Assessing the Relationship between Vitiligo and Major Depressive Disorder Severity: A Cross-Sectional Study

Amr Molla, Raed Jannadi, Hamza Alayoubi, Haya Altouri, Maryam Balkhair, Dareen Hafez

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Abstract

Background: Vitiligo, a common dermatological disorder in Saudi Arabia, is associated with significant psychological impacts. This study explores the relationship between vitiligo and the severity of Major Depressive Disorder (MDD), highlighting the broader implications on mental health among affected individuals.

Objective: This study aims to assess the prevalence and predictors of depression among adult vitiligo patients. Moreover, examining the relationship between MDD severity and vitiligo, utilizing the VASI and Patient Health Questionnaire-9 (PHQ-9) scales to assess the extent and severity of both conditions.

Methods: Employing a cross-sectional design, the research utilized the Vitiligo Area Severity Index (VASI) and the Patient Health Questionnaire-9 (PHQ-9) to measure the extent of vitiligo and depression severity respectively. The study involved 340 diagnosed vitiligo patients from various healthcare settings. Logistic and ordinal regression analysis were applied to evaluate the impact of sociodemographic variables and vitiligo types on MDD severity.

Results: the prevalence of MDD was 58.8%. The analysis further revealed that depression severity varied notably; 24.7% of patients experienced mild depression, 31.1% moderate, 22.6% moderately severe, and 21.6% severe depression. Female patients, those who are divorced or have lower incomes, and patients with acrofacial or vulgaris types of vitiligo experience more severe depression.

Conclusions: The findings suggest that vitiligo contributes to an increased risk of severe depression, highlighting the need for integrated dermatological and psychological treatment approaches to address both the physical and mental health aspects of the disease. Clinical Trial: NAD

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Abstract

Background: Vitiligo, a common dermatological disorder in Saudi Arabia, is associated with significant psychological impacts. This study explores the relationship between vitiligo and the severity of Major Depressive Disorder (MDD), highlighting the broader implications on mental health among affected individuals.

Objectives: To assess the prevalence and predictors of depression among adult vitiligo patients, and to examine the relationship between MDD severity and vitiligo.

Methods: Employing a cross-sectional design, the research utilized the Vitiligo Area Severity Index (VASI) and the Patient Health Questionnaire-9 (PHQ-9) to measure the extent of vitiligo and depression severity respectively. The study involved 340 diagnosed vitiligo patients from various healthcare settings. Logistic and ordinal regression analysis were applied to evaluate the impact of sociodemographic variables and vitiligo types on MDD severity.

Results: The prevalence of MDD was 58.8% (200 out of 340 participants). Depression severity varied notably: 24.7% of patients experienced mild depression, 31.1% moderate, 22.6% moderately severe, and 21.6% severe depression. Female patients had higher odds of severe depression compared to males (aOR = 3.14, 95% CI: 1.93-5.1, P < .001). Age was inversely related to depression severity, with patients over 60 years showing significantly lower odds (aOR = 0.1, 95% CI: 0.03-0.39, P < .001). Lower income was associated with higher depression severity (aOR = 10.2, 95% CI: 3.25-31.8, P < .001). Vitiligo types also influenced depression severity; vulgaris (aOR = 5.3, 95% CI: 2.6-10.9, P < .001) and acrofacial vitiligo (aOR = 2.8, 95% CI: 1.5-5.1, P < .001) were significantly associated with higher depression levels compared to focal vitiligo.

Conclusion: The findings suggest that vitiligo contributes to an increased risk of severe depression, highlighting the need for integrated dermatological and psychological treatment approaches to address both the physical and mental health aspects of the disease.

Keywords: Vitiligo, Major Depressive Disorder (MDD), PHQ-9, Depression Severity, Saudi Arabia, Cross-Sectional Study

Introduction

Skin, the largest organ of the human body, serves as the visible exterior that covers internal structures. Vitiligo is a chronic, relapsing skin disorder characterized by well-defined milky-white, depigmented macules and patches resulting from the destruction of melanocytes [1]. This condition is often associated with other autoimmune disorders, particularly thyroid autoimmune diseases. Beyond the physical manifestations, vitiligo imposes a significant psychological burden due to its impact on cosmetic appearance, leading to potential stigmatization and misconceptions within social interactions. Consequently, individuals with vitiligo are at an elevated risk of developing major depressive disorder (MDD) [2].

Major depressive disorder is marked by persistent sadness, loneliness, and disinterest, typically triggered by fear, trauma, or other significant stressors. This condition not only affects mood and interest but also impairs cognitive functions, influencing emotions, sleep, and appetite. These changes can alter behavior, making individuals appear irritable or despondent, with severe cases potentially leading to suicidal ideation [3]. The prevalence of MDD for lifetime is 16.2% [4]. According to a meta-analysis study, the prevalence of depression among vitiligo patients is 25.3% [5].

Patients with vitiligo often exhibit a dysregulated immune system, which may be exacerbated by concomitant depression. Clinical and animal studies suggest that depression can aggravate vitiligo, as both conditions share similar leukocyte signatures and inflammatory genetic mechanisms associated with systemic autoimmune inflammation. This overlap suggests a shared pathophysiological pathway, potentially increasing the risk of an inflammatory brain-skin axis, offering new insights into their bidirectional relationship and their classification within a socially stress-stigmatized model [6].

Recent studies have highlighted specific gene expression profiles associated with vitiligo, revealing significant molecular mechanisms underlying the condition. Changes in the expression of interleukin (IL)-10 family cytokines (IL26, IL-28A, IL28B, IL29) and their receptor subunits (IL20RB, IL22RA2, IL28RA), along with other genes related to melanocyte function such as MDM1, IFNA1, IFNB1, IFNG, and ICAM1, have been observed in the skin and peripheral blood mononuclear cells (PBMC) of vitiligo patients. These genes are implicated in pathways regulating melanocyte survival, apoptosis, development, migration, and melanogenesis, suggesting their role in vitiligo pathogenesis [7]. Additionally, increased dopamine levels and altered expression of enzymes in the dopamine pathway, including DDC, MAOA, and MAOB, have been noted in vitiligo patients' skin and blood. This suggests that the dopamine pathway may influence melanogenesis directly or through the melanocortin pathway [8]. Furthermore, another study supports the role of IL-10 family cytokines in vitiligo pathogenesis, particularly emphasizing the involvement of IL-22. Altered expression patterns of IL20RB, IL22RA2, IL-28A, IL28B, IL28RA, MDM1, IFNA1, IFNB1, IFNG, and ICAM1 in vitiligo skin

and PBMCs further underscore their significance in the disease [9].

Global studies indicate that vitiligo significantly affects mental health, often leading individuals to self-isolation and avoidance of social gatherings, thereby severely affecting quality of life. Acceptance and active coping can mitigate stress and anxiety; however, the appearance-related impacts of vitiligo and MDD can lead to social withdrawal, sensitivity to perceived societal judgments, and overall deterioration in personal and professional life, culminating in diminished self-esteem and confidence [10, 11].

Inspired by the Psoriasis Area and Severity Index (PASI), the Vitiligo Area Severity Index (VASI) employs hand units to quantify affected skin areas, where one hand unit approximates one percent of total body skin. The VASI score is calculated by multiplying the area of vitiligo (in hand units) by the degree of depigmentation within each measured patch [12].

This study aims to assess the prevalence and predictors of depression among adult vitiligo patients. Moreover, examining the relationship between MDD severity and vitiligo, utilizing the VASI and Patient Health Questionnaire-9 (PHQ-9) scales to assess the extent and severity of both conditions.

Methodology

Study Design and Sample

This is a cross-sectional study aimed to investigate the relationship between MDD and vitiligo in Saudi Arabia. The study was targeting adult patients diagnosed with vitiligo based on VASI and Wood's lamp examination, that revealed depigmented patches or macules that occurs at typical vitiligo sites. A total of 340 adult vitiligo patients were selected by simple random sampling method for the study, which was conducted from April 2023 to April 2024 at participating hospitals across Saudi Arabia.

The inclusion and exclusion criteria for participation were as follows:

Inclusion Criteria:

a. Patients diagnosed with vitiligo, as determined by the Vitiligo Area and Severity Index (VASI).
b. Ages ranging from 18 to 85 years.
c. Resident in Saudi Arabia during the study period.
d. Able to provide informed consent and complete the study assessments.

VASI score measures the extent and severity of vitiligo by evaluating the body's surface area affected by vitiligo and quantifies the degree of skin depigmentation. The index divides the body into segments, with each segment's depigmentation severity scored on a scale from 0% (no depigmentation) to 100% (complete depigmentation). The score for each segment is calculated by multiplying the affected body surface area percentage by the depigmentation level, which provides a comprehensive measure of the disease's severity [13].

Exclusion Criteria:

a. Known pre-existing mental health disorders prior to the diagnosis of vitiligo (e.g., diagnosed major depressive disorder, bipolar disorder, schizophrenia).
b. Other forms of skin depigmentation not classified as vitiligo, such as albinism or chemical leukoderma.

c. Cognitive impairments or any conditions that might hinder comprehension of the questionnaire or informed consent process.

d. Pregnant or lactating women, due to potential hormonal effects on skin condition and mood.

Data Collection

Data were collected by using a web-based questionnaire conducted through social media of the patient contact number or email, phone call, or interview clinic during the period of the study. The questionnaire was divided into two parts. The first part captured sociodemographic information such as sex, age, marital status, nationality, job, and monthly income. While, the second part consisted of the PHQ-9 to assess symptoms of depression.

Study Variables

A. Independent variable: Vitiligo type

In this study, the independent variable was the type of vitiligo, categorized according to the revised classification from the Vitiligo Global Issues Consensus Conference (2012) [14]. This system classifies vitiligo into three primary clinical forms. Non-segmental vitiligo encompasses generalized vitiligo (formerly known as vulgaris), acrofacial vitiligo with its subtype referred to as 'lip-tip' vitiligo, and vitiligo universalis. Segmental vitiligo is characterized by a unilateral, asymmetric distribution. Unclassified vitiligo includes cases that do not evolve into either segmental or non-segmental forms within long period, such as focal vitiligo and single mucosal vitiligo affecting either genital areas or the oral cavity.

B. Dependent variable: Major Depressive Disorder

Patient Health Questionnaire-9 (PHQ-9) score was used to assess the severity of depressive symptoms. The PHQ-9 is a clinician-administered instrument that screens for depression and grades symptom severity based on the criteria from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) [15, 16]. Respondents rate how often they have experienced each of the nine DSM-IV criteria for depression over the past two weeks on a scale from zero ("not at all") to three ("nearly every day"). The total possible score ranges from zero to 27, with higher scores indicating greater depression severity. The depression severity categories are:

0-4:	None to minimal depression
5-9:	Mild depression
10-14:	Moderate depression
15-19:	Moderately severe depression
20-27:	Severe depression

Two variables were created based on PHQ-9 score. First, depression severity variable was coded as follows: 0 = non, 1= mild, 2= moderate, 3= moderately severe, and 4= severe depression. Binary depression variable was categorized into two groups whether the patient has depression (mild to severe) or not (non/minimal).

Covariates

In this study, the covariates include gender, age, nationality, marital status, job, and monthly income. Gender was categorized as male or female. Age was divided into three groups: 18-25 years, 26-60 years, and over 60 years, with the 26-60 age group serving as the reference category in multivariate analysis. Nationality was classified as either Saudi or non-Saudi. Income levels were categorized into four groups, ranging from less than 810 USD per month for the low-income group to over 5,265 USD per month for the high-income group, with the moderately high-income group (ranging from 2,430 USD to 5,265 USD per month) used as the reference in regression analysis. Marital status was classified as single, married, or divorced, with married participants considered the reference group. Job status was divided into three categories: employed, unemployed, or student.

Data Management and Analysis

Data were collected electronically and analyzed using SPSS software version 29. For bivariate analysis, Chi-square test was used to investigate the association between categorical variables. Monte Carlo simulation method was applied when indicated as an alternative to standard chi-square test. Logistic regression analysis was conducted to explain the variability of depression occurrence by including sex, age, nationality, marital status, income, job and vitiligo types in the final model. Similarly, the same model was applied in ordinal logistic regression analysis to predict depression severity. *P*-value less than 0.05 was considered a statistically significant.

Results

Sociodemographic Characteristics

Table 1 shows the sociodemographic characteristics of the study sample stratified by depression status. The prevalence of depression among vitiligo patients was 58.8%, with 200 out of 340 participants suffering from depression. A significant gender difference in depression prevalence was observed. Females showed a higher prevalence, with 109 out of 156 (69.9%) experiencing depression compared to 91 out of 184 males (49.5%), and this difference was statistically significant (*P* < .001). Moreover, age played a significant role in depression among vitiligo patients. The 18-25 age group had the highest depression rate, with 51 out of 69 participants (73.9%) experiencing depression, followed by the 26-60 age group with 146 out of 248 participants (58.9%) experiencing depression, while those over 60 years had a much lower rate of 3 out of 23 participants (13%) experiencing depression (*P* < .001). Marital status was significantly associated with depression development, where divorced and single individuals were more likely to be depressed, with 34 out of 41 divorced participants (82.9%) and 115 out of 153 single participants (75.2%) experiencing depression, compared to 51 out of 146 married patients (34.9%) (*P* < .001). Depression development varied significantly across income levels. The lowest income group had a higher depression proportion, with 181 out of 253 participants (71.5%) experiencing depression. In contrast, individuals in the high-moderate income category showed a much lower depression prevalence, with 6 out of 43 participants (14%) experiencing depression (*P* < .001). (Table. 1).

Table 1: Demographic and Socioeconomic Influences on Depression Status among Vitiligo Patients

Variables		Total	Depression		P-Value
			Yes	No	
		N (%) 340 (100)	N (%) 200 (58.8)	N (%) 140 (41.2)	P-Value
Gender	Male	184 (54.1)	91 (49.5)	93 (50.5)	<.001
	Female	156 (45.9)	109 (69.9)	47 (30.1)	
Age Groups (Y)	18-25	69 (20.3)	51 (73.9)	18 (26.1)	<.001
	26-60	248 (72.9)	146 (58.9)	102 (41.1)	
	>60	23 (6.8)	3 (13)	20 (87)	
Nationality	Saudi	290 (85.3)	175 (60.3)	115 (39.7)	.17
	Non-Saudi	50 (14.7)	25 (50)	25 (25)	
Marital Status	Single	153 (45)	115 (75.2)	38 (24.8)	<.001
	Divorced	41 (12.1)	34 (82.9)	7 (17.1)	
	Married	146 (42.9)	51 (34.9)	95 (65.1)	
Income	Low	253 (74.4)	181 (71.5)	72 (28.5)	<.001 [a]
	Low-moderate	32 (9.4)	10 (31.3)	22 (68.8)	
	High-moderate	43 (12.6)	6 (14)	37 (86)	
	High	12 (3.5)	3 (25)	9 (75)	
Job	Yes	128 (37.6)	46 (35.9)	82 (64.1)	<.001
	No	183 (53.8)	133 (72.7)	50 (27.3)	
	Student	29 (8.5)	21 (72.4)	8 (27.6)	

[a] P-Value calculated by using the Monte Carlo simulation

Bivariate Association of Depression Severity with Sociodemographic Characteristics

Table 2 illustrates the bivariate association of depression severity and various sociodemographic characteristics of the study sample. Males were less likely to experience severe depression compared to females, with 2 out of 184 males (1.1%) experiencing severe depression versus 35 out of 156 females (22.4%) ($P < .001$). Furthermore, age group analysis reveals that most (20 out of 23, 87%) of the older vitiligo patients (>60 years) did not suffer from depression, while the youngest age group (18-25 years) had more representation in the moderate and moderately severe categories, with 18 out of 69 (26.1%) experiencing moderate depression and 12 out of 69 (17.4%) experiencing moderately severe depression ($P < .001$). Marital status was significantly associated with depression severity, where divorced individuals exhibited higher rates of severe depression, with 13 out of 41 (31.7%) experiencing severe depression compared to 22 out of 153 singles (14.4%) and 2 out of 146 married individuals (1.4%) ($P < .001$). Moreover, the low-income group notably had higher rates of moderate to severe depression compared to higher income groups. For instance, in the low-income group, 91 out of 253 participants (36%) experienced moderate to severe depression, whereas in the high-moderate income group, only 2 out of 43 participants (4.7%) experienced moderate to severe depression ($P < .001$). (Table.2).

Table 2: Variation in Depression Severity across Demographic and Socioeconomic Characteristics of Vitiligo Patients

Variables		Total	None	Mild	Moderate	Moderately Severe	Severe	P-Value
		N (%) 340 (100)	N (%) 140 (41.2)	N (%) 62 (18.2)	N (%) 61 (17.9)	N (%) 40 (11.8)	N (%) 37 (10.9)	
Gender	Male	184 (54.1)	93 (50.5)	44 (23.9)	32 (17.4)	13 (7.1)	2 (1.1)	<.001
	Female	156 (45.9)	47 (30.1)	18 (11.5)	29 (18.6)	27 (17.3)	35 (22.4)	
Age Groups (Y)	18-25	69 (20.3)	18 (26.1)	14 (20.3)	18 (26.1)	12 (17.4)	7 (10.1)	<.001 [a]
	26-60	248 (72.9)	102 (41.1)	48 (19.4)	40 (16.1)	28 (11.3)	30 (12.1)	
	>60	23 (6.8)	20 (87)	0 (0)	3 (13)	0 (0)	0 (0)	
Nationality	Saudi	290 (85.3)	115 (39.7)	49 (16.9)	55 (19)	36 (12.4)	35 (12.1)	.11
	Non-Saudi	50 (14.7)	25 (50)	13 (26)	6 (12)	4 (8)	2 (4)	
Marital Status	Single	153 (45)	38 (24.8)	36 (23.5)	36 (23.5)	21 (13.7)	22 (14.4)	<.001 [a]
	Divorced	41 (12.1)	7 (17.1)	2 (4.9)	7 (17.1)	12 (29.3)	13 (31.7)	
	Married	146 (42.9)	95 (65.1)	24 (16.4)	18 (12.3)	7 (4.8)	2 (1.4)	
Income	Low	253 (74.4)	72 (28.5)	54 (21.3)	52 (20.6)	39 (15.4)	36 (14.2)	<.001 [a]
	Low-moderate	32 (9.4)	22 (68.8)	3 (9.4)	5 (15.6)	1 (3.1)	1 (3.1)	
	High-moderate	43 (12.6)	73 (86)	4 (9.3)	2 (4.7)	0 (0)	0 (0)	
	High	12 (3.5)	9 (75)	1 (8.3)	2 (16.7)	0 (0)	0 (0)	
Job	Yes	128 (37.6)	82 (64.1)	20 (15.6)	15 (11.7)	6 (4.7)	5 (3.9)	<.001 [a]
	No	183 (53.8)	50 (27.3)	34 (18.6)	39 (21.3)	29 (15.8)	31 (16.9)	
	Student	29 (8.5)	8 (27.6)	8 (27.6)	7 (24.1)	5 (17.2)	1 (3.4)	

[a] *P*-Value calculated by using the Monte Carlo simulation

Association of Vitiligo Types with Depression Severity

Vitiligo types varied significantly in their association with depression severity. Acrofacial vitiligo was the most common type, affecting 165 patients (48.5%). This group showed a higher proportion of moderate to severe depression, with 73 out of 165 patients (44.2%) experiencing moderate to severe depression compared to a more localized focal vitiligo, with 16 out of 65 patients (24.7%) experiencing moderate to severe depression. Vulgaris vitiligo was observed in 73 patients (21.5%) and revealed the highest proportion of moderate to severe depression, with 42 out of 73 patients (57.6%) experiencing moderate to severe depression. On the other hand, universalis vitiligo appeared in 11 patients (3.2%), with a majority, 10 out of 11 patients (90.9%), having no depression, and the remaining proportion, 1 out of 11 patients (9.1%), experienced mild depression. Similarly, genital vitiligo affected 16 patients (4.7%), mostly with no depression, with 10 out of 16 patients (62.5%) having no depression, and lesser extents of mild, with 3 out of 16 patients (18.8%), moderate, with 2 out of 16 patients (12.5%), and moderately severe, with 1 out of 16 patients (6.3%) depression. See (Table. 3).

Table 3: Correlation between Vitiligo Types and Depression Severity among Patients

	Variables	None N (%)	Mild N (%)	Moderate N (%)	Moderately Severe N (%)	Severe N (%)	Total N (%)	P-Value
Vitiligo Types	**Acrofacial**	61 (37)	31 (18.8)	34 (20.6)	20 (12.1)	19 (11.5)	165 (48.5)	.01 [a]
	Vulgaris	24 (32.9)	7 (9.6)	18 (24.7)	14 (19.2)	10 (13.7)	73 (21.5)	
	Focal	33 (50.8)	16 (24.6)	7 (10.8)	4 (6.2)	5 (7.7)	65 (19.1)	
	Universalis	10 (90.9)	1 (9.1)	0 (0)	0 (0)	0 (0)	11 (3.2)	
	Segmental	2 (20)	4 (40)	0 (0)	1 (10)	3 (30)	10 (2.9)	
	Genital	10 (62.5)	3 (18.8)	2 (12.5)	1 (6.3)	0 (0)	16 (4.7)	
	Total	140 (41.2)	62 (18.2)	61 (17.9)	40 (11.8)	37 (10.9)	340 (100)	

[a] *P*-Value calculated by using the Monte Carlo simulation

Logistic Regression Analysis of Depression Risk Factors

Logistic regression analysis indicates that the age group over 60 years is significantly less likely to develop MDD compared to the reference group (26-60 years), with an adjusted odds ratio (aOR) of 0.12 (95% CI: 0.03-0.48, *P*= .002). Females did not have a statistically significant higher risk of

developing depression compared to males, with an aOR of 1.29 (95% CI: 0.7-2.39, *P*=.42). Individuals with low income had a significantly higher risk of developing MDD, with an aOR of 9.5 (95% CI: 2.9-30.9, *P* <.001) compared to the moderately-high income reference group. Additionally, single patients had an aOR of 2.78 (95% CI: 1.29-5.98, *P*= .01), and divorced individuals had an aOR of 3.86 (95% CI: 1.28-11.67, *P*= .02) of having depression compared to married patients. Compared to a localized focal vitiligo, segmental vitiligo showed the highest risk of depression development, with an aOR of 6.37 (95% CI: 1.04-38.8, *P*= .045), followed by vulgaris and acrofacial types that showed significantly increased risks, with aORs of 3.5 (95% CI: 1.46-8.38, *P*= .005) and 2.45 (95% CI: 1.2-4.98, *P*= .01), respectively. In contrast, universalis vitiligo was associated with a significantly lower depression risk, with an aOR of 0.07 (95% CI: 0.01-0.59, *P*= .02). (Table 4).

Table 4: Logistic Regression Analysis of Study variables influencing on Major Depressive Disorder Development among Vitiligo Patients

Variables		aOR[a] (95% CI)	*P*-Value
Age Groups (Y)	26-60 (Ref)	1	
	18-25	0.67 (0.27-1.65)	.38
	>60	0.12 (0.03-0.48)	.002
Gender	Male (Ref)	1	
	Female	1.29 (0.7-2.39)	.42
Income	Moderately-High (Ref)	1	
	High	2.95 (0.51-17.1)	.23
	Moderate	2.61 (0.78-8.78)	.12
	Low	9.5 (2.9-30.9)	<.001
Marital Status	Married (Ref)	1	
	Single	2.78 (1.29-5.98)	.01
	Divorced	3.86 (1.28-11.67)	.02
Vitiligo Types	Focal (Ref)	1	
	Universalis	0.07 (0.01-0.59)	.02
	Genital	1.24 (0.29-5.27)	.77
	Acrofacial	2.45 (1.2-4.98)	.01
	Vulgaris	3.5 (1.46-8.38)	.005
	Segmental	6.37 (1.04-38.8)	.045

[a] aOR was calculated by including age, gender, nationality, marital status, income, job, and vitiligo types.

Ordinal Logistic Regression Analysis of Depression Severity

Table 5 demonstrates the ordinal logistic regression of depression severity by modeling depression in an ascending severity direction ranging from minimal to severe depression. Gender significantly influences the severity of depression, with females having a higher risk (aOR = 3.14, 95% CI: 1.93-5.1, *P* <.001) compared to males. Moreover, the age group over 60 years has a significantly lower risk of developing severe depression compared to the reference group (26-60 years), with an aOR of 0.1 (95% CI: 0.03-0.39, *P* <.001). Being divorced is associated with a higher risk of suffering from severe depression (aOR = 5.8, 95% CI: 2.6-12.9, *P* <.001) compared to married patients. Low-income patients were linked to a higher severity of depression, showing an aOR of 10.2 (95% CI: 3.25-31.8, *P* <.001) compared to the moderately high-income group. The type of vitiligo shows a significant role in depression severity, with vulgaris (aOR = 5.3, 95% CI: 2.6-10.9, *P* <.001) and acrofacial (aOR = 2.8, 95% CI: 1.5-5.1, *P* <.001) types associated with a higher depression severity compared to focal vitiligo. On the other hand, universalis vitiligo shows a significantly lower association with severe depression (aOR = 0.05, 95% CI: 0.01-0.5, *P*= .01) See (Table 5).

Table 5: Ordinal Logistic Regression of Factors Affecting Depression Severity in Vitiligo Patients

Variables		aOR[a] (95% CI)	*P*-Value
Age Groups (Y)	26-60 (Ref)	1	

	18-25	0.97 (0.51-1.86)	.93
	>60	0.1 (0.03-0.39)	<.001
Gender	Male (Ref)	1	
	Female	3.14 (1.93-5.1)	<.001
Income	Moderately-High (Ref)	1	
	High	4.1 (0.71-23)	.12
	Moderate	3.1 (0.91-10.6)	.07
	Low	10.2 (3.25-31.8)	<.001
Marital Status	Married (Ref)	1	
	Single	2.7 (1.5-5.1)	.001
	Divorced	5.8 (2.6-12.9)	<.001
Vitiligo Types	Focal (Ref)	1	
	Universalis	0.05 (0.01-0.5)	.01
	Acrofacial	2.8 (1.5-5.1)	<.001
	Vulgaris	5.3 (2.6-10.9)	<.001
	Segmental	4.4 (1.2-15.9)	.02
	Genital	1.7 (0.5-6.2)	.43

[a] aOR was calculated by including age, gender, nationality, marital status, income, job, and vitiligo types.

Discussion

This study quantitatively assessed the prevalence and predictors of depression among patients with vitiligo in Saudi Arabia, utilizing the VASI and PHQ-9. Our findings revealed a significant association between vitiligo and increased severity of MDD, with a prevalence of 58.8% among the vitiligo population, substantially higher than the 16.2% lifetime prevalence reported for the general population [3, 4]. It is notable that MDD exhibits a higher severity among certain subgroups within the vitiligo patient population. Specifically, females, divorced individuals, and those with lower income levels tend to experience more severe forms of depression. Additionally, the type of vitiligo also influences the severity of MDD, with acrofacial and vulgaris vitiligo associated with higher depression levels. These insights are crucial for tailoring more effective, targeted interventions for these vulnerable subgroups.

This study's strengths include the utilization of validated tools like the VASI and the PHQ-9, which enhance the reliability of our depression severity assessments. Additionally, our significant sample size and random sampling methodology provide a robust statistical basis for generalization within the target population. In addition, the PHQ-9 questionnaires were administered by professional psychiatrists to assess MDD severity. However, the study also faces limitations. Being a cross-sectional study, it does not support causal inferences between vitiligo and the onset of MDD. Our findings might also not be applicable to other regions or ethnic groups since the study was geographically confined to Saudi Arabia. Moreover, excluding individuals with pre-existing mental health conditions might lead to an underestimation of the actual psychological impact of vitiligo, as it does not consider those who might have developed MDD prior to the onset of vitiligo.

The observed high prevalence of MDD among patients with vitiligo supports the hypothesis that chronic skin diseases are significantly associated with psychiatric morbidities. This correlation is likely due to the visible and stigmatizing nature of vitiligo, which can lead to social withdrawal and significant psychological stress, thereby increasing the risk of depression. The results are consistent with findings from similar studies, which reported depression prevalence rates of 80% and 51.5%

respectively [17, 18], emphasizing the need for a multidisciplinary approach to managing patients with vitiligo, considering both dermatological and psychological aspects.

The findings from this study are primarily applicable to the adult population with vitiligo in Saudi Arabia. While these results provide valuable insights into the psychological impact of vitiligo, caution should be used when generalizing to populations in different settings or with different cultural backgrounds. Further research in varied demographic and ethnic groups is necessary to understand fully the global implications of these findings.

Recent studies have identified genetic associations related to immune-regulating genes in major depressive disorder (MDD). A case-control genetic association study involving the IKBKE gene, which encodes the IKKε protein involved in innate immunity and pro-inflammatory responses, revealed significant associations between IKBKE SNPs and MDD, as well as suggestive associations with panic disorder (PD) [19]. Additionally, polymorphisms in the limbic system-associated membrane protein (LSAMP) gene have shown strong associations with MDD and suggestive associations with PD, suggesting a potential role for LSAMP in mood and anxiety disorders [20]. These genetic findings are particularly relevant to the immune dysregulation observed in vitiligo patients, where immune-related genes play a crucial role in the pathogenesis of the disease. The pro-inflammatory properties of the IKBKE gene and its involvement in innate immunity could provide a mechanistic link between the immune responses in vitiligo and the increased susceptibility to mood disorders such as MDD. Similarly, the LSAMP gene's association with mood disorders highlights the potential overlap in genetic pathways that may contribute to both vitiligo and MDD. The shared genetic markers and pathways between vitiligo and MDD suggest that immune dysregulation may be a common underlying factor. For instance, the involvement of pro-inflammatory cytokines and immune-modulating genes in both conditions underscores the importance of understanding how immune system alterations can influence both skin pathology and psychiatric outcomes. Further research into these shared genetic and molecular pathways could provide deeper insights into the comorbidity of vitiligo and mood disorders, potentially leading to more integrated therapeutic approaches targeting both the immune system and mental health.

Future research should employ longitudinal designs to explore the causal relationships between vitiligo and depression. Studies testing the effectiveness of integrated treatment approaches for the physical and psychological aspects of vitiligo would also be beneficial. Expanding research to include diverse populations can help determine the broader applicability of these findings and explore cultural influences on the psychological impacts of vitiligo.

Conclusion

In summary, this cross-sectional study has highlighted a significant association between vitiligo and the severity of Major Depressive Disorder among patients, with a notably high prevalence of depression observed. The findings underscore the profound psychological impact of vitiligo,

reinforcing the need for comprehensive treatment approaches that address both the dermatological and psychological aspects of the disorder. Future research should focus on longitudinal studies to explore the causative mechanisms between vitiligo and depression and evaluate the effectiveness of integrated treatment strategies.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception,

study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took

part in drafting, revising or critically reviewing the article; gave final approval of the version to be

published; have agreed on the journal to which the article has been submitted; and agree to be

accountable for all aspects of the work.

Data Availability Statement

The data that support the findings of this research are available from the corresponding author
upon reasonable request. Due to legal and ethical considerations, the data cannot be made publicly
available. Requests for data access should be directed to **Amr Molla** at amolla@taibahu.edu.sa.

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