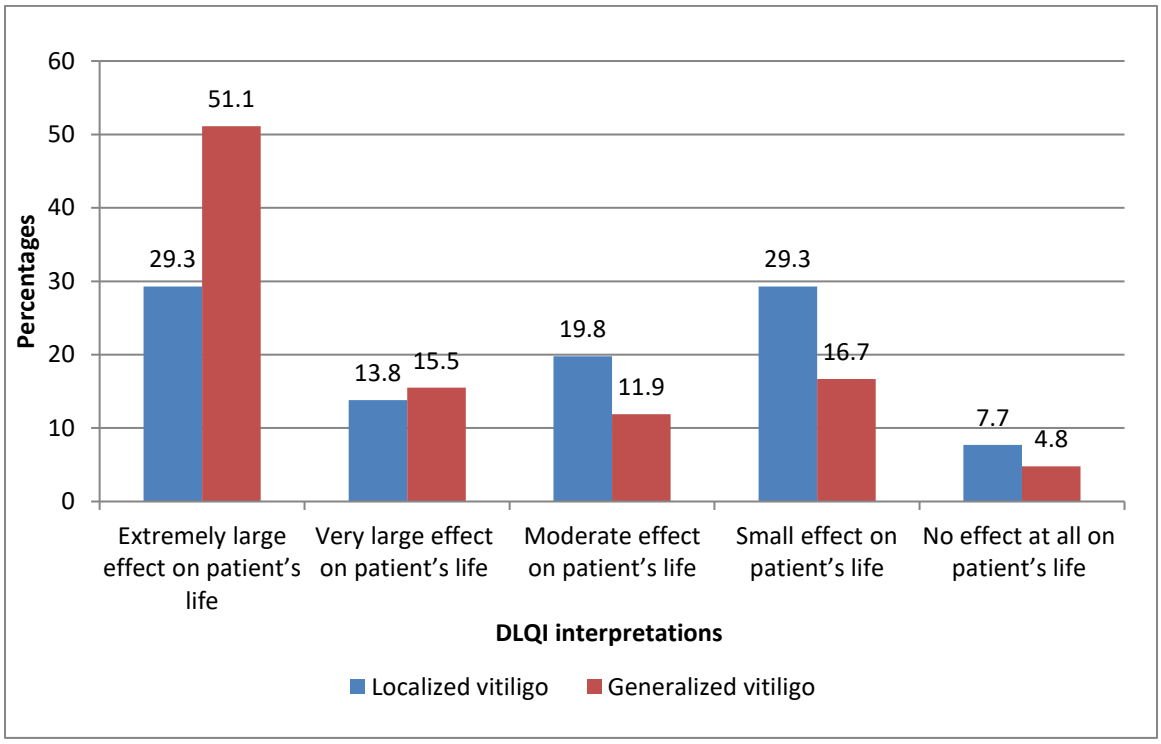

Figure 15: DLQI interpretations in localized and generalized vitiligo

Apart from item 4 of the DLQI questionnaire, all other domains of QoL showed significantly higher ($p<0.05$) DLQI scores in generalized vitiligo compared to localized type. Among various domains of QoL, the treatment domain (Item 10) had the highest impact on QoL in both types of vitiligo. The mean DLQI scores of different domains are shown in **Table 10.**

Table 10: Comparison between localized vitiligo and generalized vitiligo for different items of the DLQI scales

DLQI Items	Mean ± SD			P-Value
	Localized vitiligo (n=116)	Generalized vitiligo (n=84)	Total	LV vs. GV
Item 1	0.8 ± 1.1	1.4 ± 1.3	1.1 ± 1.2	<0.001**
Item 2	1.1 ± 1.2	1.6 ± 1.3	1.3 ± 1.2	0.001*
Item 3	0.4 ± 0.6	0.7 ± 0.8	0.5 ± 0.7	0.002*
Item 4	0.6 ± 0.7	0.7 ± 0.7	0.6 ± 0.7	0.06
Item 5	0.3 ± 0.6	0.6 ± 0.7	0.5 ± 0.6	0.002*
Item 6	0.4 ± 0.6	0.6 ± 0.7	0.5 ± 0.6	0.006*
Item 7	0.6 ± 0.8	1.0 ± 1.0	0.8 ± 0.9	0.001*
Item 8	1.0 ± 0.9	1.3 ± 1.1	1.1 ± 1.0	0.01*
Item 9	1.2 ± 1.2	1.4 ± 1.3	1.3 ± 1.3	0.09
Item 10	1.5 ± 1.1	1.9 ± 1.0	1.7 ± 1.1	0.003*

LV-Localized vitiligo; GV-Generalized vitiligo; SD- Standard deviation; ***** Statistically significant; ** Highly significant ($P \leq 0.01$).

5.3 Depression in vitiligo

In our study, the prevalence of depression was 89.5% (n = 179) in vitiligo patients. Severe and very severe depression was observed among 27.4% and 36.9 % of generalized vitiligo patients, respectively. Whereas, the proportion of severe and very severe depression among localized vitiligo patients was 18.1 % and 2.6 %, respectively**.** The Mean (±SD) HAM-D score and prevalence of depression are presented in Table 11 & **Figure16.**

Table 11: Comparison of the mean (±SD) HAM-D scores between localized and generalized vitiligo

Severity of depression	Localized type (n=116)		Generalized type (n=84)		P-value
	n (%)	Mean (±SD) HAM-D score	n (%)	Mean (±SD) HAM-D score	
Normal	15 (13)	4.71±2.39	6 (7.1)	3.83±1.83	<0.001**
Mild Depression	46 (39.6)	10.42±1.84	6 (7.1)	8.83±2.31	
Moderate Depression	31 (26.7)	15.40±1.42	18 (21.5)	14.94±1.29	
Severe Depression	21 (18.1)	19.65±1.26	23 (27.4)	20.90±1.10	
Very Severe Depression	3 (2.6)	23.33±1.42	31 (36.9)	32.43±4.76	

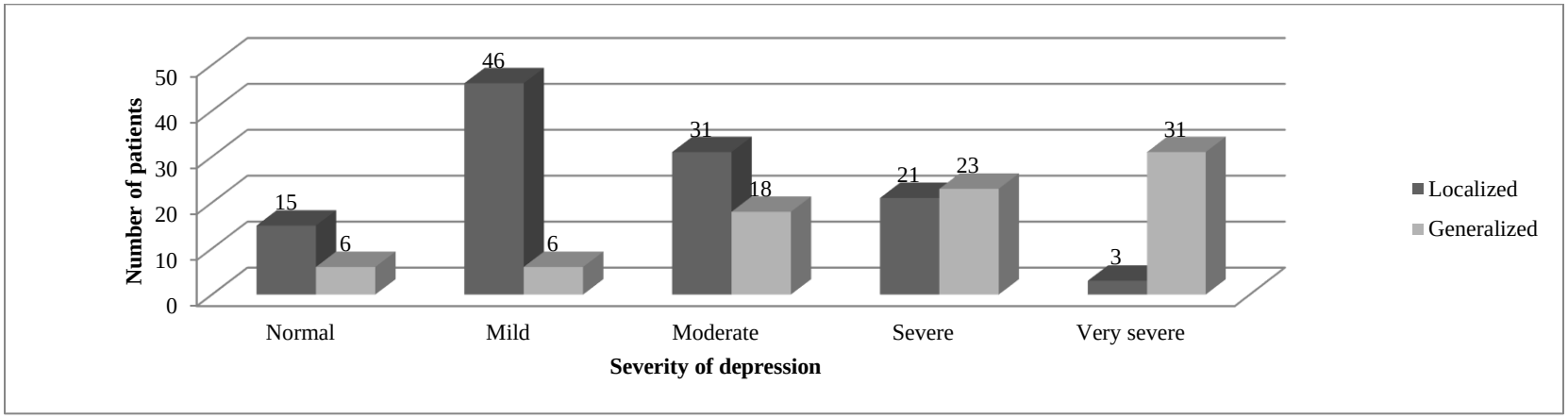

Figure 16: Comparison of the severity of depression between localized and generalized vitiligo

The most common depressive symptoms observed among localized vitiligo patients were feeling of guilt (13%), followed by insomnia (12%), anxiety (7.5%), sexual problems (5%), etc. In generalized vitiligo, the most common depressive symptoms were insomnia (24%), followed by anxiety (10.5%), feeling of guilt (8%), sexual problems (7.5%), etc. The overall prevalence of depressive symptoms in localized and generalized vitiligo is presented in **Table 12**.

Table 12: Comparison of prevalence of symptoms between localized and generalized vitiligo

Symptoms	Localized vitiligo	Generalized vitiligo	Total prevalence
	N (%)	N (%)	N (%)
Insomnia	24 (12)	48 (24)	72 (36)
Feeling of guilt	26 (13)	16 (8)	42 (21)
Anxiety	15 (7.5)	21 (10.5)	36 (18)
Sexual problems	10 (5)	15 (7.5)	25 (12.5)
Suicidal ideation	8 (4)	13 (6.5)	21 (10.5)
Suicidal attempts	0 (0)	6 (3)	6 (3)

5.4. Comparison between synthetic and herbal medicine

In this study, a total of 43 medical records of vitiligo patients were assessed for eligibility. Of these, 24 were prescribed with only Aloe Vera gel and 19 with tacrolimus 0.1% ointment. During the 24-week treatment, four patients (two from each group) were no longer available for follow-up. As a result, the study ultimately included a total of 39 medical records for analysis.

The majority of the patients, (59% in Aloe Vera and 58.9% in tacrolimus), enrolled in the study. The mean (±SD) age of the Aloe Vera and tacrolimus group patients was 9.6 ± 6.7 months and 11.5 ± 10.6 months, respectively. Patient characteristics and clinical data are shown in **Table 13**. Patient demographics and clinical characteristics of each patient treated with Aloe Vera gel and tacrolimus are shown in **Tables 14 & 15** respectively.

Table 13: Patient Demographics and Clinical Characteristics at Baseline

Characteristics	**Aloe Vera (N=22) n (%)**	**Tacrolimus (N=17) n (%)**
Gender		
Male	13 (59.1%)	11(64.7%)
Female	9 (40.9%)	6 (35.3%)
Mean age in years ± (SD)	31.7± (8.8)	29.1± (7.4)
Types, n (%)		
Generalized	9 (41%)	7 (41.1%)
Localized	13 (59%)	10 (58.9%)
Disease duration (months), mean (±SD)	9.6 (±6.7)	11.5 (±10.6)
Associated autoimmune diseases, n (%)		
Yes	3 (13.6%)	2 (11.8%)
No	19 (86.3%)	15 (88.2%)
Past history of repigmentation, n (%)		
No	21 (95.4%)	17 (100%)

Table 14: Clinico-demographics characteristics of each patient treated with Aloe Vera gel (n=22)

S. No	Gender	Age (years)	Admitting diagnosis	Location	Duration of disease (months)	Adverse effects	% of re-pigmentation (After 3 months)	% of re-pigmentation (After 6 months)
1	F	26	Acrofacial type	Face, hands	12	No	25%	25% (no change)
2	F	46	Contact vitiligo	foot	8	No	25%	90%
3	M	25	Focal type vitiligo	Neck	6	Burning sensation	No	25%
4	M	27	Focal type vitiligo	Hands	12	No	25%	75%
5	F	31	Segmental	Hands, right arms	24	No	25%	50%
6	M	36	Acrofacial type	Face, hands	24	No	50%	50% (no change)
7	F	28	Focal type vitiligo	hands	3	No	25%	50%
8	M	36	Acrofacial type	Face, chest, hands	12	No	50%	50%
9	M	32	Segmental	right arm, elbows	6	No	5%	25%
10	F	42	Acrofacial type	Hands, Legs, chest	12	No	25%	50%
11	M	23	Focal type	right hand	3	No	10%	25%
12	F	28	Focal	Hands	3	Pruritus	5%	25%

13	M	25	Vitiligo vulgaris	Face	7	Burning sensation	25%	75%
14	M	25	Focal type	Hand, feet	4	No	No	10 %
15	F	23	Focal	hands	2	No	5%	25%
16	M	26	Acrofacial type	Hands, face, figures	9	No	10%	25%
17	M	32	Vitiligo vulgaris	Face, hands, neck, legs	12	No	5%	25%
18	F	58	facial	face	6	No	50%	90%
19	M	48	Segmental	stomach, hands	9	No	50%	50% (no change)
20	F	52	Vitiligo vulgaris	Hands, legs Face	12	No	25%	10 %
21	M	36	Focal type	hands and neck	3	No	No	25%
22	M	34	Acrofacial type	Face, chest, hands	24	No	10%	25%

Table 15: Clinico-demographics characteristics of each patient treated with Tacrolimus (n=17)

S. No	Gender	Age (years)	Admitting diagnosis	Location	Duration of disease (months)	Adverse effects	% of re-pigmentation (After 3 months)	% of re-pigmentation (After 3 months)
1	F	24	Acrofacial type	Face, hands, neck, legs	12	Pruritus, Erythema	50%	75%
2	M	33	Focal type vitiligo	hands and neck	6	Pruritus	25%	75%
3	M	23	Vitiligo vulgaris	Genital region, hand figure's	24	Burning sensation, Erythema	No	25%
4	M	28	Focal type vitiligo	legs	1	Pruritus, Erythema	50%	90%
5	M	36	Segmental	fore arms, legs, feet	42	Pruritus, Erythema	No	50%
6	F	36	facial	hands, legs	4	Burning sensation	10%	50%
7	M	26	Focal type	Hands	6	Burning sensation, Pruritus, Erythema	25%	75%
8	F	30	Focal	Face, hands	5	Pruritus	25%	50%

9	M	28	Vitiligo vulgaris	Hands, Legs	12	Pruritus	No	25%
10	M	30	Focal	Legs, left hand	6	Pruritus, Erythema	10%	50%
11	M	46	Segmental	chest, legs, hands	18	Erythema,	25%	50%
12	M	24	Focal	legs	6	Pruritus, Erythema	5%	25%
13	F	31	Focal	hands, right arm, legs	5	Pruritus	10%	25%
14	F	41	Vitiligo vulgaris	Fingers, chest, neck	18	Pruritus, Erythema	25%	50%
15	F	20	focal	hands	3	Burning sensation, Pruritus	25%	50%
16	M	21	Acrofacial type	Hands, face, fingers	24	Erythema,	5%	25%
17	M	19	Focal type	Lower limbs, hands	4	Burning sensation, Pruritus	25%	25%

Complete repigmentation (Grade 5) was not achieved in any patients. At the end of the study period, 90% repigmentation (Grade 4) was seen in two patients as shown in **Figure 17**. Thus, on an overall basis, a good response (75–100% repigmentation) was seen only in the tacrolimus group, with 13.6% in the first follow-up and 23.5% in the second follow-up. In the Aloe Vera group, better responses (50-74%) were achieved in 18% and 11.7% of patients during follow-ups I and II. Whereas in the tacrolimus group, better responses were noticed in 18.1% and 41.1% of patients during follow-up I and II, respectively. The percentage of repigmentation for both groups is shown in **Table 16**.

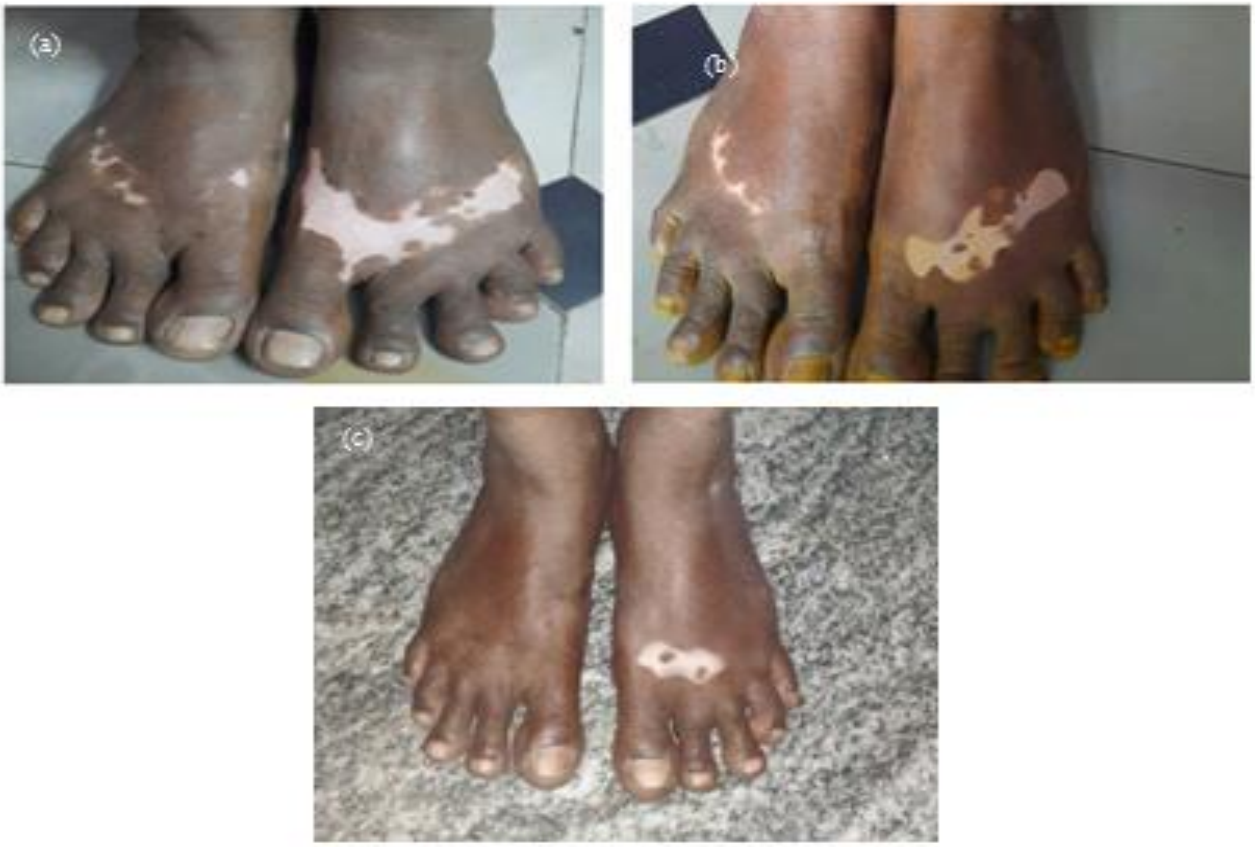

Figure 17: (a) Before Aloe Vera treatment (b) 6 months after treatment (c) 9 months after treatment

Table 16: Target lesions repigmentation rate with natural *Aloe Vera* (n=22) *and Tacrolimus* (n=17)

	3 months		6 months		
% of Re-pigmentation	***A. Vera***	***Tacrolimus***	***A. Vera***	***Tacrolimus***	**Grade**
No change	3 (13.6)	3 (17.6)	3 (13.6)	0 (0)	0
1-24	7 (31.8)	5 (29.4)	2 (9.0)	0 (0)	1
25-49	8 (36.3)	7 (41.1)	10 (45.4)	6 (35.3)	2
50-74	4 (18.1)	2 (11.7)	4 (18.1)	7 (41.1)	3
75-99	0 (0)	0 (0)	3 (13.6)	4 (23.5)	4
100	0 (0)	0 (0)	0 (0)	0 (0)	5

A total of 9% of patients in the Aloe Vera group and 29.4% of patients in the tacrolimus group experienced a stinging or burning sensation during the treatment period. In addition, some patients experienced pruritus and erythema, as shown in **Table 17**. Patients were monitored for 6 months after completion of the therapy regimen to assess pigmentation stability. During this follow-up period, no patient showed any loss of pigmentation.

Table 17: Treatment-related adverse events up to 6 months

Adverse Events	**Aloe Vera (n=22)**	**Tacrolimus (n=17)**
Stinging or Burning sensation, n (%)	2 (9)	5 (29.4)
Pruritus, n (%)	1 (4.5)	12 (70.5)
Erythema, n (%)	0 (0)	10 (58.8)

5.5. Discussion

Drug Prescribing Pattern in vitiligo

Prescription auditing is a part of medical auditing and is a quality improvement procedure. It helps to improve patient care and therapeutic outcomes. Prescription auditing is also an educational activity that, if done regularly, can help to improve prescription quality and enable patients to receive high-quality care (271).

Corticosteroid was the most commonly prescribed drug in our study. Most of the corticosteroids were given topically, followed by oral. This may be due to adverse effects associated with systemic steroid therapy. Topical steroids have added advantages in terms of less systemic absorption, fewer side effects, and convenience to use. Similar to our study Sarkar C et al. also reported that topical steroids were the most commonly prescribed drug in vitiligo (272) Topical corticosteroids (TCS) and topical calcineurin inhibitors (TCIs) play a crucial role in evidence-based therapy, leading to the re-pigmentation of sun-exposed patches in approximately 75% of patients. TCIs, such as a 0.1% tacrolimus ointment applied twice daily for six months, are recommended for use to avoid potential adverse effects on the face and on areas that are especially sensitive to corticosteroids (273) In the present study, betamethasone was the most commonly prescribed corticosteroid, followed by clobetasol propionate. In this study, steroids were prescribed in combination with topical tacrolimus. Tacrolimus is beneficial for younger patients and suitable for sensitive parts of the skin, such as the eyelids (274). According to the study by Jang and colleagues, a triple therapy approach involving systemic corticosteroids, excimer laser treatment, and topical tacrolimus has demonstrated effectiveness in treating recent-onset vitiligo (275). Early intervention with this combination therapy was likely to prevent the disease's progression and achieve more rapid and full repigmentation (275).

Tacrolimus ointment is a well-tolerated, choice for individuals who are unable to undergo routine phototherapy and too concerned about the side effects of long-term topical steroids used (276). The tacrolimus ointment 0.1% was effective in preventing the depigmentation of vitiligo patches and also effective for facial vitiligo (277,278).

The basic fibroblast growth factor (BFGF) related peptides were investigated as a potential repigmenting agent for vitiligo macules (279). Shah et al. described that BFGF-related decapeptide in combination with tacrolimus was more effective than tacrolimus alone among vitiligo patients (280).

The analog of vitamin D_3 was also demonstrated to produce good benefits for psoriasis and vitiligo recently (281). Vitamin D_3 increased the activity of tyrosinase enzymes and stimulates melanin formation (282). Vitamin D supplementation is therapeutically helpful for autoimmune diseases in animal models (283). Thus, a vitamin D supplement may be utilized as a therapy in autoimmune disorders such as vitiligo. A study conducted by Karagüzel et al. illustrated that combined therapy with oral vit. D and topical tacrolimus was more effective than topical tacrolimus alone for repigmentation (284).

Psychosocial effects of vitiligo

Many skin diseases are common in developing nations, which is one of the most common reasons for seeking medical attention (285). In our study, patients with more patch extension (Generalized) in vitiligo had lower QoL than patients with less patch extension (Localized). The probable reason could be the appearance of large numbers of wider patches on visible regions, especially on the face, hands, and feet, which may feel ugly in their overall look and appearance. The feeling of being ugly was also observed among patients with skin diseases such as psoriasis, acne, and alopecia (286). Similar to our observations, some studies have reported an association between disease extension and QoL impairments in vitiligo (287,288).

Generalized vitiligo patients aged >60 years had a lower QoL, whereas, in localized vitiligo, the age group of 25-35 years had a lower QoL. However, a previous study reported that patients aged 25-44 had lower QoL (39). In another study by Karelson et al., the average total DLQI score was highest for people aged 40-49 years (242). Our study found a high mean DLQI score (13.39) in the married generalized group. Females who develop vitiligo after marriage may experience marital issues that

may end in divorce. Young women suffering from vitiligo may be considered unclean and unsuitable for marriage and have a small chance of marriage (289).

Depression is a highly distressing mental health condition characterized by persistent low mood, negative thoughts (feelings of worthlessness), and behavioral changes (such as trouble sleeping, decreased appetite, and a sex drive). It is also a leading cause of suicide and self-harm (290). Our findings revealed that the prevalence of severe and very severe depression was higher in the generalized group than in the localized group. In our study, the prevalence of depression was 89.5%. This rate was higher than Indian study that measured depression in vitiligo (35). Dyschromic lesions in the genital region can have a more profound impact on the sexual perception and development of child patients compared to adults. This suggests that both visible and concealed areas can negatively influence self-perception (291). Patients of both types of vitiligo experienced insomnia, feelings of guilt, anxiety, sexual problems, suicidal ideations, and attempts as depressive symptoms. The rate of suicidal ideation was higher in generalized vitiligo than in localized vitiligo. In our study, the prevalence of suicidal ideation was 10.5%.

A recent systematic review reported that the prevalence of suicidal ideation ranged from 6% to 25% among vitiligo patients (292). In our study, the overall prevalence of anxiety was 18%. On the contrary, a low prevalence of anxiety (4%) was reported in a study by Balaban et al. (293). However, a high prevalence of anxiety was observed in a study conducted by Liu et al. (294).

In our study, 13% of vitiligo patients had sexual problems, which was greater (7.5%) in generalized vitiligo than in localized form. Sexual response and sexual interest are primarily psychological and susceptible to anxiety and depression (295).5.5% of people with vitiligo reported sexual impairment, according to a research study from India (296). In another study from Saudi Arabia, 53.2% of vitiligo patients reported having sexual dysfunction, which was much higher than our study's findings (297).

Synthetic and herbal medicines in vitiligo

Various therapeutic options for the management of vitiligo are corticosteroids, immunomodulators, phototherapy (UVB), photochemotherapy (PUVA), and surgery. These conventional therapies have several limitations in terms of success rate, cost of therapy, and ADRs. Treatment with PUVA increased the risk of skin cancer, corticosteroids induce skin atrophy, and UVB therapy is associated with skin boils (119). Topical corticosteroids are considered as first-line therapy for vitiligo (298) Immunomodulators like tacrolimus or pimecrolimus prove effective for individuals with limited depigmented areas, particularly on the neck and face. (299,300). One of the major findings of this study is that as an herbal therapy, topical Aloe Vera 95% gel and synthetic drug like tacrolimus 0.1% was significantly improved repigmentation and proved to be quite effective in patients suffering with stable form of vitiligo.

For thousands of years, herbal drugs have been widely used for the treatment of many skin diseases such as acne, alopecia, dermatitis, herpes simplex, herpes zoster, pruritus, psoriasis, scabies, skin cancer, wounds, burns, as well as vitiligo (301). Some of the herbal products shown to have valid therapeutic effects in the treatment of vitiligo are ginkgo biloba, khellin, cucumis melo, and picrorhizakurroa (302). Masoumech and Ali reported that the topical *Aloe Vera* gel was found to be safe, with no notable skin reactions (303). In our study, about 86% of the patients from *Aloe Vera* group and 100% from tacrolimus group achieved repigmentation at 24 weeks of follow up. Seneschal et al. found that 65% of patients treated with tacrolimus 0.1% achieved a repigmentation of the target lesion by ≥75% between the baseline and week 24 which is greater than our study results (304). According to Rokni et al., most of the patients (90%) had high improvement in the head and neck area, while a smaller proportion (30%) had good improvement in other body parts (305). Lepe et al. also reported that tacrolimus was more effective than clobetasole (274). However, no studies have been conducted on effectiveness of *Aloe Vera* in vitiligo. But effective of *Aloe Vera* is reported in other dermatological conditions like psoriasis, acne, dermatitis etc. Syed et al. illustrated that about 83.3% was noticed with moderate to excellent improvement or complete resolution of sporiatic lesions (306).

Aloe Vera is a commonly used herb that belongs to the *Liliaceae* family and grows primarily in dry areas. It contains a variety of potentially active substances, such as vitamins, enzymes, minerals, saponin, lignin, etc (307). *Aloe Vera* possesses skin protective properties and is effective against aging, UV-related skin damage, wound healing, chemical carcinogenesis, and psoriasis (307,308).

According to the most widely accepted theory for the development of vitiligo, oxidative stress causes an immunological reaction that damages melanocytes. Increased reactive oxygen species (ROS) due to oxidative stress can cause organelles and molecules to malfunction, provoking an immune response that eventually results in melanocyte death (309). Keratinocytes are the epidermis's primary cell type and connect with melanocytes. Multiple studies have demonstrated that keratinocytes mediate the harmful effects of oxidative stress by producing cytokines that attract autoreactive T cells and interfere with melanocyte signaling, ultimately leading to melanocyte death (310,311). *Aloe Vera's* antioxidant properties are well documented, and it is thought that these properties might be beneficial in vitiligo treatment (312). A study has reported that the anthraquinone components in *Aloe Vera* inhibit free radical-mediated cytotoxic effects and lipid peroxidation during the inflammatory response (313). Anthraquinone also protects the skin by reducing the production of IL-8 and DNA damage. It also increases glutathione (GSH) and superoxide dismutase (SODs) activity by which the skin defends itself against ROS-induced damage (313). *Aloe Vera* increases the proliferation and differentiation of keratinocytes by stabilizing the lysosomal membrane and increasing the expression of TFG1, bFGF, and Vegf-A in fibroblasts (314). *Aloe Vera* works by inhibiting the cyclooxygenase pathway and decreasing arachidonic acid-derived prostaglandin E2. Recently, C-glucosyl chromone, a new anti-inflammatory compound, was identified in gel extracts (308). Alprogen, a glycoprotein from *Aloe Vera*, blocks calcium influx into mast cells, preventing histamine and leukotriene release mediated by antigen-antibody interactions (315). In addition, *Aloe Vera* contains several low molecular weight compounds that can inhibit the production of reactive oxygen free radicals by activated human neutrophils (308). Acemannan is a compound in *Aloe Vera* that promotes tissue repair (316).

In our study, the tacrolimus group experienced more adverse effects at the application site. In the *Aloe Vera* group, only two patients experienced a stinging or burning sensation, and one patient experienced pruritus within the first week of the treatment. These reactions disappeared automatically without the treatment.

6. SUMMARY AND CONCLUSION

6.1. Summary

In the present study, 200 patient's prescriptions were evaluated, and 464 drugs were prescribed. The most commonly prescribed class of drugs was corticosteroids, followed by calcineurin inhibitors, vitamins, basic fibroblast growth factor, moisturizers, antihistamines, and minerals. Topical corticosteroids are considered as a first-line treatment for localized vitiligo. In cases where corticosteroids may not be suitable or for individuals with vitiligo in sensitive areas like the face and genitals, topical calcineurin inhibitors may be prescribed. These agents suppress the immune response, which is thought to be involved in the destruction of melanocytes, the pigment-producing cells. Both topical tacrolimus and corticosteroids treatments aim to encourage melanin production in depigmented areas. The prescription of vitamins, basic fibroblast growth factor, and minerals highlights an integrative approach aiming at nutritional support and tissue regeneration.

Furthermore, the study observed that the higher levels of QoL impairment and depression in individuals with generalized vitiligo compared with localized vitiligo. Generalized vitiligo typically involves a more extensive and widespread loss of skin pigmentation, affecting larger areas of the body. The visible and prominent nature of depigmented patches in multiple body regions may contribute to increased self-consciousness, negative body image, and a greater impact on overall appearance.

Regarding the efficacy and safety of *Aloe Vera* and tacrolimus, majority of the patients were responded positively with *Aloe Vera*. Though tacrolimus had a higher response rate than *Aloe Vera* gel, but it was associated with more adverse events. However, further randomized control trials are needed to evaluate the effectiveness and safety of natural *Aloe Vera* for vitiligo patients.

Study Strengths

This study provides a comprehensive evaluation of vitiligo treatment by examining multiple aspects, including drug prescribing patterns, quality of life (QoL), and depression. This study provides a holistic understanding of the patient experience and treatment outcomes. Additionally, comparing synthetic and herbal drugs prescribed for vitiligo presents valuable insights into the effectiveness of different treatment options and patient preferences. These findings can significantly inform clinical practice and guide future research on vitiligo therapies.

Study Limitations

However, the study has notable limitations. Firstly, being a single-center study limits the generalizability of the findings. Expanding the research to multiple centers would provide a broader understanding of drug prescribing patterns, QoL, and depression among vitiligo patients across various regions and populations. Secondly, the absence of a control group restricts the ability to compare treated patients with untreated ones or those receiving alternative treatments. Addressing these limitations in future research would enhance the robustness and applicability of the findings.

6.2. Conclusion

Based on the results of our study, topical and systemic corticosteroids was most commonly prescribed drugs in vitiligo, followed by topical calcineurin inhibitors in combination. However, ongoing research is essential to enhance the prescription patterns and establish more effective guidelines that can benefit those living with vitiligo. It was also shown that individuals with generalized vitiligo experienced a higher degree of depression and a more significant impact on their QoL when compared to those with localized vitiligo. The QoL is significantly impaired in patients with vitiligo and depression was also found to be prevalent in this population. In order to improve patients' condition, a holistic approach that incorporates psychological interventions, counseling, and effective therapy is recommended. With regards to the efficacy and safety of topical *Aloe Vera* gel and tacrolimus, both therapies were safe and seemed to be fairly effective for managing stable forms of vitiligo. Therefore, natural *Aloe Vera* may be used as an alternative option for the treatment of stable vitiligo. Further longitudinal randomized controlled studies with a larger sample size are recommended to confirm the beneficial effects of *Aloe Vera* and tacrolimus in vitiligo.

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APPENDIX-I

INSTITUTIONAL ETHICS COMMITTEE,
RAJIV GANDHI INSTITUTE OF MEDICAL SCIENCES,
& GENERAL HOSPITAL, KADAPA-516003.

>>><<<

ETHICS COMMITTEE REVIEW LETTER

To

Ref. No: RIMS/IEC/2019/12/19

Sri.S.Padmakar,
Student at Lovely Professional University,
In Domain Ph.D (Pharmacology)
Working as Assistant Professor at P.R.R.M.C.P
Kadapa.

Review Letter Dated: 19.12.2019, IEC, RIMS, Kadapa.

The members of Ethics Committee and discussed the study proposal entitled:

"ASSESSMENT OF DRUG PRESCRIBING PATTERN, QUALITY OF LIFE AND DEPRESSION IN GENERALIZED AND LOCALIZED VITILIGO PATIENTS OF ANDHRA PRADESH."

Under the guidance of DR.R.VENKATA RAMUDU, ASST.PROF. Dept., of PSYCIATRY, RIMS, Kadapa. Ethics Committee has approved this study. None of the members voted against the study.

The present approval is valid only for 3 years Investigator must take the reapproval after three years. Any change, modification or deviation in the protocol or any adverse event must be informed to Ethics committee. Any protocol modification or amendment must receive IEC approval.

CHAIR PERSON
INSTITUTIONAL ETHICS COMMITTEE,
RAJIV GANDHI INSTITUTE OF MEDICAL SCEINCES
& GENERAL HOSPITAL, KADAPA-516003.

APPENDIX- II

INFORMED CONSENT FORM

I,_____exercising my free power of choice, hereby give my consent

to be included as a patient in the clinical study –**Assessment of drug prescribing pattern, quality of life and depression in generalized and localized vitiligo patients of Andhra Pradesh.**

Duration of study – 3 years

I agree to the following

1. I understand that I will not be given any new study medication for participation in the study.
2. I also understand that, since I'm already taking the drug as prescribed as doctor, I become eligible be included in the study.
3. I have been informed to my satisfaction by the investigator about the purpose of the clinical study and study procedures including the investigations to monitor and safeguard my body functions.
4. I have been given the opportunity to question on all the aspects of the study, and I have understood the advice and information as provided.
5. I have informed about all medications that I have taken in the recent past and those I am currently taking for the present and past disease/disorders.
6. I also understand that the information thus gathered will be helpful in optimizing by drug therapy.

7. I understand that medical records that reveal my identity will remain confidential except that they will be provided as noted above or as may be required by law.

Signature of the patient

If illiterate,
Thumb print of participant

Study Investigators:
NAME
Contact Details-
Gmail-

I confirm that I have explained the nature, purpose, and possible benefits of the

above Study to _____

Signature of the Investigator with date

Study Site: **Government General Hospital, RIMS, Kadapa, A.P., India.**

APPENDIX-III

RAJIV GANDHI INSTITUTE OF MEDICAL SCIENCES (RIMS**)**

Government General Hospital (GGH), Kadapa, Andhra Pradesh 516002.

PATIENT DATA COLLECTION FORM

Study title: **To compare the synthetic and herbal drugs prescribed in vitiligo patients**

Name:	**O.P number:**	**Date:**
Age:	**Gender:**	

Patient chief complaints:

Past medical and medication history:

Diagnosis:

Duration of disease:

Location:

Medication Prescribed:

Percentage of re-pigmentation:

Follow up- I:

Follow up- II:

ADVERSE DRUG REACTION IF ANY:

Is there any adverse drug reaction identified? Yes ____ No ____

If yes, describe the adverse drug reaction

APPENDIX-III

RAJIV GANDHI INSTITUTE OF MEDICAL SCIENCES (RIMS)

Government General Hospital (GGH), Kadapa, Andhra Pradesh 516002.

PATIENT DATA COLLECTION FORM

Study title: Assessment of drug prescribing pattern in vitiligo

Patient Name: **Admission No:**

Age/Gender:

Date of Admission:

Department/ Ward/Unit:

Name of the Consultant Doctor/Physician:

Chief Complaints:

Provisional/Admitting diagnosis:

Duration of disease:

Past medical history:

Past medication history:

CONFORMATORY DIAGNOSIS:

PROGRESS CHART:

TREATMENT PROVIDED

DERMATOLOGY LIFE QUALITY INDEX (DLQI)

APPENDIX- IV

Name:…… **Score:** ……

Date: ……

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick ( ) one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	❒ ❒ ❒ ❒		
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	❒ ❒ ❒ ❒		
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
7.	Over the last week, has your skin prevented you from **working** or **studying**?	Yes No	❒	Not relevant	❒
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	❒ ❒		
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	❒ ❒ ❒ ❒	Not relevant	❒

HAMILTON DEPRESSION RATING SCALE (HAM-D)

Patient Name_____ **Today's Date:**

The HAM-D is designed to rate the severity of depression in patients. Although it contains 21 areas, calculate the patient's score on the first 17 answers.

---

1. DEPRESSED MOOD
(Gloomy attitude, pessimism about the future, feeling of sadness, tendency to weep)
0 = Absent
1 = Sadness, etc.
2 = Occasional weeping
3 = Frequent weeping
4 = Extreme symptoms

---

2. FEELINGS OF GUILT
0 = Absent
1 = Self-reproach, feels he/she has let people down
2 = Ideas of guilt
3 = Present illness is a punishment; delusions of guilt
4 = Hallucinations of guilt

---

3. SUICIDE
0 = Absent
1 = Feels life is not worth living
2 = Wishes he/she were dead
3 = Suicidal ideas or gestures
4 = Attempts at suicide

---

4. INSOMNIA - Initial
(Difficulty in falling asleep)
0 = Absent
1 = Occasional
2 = Frequent

---

5. INSOMNIA - Middle
(Complains of being restless and disturbed during the night. Waking during the night.)
0 = Absent
1 = Occasional
2 = Frequent

---

6. INSOMNIA - Delayed
(Waking in early hours of the morning and unable to fall asleep again)
0 = Absent
1 = Occasional
2 = Frequent

---

7. WORK AND INTERESTS
0 = No difficulty
1 = Feelings of incapacity, listlessness, indecision and vacillation
2 = Loss of interest in hobbies, decreased social activities
3 = Productivity decreased
4 = Unable to work. Stopped working because of present illness only. (Absence from work after treatment or recovery may rate a lower score).

---

8. RETARDATION
(Slowness of thought, speech, and activity; apathy; stupor.)
0 = Absent
1 = Slight retardation at interview
2 = Obvious retardation at interview
3 = Interview difficult
4 = Complete stupor

---

9. AGITATION
(Restlessness associated with anxiety.)
0 = Absent
1 = Occasional
2 = Frequent

---

10. ANXIETY - PSYCHIC
0 = No difficulty
1 = Tension and irritability
2 = Worrying about minor matters
3 = Apprehensive attitude
4 = Fears

HAMILTON DEPRESSION RATING SCALE (HAM-D)

11. ANXIETY - SOMATIC
Gastrointestinal, indigestion
Cardiovascular, palpitation, Headaches
Respiratory, Genito-urinary, etc.
0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

---

12. SOMATIC SYMPTOMS - GASTROINTESTINAL
(Loss of appetite , heavy feeling in abdomen; constipation)
0 = Absent
1 = Mild
2 = Severe

---

13. SOMATIC SYMPTOMS - GENERAL
(Heaviness in limbs, back or head; diffuse backache; loss of energy and fatiguability)
0 = Absent
1 = Mild
2 = Severe

---

14. GENITAL SYMPTOMS
(Loss of libido, menstrual disturbances)
0 = Absent
1 = Mild
2 = Severe

---

15. HYPOCHONDRIASIS
0 = Not present
1 = Self-absorption (bodily)
2 = Preoccupation with health
3 = Querulous attitude
4 = Hypochondriacal delusions

---

16. WEIGHT LOSS
0 = No weight loss
1 = Slight
2 = Obvious or severe

17. INSIGHT
(Insight must be interpreted in terms of patient's understanding and background.)
0 = No loss
1 = Partial or doubtfull loss
2 = Loss of insight

TOTAL ITEMS 1 TO 17: _____
0 - 7 = Normal
8 - 13 = Mild Depression
14-18 = Moderate Depression 19 - 22 = Severe Depression

18. DIURNAL VARIATION
(Symptoms worse in morning or evening. Note which it is.)
0 = No variation
1 = Mild variation; AM ( ) PM ( )
2 = Severe variation; AM ( ) PM ( )

---

19. DEPERSONALIZATION AND DEREALIZATION
(feelings of unreality, nihilistic ideas)
0 = Absent
1 = Mild
2 = Moderate
3 = Severe
4 = Incapacitating

---

20. PARANOID SYMPTOMS
(Not with a depressive quality)
0 = None
1 = Suspicious
2 = Ideas of reference
3 = Delusions of reference and persecution
4 = Hallucinations, persecutory

---

21. OBSESSIONAL SYMPTOMS
(Obsessive thoughts and compulsions against which the patient struggles)
0 = Absent
1 = Mild
2 = Severe

అనుబంధం- II

సమాచార సమ్మతి ఫారమ్

నేను,_____నా ఎంపిక యొక్క ఉచిత అధికారాన్ని అమలు చేస్తున్నాను, దీని ద్వారా నాకు ఇవ్వండి సమ్మతి

క్లినికల్ స్టడీలో రోగిగా చేర్చబడాలి - **ఆంధ్రప్రదేశ్‌లోని సాధారణీకరించిన మరియు స్థానికీకరించిన బొల్లి రోగులలో ఔషధాలను సూచించే నమూనా, జీవన నాణ్యత మరియు నిరాశను అంచనా వేయడం.**

అధ్యయనం యొక్క వ్యవధి - 3 సంవత్సరాలు

నేను ఈ క్రింది వాటిని అంగీకరిస్తున్నాను

1. ఇందులో పాల్గొనడం కోసం నాకు కొత్త అధ్యయన మందులు ఏవీ ఇవ్వబడవని నేను అర్థం చేసుకున్నాను చదువు.
2. నేను ఇప్పటికే డాక్టర్ సూచించినట్లుగా ఔషధాన్ని తీసుకుంటున్నాను కాబట్టి, నేను చేర్చడానికి అర్హత పొందానని కూడా నేను అర్థం చేసుకున్నాను చదువు.
3. నా శరీరాన్ని పర్యవేక్షించడానికి మరియు రక్షించడానికి పరిశోధనలతో సహా క్లినికల్ స్టడీ మరియు స్టడీ ప్రొసీజర్‌ల ప్రయోజనం గురించి పరిశోధకుడి ద్వారా నాకు సంతృప్తికరంగా తెలియజేయబడింది. విధులు.
4. అధ్యయనం యొక్క అన్ని అంశాలపై ప్రశ్నించడానికి నాకు అవకాశం ఇవ్వబడింది మరియు అందించిన సలహాలు మరియు సమాచారాన్ని నేను అర్థం చేసుకున్నాను.
5. నేను ఇటీవలి కాలంలో తీసుకున్న అన్ని మందుల గురించి మరియు ప్రస్తుతం మరియు గతం కోసం నేను ప్రస్తుతం తీసుకుంటున్న మందుల గురించి తెలియజేసాను వ్యాధి / రుగ్మతలు.
6. ఈ విధంగా సేకరించిన సమాచారం ఔషధం ద్వారా ఆప్టిమైజ్ చేయడంలో సహాయకరంగా ఉంటుందని కూడా నేను అర్థం చేసుకున్నాను చికిత్స.

7. నా గుర్తింపును బహిర్గతం చేసే వైద్య రికార్డులు గోప్యంగా ఉంచబడతాయని నేను అర్థం చేసుకున్నాను, అవి పైన పేర్కొన్న విధంగా అందించబడతాయి లేదా వారికి అవసరమైన విధంగా అందించబడతాయి చట్టం.

రోగి యొక్క సంతకం

నిరక్షరాస్యులైతే,
పాల్గొనేవారి బొటనవేలు ముద్రణ

అధ్యయన పరిశోధకులు
సంప్రదింపు వివరాలు-

నేను స్వభావం, ప్రయోజనం మరియు సాధ్యమయ్యే ప్రయోజనాలను

వివరించినట్లు ధృవీకరిస్తున్నాను పై అధ్యయనం కు ____

తేదీతో పరిశోధకుడి సంతకం

అధ్యయన సైట్:

Government General Hospital, RIMS, Kadapa, A.P., India.

డెర్మటాలజీ లైఫ్ క్వాలిటీ ఇండెక్స్ (DLQI)

పేరు : ..... **స్కోర్:** .....

తేదీ: .....

ఈ ప్రశ్నాపత్రం యొక్క లక్ష్యం గత వారంలో మీ చర్మ సమస్య మీ జీవితాన్ని ఎంత ప్రభావితం చేసిందో కొలవడమే. దయచేసి ప్రతి ప్రశ్నకు ఒక పెట్టెను ( ) టిక్ చేయండి.

1.	పైగా ది చివరిది వారం, ఎలా **దురద** , **గొంతు** , **బాధాకరమైన** లేదా **కుట్టడం** మీ చర్మం ఉందా?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	
2.	పైగా ది చివరిది వారం, ఎలా **ఇబ్బందిపడ్డాడు** లేదా **స్వీయ చేతనైన** మీరు మీ చర్మం కారణంగా ఉన్నారా?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	
3.	పైగా ది చివరిది వారం, ఎలా చాలా కలిగి ఉంది మీ చర్మం జోక్యం చేసుకున్నారు మీతో వెళ్తున్నారు **షాపింగ్** లేదా చూస్తున్నాను తర్వాత మీ **ఇల్లు** లేదా **తోట** ?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
4.	పైగా ది చివరిది వారం, ఎలా చాలా కలిగి ఉంది మీ చర్మం ప్రభావితం చేసింది ది మీరు వేసుకునే **బట్టలు ?**	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
5.	పైగా ది చివరిది వారం, ఎలా చాలా కలిగి ఉంది మీ చర్మం ప్రభావితం ఏదైనా **సామాజిక** లేదా **విశ్రాంతి** కార్యకలాపాలు?	చాలా చాలా కొంచెం కాదు అవు ను కదు	❒ ❒ ❒ ❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
6.	పైగా ది చివరిది వారం, ఎలా చాలా కలిగి ఉంది మీ చర్మం చేసింది అది మీరు ఏదైనా చేయడం కష్టం **క్రీడ** ?	చాలా కొంచెం అస్సలు కుదరదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
7.	పైగా ది చివరిది వారం, కలిగి ఉంది మీ చర్మం అడ్డుకున్నారు మీరు నుండి **పని చేస్తున్నారా** లేదా **చదువుతున్నారా** ? ఉంటే "లేదు", పైగా ది చివరిది వారం ఎలా చాలా కలిగి ఉంది మీ చర్మం ఉంది పనిలో సమస్య లేదా **అభ్యసించడం** ?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
8.	గత వారంలో, మీ చర్మం ఎంత సమస్యలను సృష్టించింది తో మీ **భాగస్వామి** లేదా ఏదైనా యొక్క మీ **దగ్గరగా స్నేహితులు** లేక **బంధువులా** ?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
9.	పైగా ది చివరిది వారం, ఎలా చాలా కలిగి ఉంది మీ చర్మం ఏదైనా కలిగించింది **లైంగిక ఇబ్బందులు** ?	చాలా చాలా కొంచెం కాదు	❒ ❒ ❒ ❒	కాదు సంబంధిత ❒
10.	**చికిత్సలో** ఎంత సమస్య ఉంది కోసం మీ చర్మం ఉంది, కోసం ఉదాహరణ ద్వారా తయారు చేయడం మీ ఇల్లు గజిబిజిగా లేదా సమయం తీసుకుంటున్నారా?		❒	కాదు సంబంధిత

డెర్మటాలజీ లైఫ్ క్వాలిటీ ఇండెక్స్ (DLQI) - ఉపయోగం కోసం సూచనలు

డెర్మటాలజీ లైఫ్ క్వాలిటీ ఇండెక్స్ ప్రశ్నాపత్రం పెద్దలలో, అంటే వయస్సు పైబడిన రోగులలో ఉపయోగం కోసం రూపొందించబడింది.
16. ఇది స్వీయ వివరణాత్మకమైనది మరియు వివరణాత్మక వివరణ అవసరం లేకుండా దాన్ని పూరించమని అడిగిన రోగికి అందజేయవచ్చు. ఇది సాధారణంగా ఒకటి లేదా రెండు నిమిషాల్లో పూర్తవుతుంది .

స్కోరింగ్

ప్రతి ప్రశ్న యొక్క స్కోరింగ్ క్రింది విధంగా ఉంది:

చాలా చాలా	స్కోర్ చేశాడు 3
ఎ చాలా	స్కోర్ చేసింది 2
ఎ తక్కువ	స్కోర్ చేసింది 1
కాదు వద్ద అన్నీ	స్కోర్ చేశాయి 0
కాదు సంబంధిత	స్కోర్ 0
ప్రశ్న 7, 'పని నిరోధించబడింది లేదా చదువుతున్నాను'	సాధించాడు 3

గరిష్టంగా 30 మరియు కనిష్టంగా 0 వచ్చే ప్రతి ప్రశ్న యొక్క స్కోర్‌ను సంగ్రహించడం ద్వారా లెక్కించబడుతుంది. ఎక్కువ స్కోర్, జీవిత నాణ్యత మరింత ఎక్కువగా ఉంటుంది . మందగించిన.

DLQI స్కోర్‌ల అర్థాన్ని ఎలా అర్థం చేసుకోవాలి

0-1	రోగి జీవితంపై ఎటువంటి ప్రభావం ఉండదు
2-5	**రోగి జీవితంపై చిన్న ప్రభావం**
6-10	**రోగి జీవితంపై మితమైన ప్రభావం**
11-20	**రోగి జీవితంపై చాలా పెద్ద ప్రభావం**
21-30	**రోగి జీవితంపై చాలా పెద్ద ప్రభావం**

HAMILTON DEPRESSION RATING SCALE (HAM-D)

రోగి పేరు_____ ఈరోజు తేదీ _____

ది HAM-D ఉంది రూపొందించబడింది కు రేటు ది తీవ్రత యొక్క నిరాశ లో రోగులు. అయినప్పటికీ అది కలిగి ఉంటుంది 21 ప్రాంతాలు, లెక్కించు ది మొదటి 17 లో రోగి యొక్క స్కోరు సమాధానాలు.

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1. అణగారిన మానసిక స్థితి
(దిగులుగా వైఖరి, నిరాశావాదం గురించి ది భవిష్యత్తు, అనుభూతి యొక్క విచారం, ధోరణి కు ఏడుపు)
0 = హాజరుకాలేదు
1 = విచారం మొదలైనవి.
2 = అప్పుడప్పుడు ఏడుపు 3
= తరచుగా ఏడుపు
4 = విపరీతమైన లక్షణాలు

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2. భావాలు అపరాధం
0 = హాజరుకాలేదు
1 = స్వీయ నింద, అతను/ ఆమె ప్రజలను నిరాశపరిచినట్లు అనిపిస్తుంది
2 = అపరాధం యొక్క ఆలోచనలు
3 = ప్రస్తుత అనారోగ్యం ఒక శిక్ష; అపరాధం యొక్క భ్రమలు
4 = అపరాధ భ్రాంతులు

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3. ఆత్మహత్య
0 = హాజరుకాలేదు
1 = జీవితం జీవించడానికి విలువైనది కాదని భావించడం 2 = అతను/ఆమె చనిపోయారని కోరుకోవడం
3 = ఆత్మహత్య ఆలోచనలు లేదా సంజ్ఞలు 4 = ఆత్మహత్య ప్రయత్నాలు

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4. నిద్రలేమి - ప్రారంభ (
పడిపోవడంలో ఇబ్బంది నిద్రలో) 0 = గైర్హాజరు
1 = అప్పుడప్పుడు
2 = తరచుగా

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5. నిద్రలేమి - మధ్య
(రాత్రి సమయంలో అశాంతి మరియు కలవరానికి గురవుతున్నట్లు ఫిర్యాదులు. రాత్రి సమయంలో మేల్కొలపడం.)
0 =
హాజరుకాలేదు
1 =
అప్పుడప్పుడు
2 = తరచుగా

6. నిద్రలేమి - ఆలస్యమైంది
(ఉదయం తెల్లవారుజామున మేల్కొలపడం మరియు మళ్లీ నిద్రపోలేకపోవడం)
0 = హాజరుకాలేదు
1 = అప్పుడప్పుడు
2 = తరచుగా

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7. పని మరియు ఆసక్తులు
0 = ఇబ్బంది లేదు
1 = అసమర్థత , ఉదాసీనత , అసమర్థత యొక్క భావాలు మరియు వాసిలేషన్
2 = అభిరుచులపై ఆసక్తి కోల్పోవడం , సామాజిక కార్యకలాపాలు తగ్గడం
3 = ఉత్పాదకత తగ్గింది
4 = పని చేయడం సాధ్యం కాదు. ప్రస్తుత అనారోగ్యం కారణంగా మాత్రమే పని మానేశారు . (చికిత్స లేదా కోలుకున్న తర్వాత పనికి హాజరుకాకపోవడం తక్కువ స్కోర్‌ని రేట్ చేయవచ్చు).

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8. రిటార్డేషన్
(ఆలోచన, ప్రసంగం మరియు కార్యాచరణ మందగించడం ; ఉదాసీనత; మూర్ఖత్వం.)
0 = హాజరుకాలేదు
1 = ఇంటర్వ్యూలో కొంచెం రిటార్డేషన్
2 = ఇంటర్వ్యూలో స్పష్టమైన రిటార్డేషన్ 3
= ఇంటర్వ్యూ కష్టం
4 = పూర్తి మూర్ఖత్వం

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9. ఆందోళన
(ఆందోళనతో ముడిపడి ఉన్న విశ్రాంతి .) 0 =
హాజరుకానిది
1 = అప్పుడప్పుడు
2 = తరచుగా

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10. ఆందోళన - సైకిక్
0 = ఇబ్బంది లేదు
1 = టెన్షన్ మరియు చిరాకు
2 = చిన్న విషయాల గురించి చింతించడం 3 = భయపడే వైఖరి
4 = భయాలు

HAMILTON DEPRESSION RATING SCALE (HAM-D)

11. ఆందోళన - సోమాటిక్ జీర్ణకోశ, అజీర్ణం కార్డియోవాస్కులర్, దడ, తలనొప్పి శ్వాసకోశ, జెనిటో-మూత్ర, మొదలైనవి
0 = హాజరుకాలేదు
1 = తేలికపాటి
2 = మితమైన
3 = తీవ్రమైన
4 = అసమర్థత

12. సోమాటిక్ లక్షణాలు - జీర్ణశయాంతర
(నష్టం యొక్క ఆకలి, భారీ భావన లో ఉదరం; మలబద్ధకం)
0 = హాజరుకాలేదు
1 = తేలికపాటి
2 = తీవ్రమైన

13. సోమాటిక్ లక్షణాలు - సాధారణం (భారం లో అవయవాలను, తిరిగి లేదా తల; విస్తరించిన వెన్ను నొప్పి; శక్తి నష్టం మరియు అలసట) 0 = గైర్హాజరు
1 = తేలికపాటి
2 = తీవ్రమైన

14. జననేంద్రియ లక్షణాలు
(లిబిడో కోల్పోవడం, బహిష్టు ఆటంకాలు) 0 = హాజరుకాలేదు
1 = తేలికపాటి
2 = తీవ్రమైన

15. హైపోకాండ్రియాసిస్
0 = ప్రస్తుతం లేదు
1 = స్వీయ-శోషణ (శరీర)
2 = ఆరోగ్యం పట్ల నిమగ్నత 3 = క్రమరహిత వైఖరి
4 = హైపోకాండ్రియాకల్ భ్రమలు

16. బరువు తగ్గడం
0 = బరువు తగ్గడం లేదు
1 = స్వల్ప
2 = స్పష్టమైన లేదా తీవ్రమైన

17. అంతర్దృష్టి
(అంతర్దృష్టిని రోగి యొక్క పరంగా అర్థం చేసుకోవాలి అవగాహన మరియు నేపథ్యం.)
0 = నష్టం లేదు
1 = పాక్షికం లేదా సందేహాస్పదమైనది నష్టం 2 = అంతర్దృష్టి కోల్పోవడం

TOTAL ITEMS 1 TO 17: _____
0 - 7 = Normal
8 - 13 = Mild Depression
14-18 = Moderate Depression
19 - 22 = Severe Depression
≥ 23 = Very Severe Depression

18. రోజువారీ వైవిధ్యం
(ఉదయం లేదా సాయంత్రం లక్షణాలు అధ్వాన్నంగా ఉంటాయి. అది ఏమిటో గమనించండి.)
0 = వైవిధ్యం లేదు
1 = తేలికపాటి వైవిధ్యం; AM ( ) PM ( ) 2 = తీవ్రమైన వైవిధ్యం; ఉదయం ( ) PM ( )

19. వ్యక్తిగతీకరణ మరియు డీరియలైజేషన్
(అవాస్తవ భావాలు, నిహిలిస్టిక్ ఆలోచనలు)
0 = హాజరుకాలేదు
1 = తేలికపాటి
2 = మితమైన
3 = తీవ్రమైన
4 = అసమర్థత

20. పారానోయిడ్ లక్షణాలు (
నిస్పృహతో కాదునాణ్యత) 0 = ఏదీ లేదు
1 = అనుమానాస్పదమైనది
2 = సూచనల ఆలోచనలు
3 = రిఫరెన్స్ మరియు పెర్సిక్యూషన్ యొక్క భ్రమలు 4 = భ్రాంతులు, వేధింపులు

21. అబ్సెషనల్ లక్షణాలు
(రోగి పోరాడే అబ్సెసివ్ ఆలోచనలు మరియు బలవంతం)
0 = హాజరుకాలేదు
1 = తేలికపాటి
2 = తీవ్రమైన

TANGIBLE OUTCOMES

List of Publications

1. **Padmakar S**, Kumari S, Pal B. A Study on Drug Prescribing Patterns in Vitiligo Patients of Andhra Pradesh in a Tertiary Care Teaching Hospital**. The Journal of the Association of Physicians of India**. 2024 May;72(5):61-64.

2. **Padmakar S**, Kumar GA, Khurana N, Kumari S, Pal B. Efficacy and safety of natural Aloe Vera gel in the treatment of stable vitiligo. **Clinical Epidemiology and Global Health.** 2023:101332.

3. **Padmakar S**, Ramudu RV, Kumari S, Pal B. Assessment of quality of life and depression in generalized and localized vitiligo patients. **Journal of Krishna Institute of Medical Sciences University.** 2023; 12(1):24-31.

4. Pal B, Kumari S, Kaur M, Wadhwa P, Murti K, Kumar R, Pandey K, Siddiqui NA, Dhingra S, **Padmakar S**. Barriers to the effective management and prevention of post kala-azar dermal leishmaniasis (PKDL) in the Indian subcontinent. **Medical Journal Armed Forces India.** 2023;79(5):500-505.

5. **Padmakar S**, Murti K, Pandey K, Kumari S, Kumar R, Siddiqui NA, Pal B. Suicidal ideation associated with vitiligo-A systematic review of prevalence and assessment. **Clinical Epidemiology and Global Health**. 2022:101140.

6. Saikarthik P, Reddy VH, Rafi SM, Basha VW, **Padmakar S**. A Systematic Review on Prevalence and Assessment of Sexual Dysfunction in Vitiligo. **The Journal of the Association of Physicians of India**. 2022;70(10):11-2.

7. **Padmakar S**, Alishar S, Tabasum MA. A case report on Alagille syndrome and its clinical features. International **Journal of Research in Pharmaceutical Sciences**. 2021;12:18-21.

8. **Padmakar S**. A Case Report on Neurofibromatosis Associated with Infective Mass Tumor**. Indian Journal of Pharmacy & Drugs Studies**. 2021;19:34-6.

9. **Padmakar S**. Slurred speech and tremors resulting from antipsychotic therapy in a patient with bipolar disorder: a case report. **Asian Journal of Pharmaceutical and Clinical Research**. 2021;29:1-2.

Conference and proceedings

1. Participated in "4th Indo Swiss Virtual International Conference Current Scenario & Challenges in Pharmacy Practice & Pharmaceutical Sciences" 2-day conference at Vijaya Institute of Pharmaceutical Sciences for women, Vijayawada, Andhra Pradesh, May 20th-21st May 2022.

2. Participated in "Opportunities and challenges in clinical Research and Pharmacovigilance in India" 2-day conference at Seven Hills College of Pharmacy" 2-day conference at Tirupati, Andhra Pradesh, 17th-18th Sep 2021.

3. Participated in "1st International Conference on Health Economics and Outcomes Research" a 2-day conference at Narayana Pharmacy College, Nellore, Andhra Pradesh, 26th & 27th April, 2019.