

Depression and anxiety among patients on antihyperlipidemic medications

A Saudi cross-sectional study

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Abstract

Antihyperlipidemic medications (AHLM) are widely prescribed, but their potential neuropsychiatric effects have been insufficiently studied in Saudi Arabia. This study assesses the prevalence of anxiety and depression among patients prescribed AHLM. A convenience sampling method was employed for a cross-sectional study conducted at a tertiary care hospital in Riyadh, Saudi Arabia, involving adults aged 18 years and older receiving AHLM. The study's tools consisted of a questionnaire developed by the research team to assess sociodemographic characteristics, the Arabic versions of the Generalized Anxiety Disorder 7 (GAD-7), and the Patient Health Questionnaire 9 (PHQ-9). Among 373 participants, the prevalence of anxiety symptoms (GAD-7 score ≥ 10) was 13.94%, while depressive symptoms (PHQ-9 score ≥ 10) were observed in 15.82%. Although AHLM use was not significantly associated with the GAD-7 score, it was significantly associated with a high PHQ-9 score in the multivariate model ($P = .034$). Sleep problems were significantly associated with both anxiety and depression ($P < .001$). Physical inactivity was associated with higher anxiety and depression symptoms; for anxiety, regular exercise displayed a significant association in the univariate model ($\beta = -0.34$; $P = .004$), and for depression, the association remained significant in both the univariate ($\beta = -0.43$; $P < .001$) and the multivariate models ($\beta = -0.30$; $P = .005$). The findings indicate that AHLM use is linked to depressive symptoms, suggesting the need for routine mental health screening in individuals with risk factors, such as sleep disturbances and smoking.

Abbreviations: AHLM = antihyperlipidemic medications, BMI = body mass index, GAD-7 = Generalized Anxiety Disorder 7, PHQ-9 = Patient Health Questionnaire 9.

Keywords: antidyslipidemic, anxiety, depression, Saudi Arabia

1. Introduction

Globally, an estimated 3.8% of the population experiences depression^[1] and 4% experiences anxiety,^[2] representing a major public-health challenge. Depression demonstrates particularly strong comorbidity with cardiovascular diseases, creating complex clinical challenges for patient management.^[3] A population-based study found that patients with anxiety disorders had significantly higher prevalence and incidence rates of hyperlipidemia than the general population.^[4] Similarly, hyperlipidemia patients exhibited an increased risk of new-onset anxiety and depression, particularly in head- and neck-cancer patients.^[5] The growing recognition of this interconnection has spurred interest in how cardiovascular disease medications might influence mental health outcomes.

Statins are among the most prescribed classes of drugs worldwide.^[6] Statins are recommended for the primary and secondary prevention of cardiovascular events.^[7] While earlier studies suggested a possible positive association between statin use and neuropsychiatric adverse effects, including increased anxiety,^[8] depression,^[9] and suicidality,^[8] more recent studies have reported either no significant relationship or even protective effects on mental health outcomes.^[10–13] Understanding the neuropsychiatric impact of statins has substantial public-health importance. Although some studies have demonstrated antidepressant benefits through anti-inflammatory mechanisms,^[14,15] other studies have reported adverse neuropsychiatric effects, including anxiety, irritability, and sleep disturbances,^[8] creating ongoing therapeutic dilemmas.

Informed consent was obtained from all the participants in the study.

The authors have no funding and conflicts of interests to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethical approval for this study was obtained from the IRB at the College of Medicine, King Saud University, Riyadh, Saudi Arabia (Research Project No. E-24-9246). Confidentiality was strictly maintained, with all data anonymized and access restricted to authorized personnel only.

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The neuropsychiatric impact of statins operates through multiple concurrent pathways. There is evidence of a link between inflammation and depression. Several articles have referred to elevated levels of pro-inflammatory cytokines and C-reactive protein in psychiatric disorders, including depression.^[14,16] Statins also improve endothelial function and cerebral blood flow, which could support mood regulation by optimizing neurovascular coupling and neurotransmitter delivery.^[17] However, the pharmacological reduction of cholesterol biosynthesis may impair critical neurological processes, as cholesterol is an essential component of neuronal membranes and neurotransmitter systems.^[18,19] Furthermore, a case series found behavioral changes following hyperlipidemia treatment initiation, including emotional lability and cognitive disturbances.^[8]

This present study examined the association between statin therapy, anxiety, and depression in patients at a tertiary university hospital in Riyadh, Saudi Arabia. The findings help fill an important gap in the literature concerning the topic in Saudi Arabia.

2. Methodology

2.1. Study design, setting, and participants

This study involved cross-sectional research conducted at King Khalid University Hospital, a tertiary care hospital in Riyadh, Saudi Arabia, to investigate the effects of antihyperlipidemic medications (AHLM) on depression and anxiety. The study was conducted from December 2024 to July 2025, with the data collection between February and March 2025.

The study's inclusion criteria were patients aged 18 years and older who were prescribed AHLM, regardless of the reason for the prescription. Although the inclusion criteria were patients who had been prescribed AHLM, it is worth mentioning that 22 participants (5.9% of the total sample of 373) stated they were not taking medication in one of the survey's questions asking about AHLM; this response probably indicates some had used the medication(s) in the past but had since discontinued, or they were non-compliant at the time of data collection. These participants were not excluded from the analysis.

On the other hand, the study's exclusion criteria included a history of major psychiatric disorders preceding dyslipidemia diagnosis, communication barriers due to conditions such as stroke or language limitations, and concurrent use of psychotropic medications. Eligibility was confirmed by reviewing hospital records. The research team conducted the data collection via phone calls. For individuals who did not respond to the calls, a survey link was sent, enabling them to complete it independently.

The sample size was calculated using the Raosoft Digital Sample Size Calculator (<http://www.raosoft.com/samplesize.html>). The initial calculation indicated a required sample size of 362 participants; however, the final sample included 373 individuals. A non-probability convenience sampling method was employed to recruit participants.

2.2. Study instruments

Our study instrument consisted of a questionnaire developed by the research team, in addition to the Arabic validated versions of the Generalized Anxiety Disorder 7 (GAD-7) and the Patient Health Questionnaire 9 (PHQ-9).

The questionnaire developed by the research team included sections addressing demographic and clinical characteristics, psychiatric history, and lifestyle factors. Other questions explored potential confounding variables, including sex, age, height, weight, education level, and marital, employment, and financial status. Additional areas included physical activity level, sleep quality, tobacco and alcohol use, and history of medical and psychological conditions.

The GAD-7 scale is a valid and reliable tool used for screening and assessing the severity of generalized anxiety disorder.^[20] The tool consists of 7 items, with a raw score ranging from 0 to 21. The scale classifies anxiety severity into 4 categories: minimal anxiety (0–4), mild anxiety (5–9), moderate anxiety (10–14), and severe anxiety (15–21). A score of 10 or more is considered the cutoff point for identifying GAD, with sensitivity of 89% and specificity of 82%.^[21] The tool has excellent reliability, with a Cronbach alpha of 0.92 and good test–retest reliability.^[22] In our study, we used the Arabic version of GAD-7.

The PHQ-9 has been identified as one of the most reliable screening tools for depression.^[23] A comprehensive systematic review analyzed 42 studies and found PHQ-9 sensitivity ranging from 0.37 to 0.98 and specificity from 0.42 to 0.99, with most studies using a cutoff score of 10, indicating its diagnostic accuracy.^[24] The PHQ-9 consists of 9 multiple-choice questions, with a total score ranging from 0 to 27. A score of 10 or higher indicates a sensitivity of 88% and specificity of 88%.^[25] The severity of depression is categorized as follows: minimal depression (0–4), mild depression (5–9), moderate depression (10–14), moderately severe depression (15–19), and severe depression (20–27). The PHQ-9 is available in the public domain, meaning it can be used freely without needing permission from the original authors.^[26] In our study, we used the Arabic version of PHQ-9.

2.3. Ethical considerations

Ethical approval for this study was obtained from the Institutional Review Board at the College of Medicine, King Saud University, Riyadh, Saudi Arabia (Research Project No. E-24-9246). All the participants provided informed consent before enrollment. Confidentiality was strictly maintained, with all data anonymized and access restricted to authorized personnel only.

2.4. Statistical analyses

Statistical analyses were performed using R Software version 4.4.0 (R Foundation for Statistical Computing, Vienna, Austria). The internal consistency of the questionnaire scales was measured to test the reliability using Cronbach alpha coefficient, with an alpha equal to or >0.7 being considered satisfactory. Continuous variables were tested for normality using the Shapiro test and are presented as mean $\pm$ standard deviation and median. The Mann–Whitney and Kruskal–Wallis tests were used for bivariate analysis, as normality assumptions were unmet. Categorical variables are presented as frequency (percentage). Fisher tests evaluated the difference between proportions. Univariate and multivariate linear regression analyses were conducted to assess potential predictors of anxiety and depression (dependent variables: GAD-7 and PHQ-9 scores). A 2-tailed *P*-value of less than .05 was considered statistically significant.

3. Results

3.1. Sociodemographic and clinical characteristics of patients

We analyzed the responses of 373 participants, most of whom ($n = 224$; 60.05%) were male. Of the total study participants, nearly one-third (31.64%) were in the age group between 55 to 64 years old, and 31.10% of the respondents were in the age group older than 65. Furthermore, 42.32% of the patients were overweight, and 35.85% were obese. Most patients in the study, 89.54%, were Saudi, and 78.28% were married. Postgraduate education (45.31%) and higher education (21.72%) were the most prevalent levels of education in the sample. Of those

Table 1
Clinical and sociodemographic characteristics of the patients.

Age group (yr)	N = 373
18–24	1 (0.27%)
25–34	15 (4.02%)
35–44	38 (10.19%)
45–54	85 (22.79%)
55–64	118 (31.64%)
≥65	116 (31.10%)
Gender	
Male	224 (60.05%)
Female	149 (39.95%)
BMI (kg/m ²) (n = 371)	
<18.5	5 (1.35%)
18.5–24.9	76 (20.49%)
25–29.9	157 (42.32%)
≥30	133 (35.85%)
Nationality	
Saudi	334 (89.54%)
Non-Saudi	39 (10.46%)
Marital status	
Single	20 (5.36%)
Married	292 (78.28%)
Divorced	25 (6.70%)
Widower	36 (9.65%)
Education level	
Primary school	62 (16.62%)
Secondary school	61 (16.35%)
High school	81 (21.72%)
Postgraduate	169 (45.31%)
Employment status	
Unemployed	103 (27.61%)
Employed	123 (32.98%)
Retired	144 (38.61%)
Student	3 (0.80%)
Monthly income	
<10,000	163 (43.70%)
10,000–20,000	163 (43.70%)
>20,000	47 (12.60%)
Regular exercise	139 (37.27%)
Sleep problems	149 (39.95%)
Antihyperlipidemic medications	351 (94.10%)
Antihyperlipidemic medications duration	
<1 yr	51 (14.53%)
1–5 yr	114 (32.48%)
>5 yr	186 (49.87%)
How committed are you to taking antihyperlipidemic medications as prescribed by your doctor?	
Always	238 (63.81%)
Often	62 (16.62%)
Sometimes	40 (10.72%)
Rarely	6 (1.61%)
Smoking	43 (11.53%)
Type of smoking*	
Tobacco smoking	30 (8.04%)
Electronic cigarette	7 (1.88%)
Shisha	14 (3.75%)
Chronic diseases	245 (65.68%)
Type of chronic diseases*	
Diabetes	166 (44.50%)
Hypertension	163 (43.70%)
Cardiac disease	17 (4.56%)
Dyslipidemia	8 (2.14%)
Hypothyroidism	22 (5.90%)
Others	37 (9.92%)
Psychiatric diseases	39 (10.46%)
Type of psychiatric diseases*	
Anxiety	20 (5.36%)
Depression	15 (4.02%)
Other psychiatric disorders	6 (1.61%)
Duration of psychiatric diseases	
<1 yr	11 (2.95%)
1–5 yr	13 (3.49%)
>5 yr	15 (4.02%)

BMI = body mass index.

*More than 1 answer was allowed.

surveyed, 144 (38.61%) were retired and 123 (32.98%) were employed. The income levels of these patients were almost 12% earned more than SAR 20,000, and 87.40% of patients earned less than SAR 20,000 per month. Additionally, more than one-third (37.27%) exercised regularly, and 39.95 had sleep problems. Most patients (351; 94.10%) had taken AHLM, and half the sample (49.87%) had taken them for more than 5 years. Nearly two-thirds (63.81%) of the study patients had always committed to taking AHLM as prescribed, followed by 16.62% who had often committed. Smoking was admitted by 43 (11.53%) patients. Within the study population, 65.68 % had chronic diseases, with diabetes being the most prevalent (44.50%, n = 166), followed by hypertension 163 (43.70%). Thirty-nine patients (10.46%) had been diagnosed with psychiatric disorders during their lifetime, and 15 out of those 39 had been diagnosed with a duration of more than 5 years. A total of 5.36% (n = 20) of the respondents had anxiety, while 4.02% (n = 15) had a depression diagnosis. See Table 1 for the sociodemographic and clinical characteristics of participants.

3.2. GAD-7 and PHQ-9 scores

Of the participants, 39.41% (n = 147) screened positively for anxiety, and 47.45% (n = 177) screened positively for depression. The results of the GAD-7 and PHQ-9 tests and their interpretations are presented in Table 2. The internal consistency of the 2 scales was good, with Cronbach alphas of 0.87 for GAD-7 and 0.84 for PHQ-9. The overall mean GAD-7 and PHQ-9 scores of the patients were 4.65 ± 4.43 and 5.31 ± 4.89 , respectively. Segregating the results based on the detected symptoms' intensity, of the 373 participants who completed the GAD-7, 95 (25.47%) had mild symptoms of anxiety, 38 (10.19%) had moderate anxiety, and 14 (3.75%) had severe anxiety. Regarding the PHQ-9, 118 (31.64%) reported mild symptoms of depression, 37 (9.92%) had moderate depression, 13 (3.49%) had moderately severe depression, and 9 (2.41%) had severe depression.

3.3. Association of generalized anxiety disorder and depression symptoms evaluated using the GAD-7 and PHQ-9 with antihyperlipidemic medications

Table 3 lists the associations between GAD-7 and PHQ-9 severity levels and AHLM. There is a statistically significant association between the GAD-7 severity levels and AHLM. Patients who reported taking AHLM (n = 351) demonstrated mild anxiety at 26.50%, moderate anxiety at 9.40%, and severe anxiety at 3.42% compared with 9.09%, 22.73%, and 9.09%, respectively, in patients who reported not taking AHLM. Mild and moderate depression were experienced by 32.19% and 9.97%, respectively, of the patients taking AHLM, compared with 22.73% and 9.09% of the patients not taking them; however, this difference is not significant. The scores of the GAD-7 and PHQ-9 regarding AHLM and the duration and commitment of patients taking them as prescribed by their physicians are listed in Table 4. There is no significant association between the GAD-7 or PHQ-9 scores with these factors.

3.4. Association of generalized anxiety disorder evaluated using GAD-7 with antihyperlipidemic medications and other variables

Table 5 lists the results of the univariate and multivariate linear regression models examining the association between the GAD-7 score and the related variables. The univariate analysis indicated that a high GAD-7 score was associated more with patients in the age groups 25 to 34 ($\beta = 0.71$; $P = .020$) and 35 to 44 ($\beta = 0.49$; $P = .017$) than with those in the age group older than 65, as well as more with obese patients

Table 2
Statistics of GAD-7 anxiety scores and PHQ-9 depression scores.

	Cronbach alpha	Mean $\pm$ SD, median	Min-max	Level of severity	
GAD-7	0.87	4.65 $\pm$ 4.43, 3	0–21	No anxiety (0–4)	226 (60.59%)
				Mild anxiety (5–9)	95 (25.47%)
				Moderate anxiety (10–14)	38 (10.19%)
				Severe anxiety (15–21)	14 (3.75%)
PHQ-9	0.84	5.31 $\pm$ 4.89, 4	0–25	No depression (0–4)	196 (52.55%)
				Mild depression (5–9)	118 (31.64%)
				Moderate depression (10–14)	37 (9.92%)
				Moderately severe depression (15–19)	13 (3.49%)
				Severe depression (20–27)	9 (2.41%)

GAD-7 = Generalized Anxiety Disorder 7-item scale; PHQ-9 = Patient Health Questionnaire 9-item scale.

Table 3
Relationship between GAD-7 anxiety severity and PHQ-9 depression severity with antihyperlipidemic medications use.

	Antihyperlipidemic medications		P-value
	No (N = 22)	Yes (N = 351)	
GAD-7			.031*
No anxiety (0–4)	13 (59.09%)	213 (60.68%)	
Mild anxiety (5–9)	2 (9.09%)	93 (26.50%)	
Moderate anxiety (10–14)	5 (22.73%)	33 (9.40%)	
Severe anxiety (15–21)	2 (9.09%)	12 (3.42%)	
PHQ-9			.232
No depression (0–4)	12 (54.55%)	184 (52.42%)	
Mild depression (5–9)	5 (22.73%)	113 (32.19%)	
Moderate depression (10–14)	2 (9.09%)	35 (9.97%)	
Moderately severe depression (15–19)	1 (4.55%)	12 (3.42%)	
Severe depression (20–27)	2 (9.09%)	7 (1.99%)	

GAD-7 = Generalized Anxiety Disorder 7-item scale; PHQ-9 = Patient Health Questionnaire 9-item scale.

* $P < .05$.

Table 4
Relationship between GAD-7 anxiety score and PHQ-9 depression score with antihyperlipidemic medications.

	Anxiety score		Depression score	
	Mean $\pm$ SD, median	P-value	Mean $\pm$ SD, median	P-value
Antihyperlipidemic medications		.959		.427
Yes	4.58 $\pm$ 4.31, 3		5.29 $\pm$ 4.76, 4	
No	5.68 $\pm$ 6.13, 2.5		5.64 $\pm$ 6.74, 2.5	
Antihyperlipidemic medications		.163		.139
<1 yr	3.84 $\pm$ 3.88, 2		4.72 $\pm$ 5.37, 4	
1–5 yr	4.96 $\pm$ 4.16, 4		5.40 $\pm$ 4.15, 5	
>5 yr	4.55 $\pm$ 4.50, 3		4.38 $\pm$ 4.94, 4	
How committed are you to taking antihyperlipidemic medications?		.293		.165
Always	4.41 $\pm$ 4.44, 3		5.09 $\pm$ 4.87, 4	
Often	5.08 $\pm$ 3.90, 4		5.75 $\pm$ 4.68, 5	
Sometimes	5.08 $\pm$ 3.59, 5		5.08 $\pm$ 3.59, 5	
Rarely	4.50 $\pm$ 8.17, 1.5		4.50 $\pm$ 8.17, 1.5	

GAD-7 = Generalized Anxiety Disorder 7-item scale; PHQ-9 = Patient Health Questionnaire 9-item scale.

* $P < .05$.

than with patients with normal weight ($\beta = 0.35$; $P = .025$). Similarly, patients with sleep problems ($\beta = 0.74$; $P < .001$), patients who smoked ($\beta = 0.42$; $P = .018$), and patients with psychiatric diseases ($\beta = 1.06$; $P < .001$) were more associated with a high GAD-7 score. Additionally, the univariate analysis indicated that a low GAD-7 score was more associated with males than females ($\beta = -0.46$; $P < .001$), more with patients with postgraduate degrees than with patients with primary education ($\beta = -0.50$; $P = .002$), more with retired patients than with employed patients ($\beta = -0.44$; $P = .001$), more with patients with a monthly income of 10,000 to 20,000 ($\beta = -0.42$; $P < .001$) and those who had > 20,000 ($\beta = -0.76$; $P < .001$) than with patients with <10,000, and more with patients who exercised regularly ($\beta = -0.34$; $P = .004$). The multivariate linear regression model indicated the factors significantly associated with the GAD-7 score: retired patients compared with employed patients ($\beta = -0.40$; $P = .012$), patients with a monthly income of 10,000 to 20,000 ($\beta = -0.29$; $P = .035$) and patients with a monthly income of > 20,000 compared with those with <10,000 ($\beta = -0.61$; $P = .001$) were associated with a low GAD-7 score. In contrast, patients with sleep problems ($\beta = 0.55$; $P < .001$), patients who smoked ($\beta = 0.43$; $P = .012$), and patients with psychiatric diseases ($\beta = 0.75$; $P < .001$) were significantly associated with a high GAD-7 score. AHLM were not significantly associated with the GAD-7 score.

3.5. Association of depression symptoms evaluated using PHQ-9 with antihyperlipidemic medications and other variables

Table 6 contains the results of the univariate and multivariate linear regression models examining the association between the PHQ-9 score and the related variables. The univariate analysis revealed that a high PHQ-9 score was associated more with patients in the age group between 25 to 34 than with those in the age group older than 65 ($\beta = 0.89$; $P = .004$), more with unemployed patients than with employed patients ($\beta = 0.35$; $P = .018$), and more with patients with sleep problems ($\beta = 0.95$; $P < .001$) and patients with psychiatric diseases ($\beta = 1.20$; $P < .001$). Moreover, the univariate analysis indicated that a low PHQ-9 score was associated more with males than females ($\beta = -0.53$; $P < .001$), with Saudi patients ($\beta = -0.47$; $P = .014$), with married patients more than single patients ($\beta = -0.77$; $P = .003$), with patients with secondary education ($\beta = -0.51$; $P = .012$) and postgraduate education ($\beta = -0.53$; $P = .002$) more than with patients with primary education, with patients with a monthly income of 10,000 to 20,000 ($\beta = -0.32$; $P = .009$) and a monthly income of > 20,000 ($\beta = -0.76$; $P < .001$) more than with those with <10,000, with retired patients more than with employed patients ($\beta = -0.32$; $P = .018$), and with patients who exercised regularly ($\beta = -0.43$; $P < .001$). The multivariate linear regression

Table 5**Univariate and multivariate linear regression analysis of variables associated with anxiety.**

Variable	Univariate		Multivariate	
	Coefficient β (95% CI)	P-value	Coefficient β (95% CI)	P-value
Age group (yr)				
18–24	0.72 (-1.45 to 2.89)	.515	0.61 (-1.68 to 2.90)	.599
25–34	0.71 (0.11 to 1.30)	.020*	0.48 (-0.22 to 1.19)	.181
35–44	0.49 (0.09 to 0.90)	.017*	0.18 (-0.28 to 0.65)	.436
45–54	0.14 (-0.17 to 0.45)	.379	-0.04 (-0.39 to 0.31)	.832
55–64	0.03 (-0.26 to 0.31)	.857	-0.12 (-0.40 to 0.16)	.396
Gender				
Male	-0.46 (-0.69 to -0.24)	<.001*	-0.24 (-0.54 to 0.06)	.115
BMI (kg/m ²)				
<18.5	-0.23 (-1.22 to 0.77)	.655	-0.33 (-1.33 to 0.66)	.514
25–29.9	0.09 (-0.21 to 0.39)	.572	0.15 (-0.12 to 0.41)	.284
≥30	0.35 (0.04 to 0.66)	.025*	0.18 (-0.10 to 0.45)	.206
Nationality				
Saudi	-0.16 (-0.53 to 0.21)	.385	0.02 (-0.33 to 0.36)	.923
Marital status				
Married	-0.41 (-0.90 to 0.08)	.102	0.01 (-0.55 to 0.57)	.965
Divorced	0.09 (-0.55 to 0.73)	.782	0.19 (-0.50 to 0.88)	.594
Widower	0.35 (-0.24 to 0.94)	.248	0.40 (-0.27 to 1.08)	.240
Educational level				
Secondary school	-0.34 (-0.73 to 0.05)	.089	-0.09 (-0.47 to 0.29)	.636
High school	-0.35 (-0.71 to 0.02)	.060	0.01 (-0.38 to 0.40)	.958
Postgraduate	-0.50 (-0.82 to -0.18)	.002*	-0.09 (-0.50 to 0.33)	.687
Employment status				
Unemployed	0.14 (-0.14 to 0.43)	.318	-0.35 (-0.76 to 0.05)	.086
Retired	-0.44 (-0.70 to -0.18)	.001*	-0.40 (-0.72 to -0.09)	.012*
Student	-0.11 (-1.35 to 1.14)	.863	-0.11 (-1.26 to 1.05)	.857
Monthly income				
10,000–20,000	-0.42 (-0.66 to -0.19)	<.001*	-0.29 (-0.56 to -0.02)	.035*
>20,000	-0.76 (-1.11 to -0.41)	<.001*	-0.61 (-0.97 to -0.24)	.001*
Regular exercise	-0.34 (-0.57 to -0.11)	.004*	-0.20 (-0.42 to 0.01)	.062
Sleep problems	0.74 (0.52 to 0.96)	<.001*	0.55 (0.34 to 0.76)	<.001*
Antihyperlipidemic medications	-0.09 (-0.57 to 0.39)	.707	0.08 (-0.38 to 0.53)	.747
Smoking	0.42 (0.07 to 0.78)	.018*	0.43 (0.09 to 0.76)	.012*
Chronic diseases	0.10 (-0.14 to 0.34)	.411	-0.02 (-0.25 to 0.22)	.878
Psychiatric diseases	1.06 (0.71 to 1.41)	<.001*	0.75 (0.40 to 1.09)	<.001*

BMI = body mass index, CI = confidence interval.

* $P < .05$.

model found that Saudi patients ($\beta = -0.45$; $P = .010$), patients with a monthly income of $>20,000$ compared with those with $<10,000$ ($\beta = -0.50$; $P = .006$), and patients who exercised regularly ($\beta = -0.30$; $P = .005$) had a low PHQ-9 score. In contrast, patients with sleep problems ($\beta = 0.76$; $P < .001$), smokers ($\beta = 0.34$; $P = .039$), and those with psychiatric diseases ($\beta = 0.95$; $P < .001$) had a significantly high PHQ-9 score. Finally, patients who took AHLM also had a significantly high PHQ-9 score ($\beta = 0.48$; $P = .034$).

4. Discussion

Our study was primarily designed to evaluate the correlation between AHLM and the prevalence and severity of anxiety and depressive symptoms in patients receiving AHLM. In addition to this main objective, we explored whether certain demographic or clinical factors affect the relationship between AHLM and mental health outcomes.

The results reveal a significant association between AHLM use and an increase in depressive symptoms. An experimental study using chronic statin exposure in human cell models^[27] found that prolonged statin use impairs the function of 5-hydroxytryptamine 1A receptors, which play a critical role in mood regulation. Another study^[28] demonstrated that depleting essential fats in the cell membrane, such as cholesterol and sphingolipids, reduced serotonin binding on 5-hydroxytryptamine 7

receptors, potentially impairing the brain signaling involved in mood regulation. In contrast, some clinical trials have found no significant effect of statins regarding depression. For instance, a 12-week double-blind placebo-controlled randomized control trial, involving patients with treatment-resistant depression,^[29] found no difference in depressive symptom reduction between adjunctive simvastatin and placebo groups despite assessing relevant immune-metabolic markers, such as C-reactive protein and lipid profiles. Nonetheless, a body of evidence suggests that AHLM, particularly statins, may reduce the risk or severity of depression. A systematic review of 5 randomized control trials concluded that statins, when used alongside antidepressants, can moderately improve depression scores.^[30] Similarly, a large population-based cohort study^[31] found that statin use was associated with a significantly reduced risk of developing depression in patients with asthma chronic obstructive pulmonary disease overlap syndrome, suggesting a potential protective effect. Given the conflicting evidence,^[27,31] clinicians should be aware that AHLM could contribute to depressive symptoms in some patients.^[27,28]

Our results indicate no significant association between AHLM and anxiety symptoms, as measured by the GAD-7 scale. This finding was further confirmed by multivariate regression analysis. In the literature, many studies have explored the association between AHLM and anxiety. For instance, the interaction between the 5-hydroxytryptamine 1A and 5-hydroxytryptamine 7 receptors (both involved in emotional

Table 6
Univariate and multivariate linear regression analysis of variables associated with depression.

Variable	Univariate		Multivariate	
	Coefficient β (95% CI)	P-value	Coefficient β (95% CI)	P-value
Age group (yr)				
18–24	0.73 (-1.51 to 2.96)	.523	0.04 (-2.19 to 2.27)	.974
25–34	0.89 (0.28 to 1.50)	.004*	0.33 (-0.36 to 1.02)	.344
35–44	0.24 (-0.18 to 0.65)	.267	-0.07 (-0.52 to 0.38)	.754
45–54	0.12 (-0.20 to 0.44)	.449	0.01 (-0.33 to 0.35)	.965
55–64	-0.01 (-0.31 to 0.28)	.923	-0.16 (-0.43 to 0.10)	.228
Gender				
Male	-0.53 (-0.76 to -0.30)	<.001*	-0.14 (-0.44 to 0.15)	.338
BMI (kg/m ²)				
<18.5	-0.09 (-0.61 to 0.44)	.745	-0.12 (-0.65 to 0.41)	.646
25–29.9	0.09 (-0.07 to 0.25)	.266	0.11 (-0.03 to 0.26)	.120
≥30	0.16 (-0.00 to 0.32)	.052	0.07 (-0.08 to 0.22)	.351
Nationality				
Saudi	-0.47 (-0.85 to -0.09)	.014*	-0.45 (-0.78 to -0.11)	.010*
Marital status				
Married	-0.77 (-1.27 to -0.27)	.003*	-0.41 (-0.96 to 0.13)	.135
Divorced	-0.25 (-0.89 to 0.40)	.459	-0.10 (-0.77 to 0.57)	.774
Widower	0.08 (-0.52 to 0.69)	.787	-0.03 (-0.68 to 0.63)	.933
Educational level				
Secondary school	-0.51 (-0.91 to -0.11)	.012*	-0.16 (-0.53 to 0.21)	.392
High school	-0.32 (-0.69 to 0.06)	.096	0.12 (-0.25 to 0.50)	.529
Postgraduate	-0.53 (-0.86 to -0.20)	.002*	-0.03 (-0.43 to 0.38)	.898
Employment status				
Unemployed	0.35 (0.06 to 0.64)	.018*	0.00 (-0.39 to 0.40)	.997
Retired	-0.32 (-0.59 to -0.06)	.018*	-0.21 (-0.51 to 0.10)	.179
Student	0.63 (-0.64 to 1.91)	.331	0.74 (-0.39 to 1.86)	.198
Monthly income				
10,000–20,000	-0.32 (-0.57 to -0.08)	.009*	-0.06 (-0.32 to 0.21)	.672
>20,000	-0.76 (-1.12 to -0.40)	<.001*	-0.50 (-0.86 to -0.14)	.006*
Regular exercise	-0.43 (-0.66 to -0.19)	<.001*	-0.30 (-0.51 to -0.09)	.005*
Sleep problems	0.95 (0.73 to 1.16)	<.001*	0.76 (0.55 to 0.96)	<.001*
Antihyperlipidemic medications	0.23 (-0.26 to 0.72)	.357	0.48 (0.04 to 0.93)	.034*
Smoking	0.27 (-0.10 to 0.63)	.151	0.34 (0.02 to 0.67)	.039*
Chronic diseases	0.11 (-0.13 to 0.36)	.358	-0.08 (-0.31 to 0.15)	.476
Psychiatric diseases	1.20 (0.84 to 1.56)	<.001*	0.95 (0.62 to 1.28)	<.001*

BMI = body mass index, CI = confidence interval.

* $P < .05$.

regulation) may be influenced by cholesterol-rich areas of the cell membrane, suggesting a link between lipid metabolism and the development of anxiety.^[32] In contrast, several large-scale clinical studies have reported no significant association between AHLM and anxiety symptoms. A Swedish nationwide cohort study^[15] found no relationship between statin use and the risk of anxiety disorders, and the results remained consistent across different treatment periods of AHLM. However, some studies have suggested a potential protective effect of statins against anxiety. For example, a cohort study of patients with asthma chronic obstructive pulmonary disease overlap syndrome found a significantly lower risk of anxiety among statin users, even after adjusting for multiple confounding factors, including the use of inhaled and oral corticosteroids.^[31] Similarly, a meta-analysis reported that statin use was significantly associated with a lower risk of anxiety symptoms in patients with cardiovascular disease.^[33] Given the lack of a significant association between AHLM use and anxiety symptoms, as measured by the GAD-7 in our study, future Saudi research is warranted to explore this relationship, probably using larger and more diverse populations and alternative anxiety-assessment tools.

Regarding the age of participants, our univariate analysis findings indicate that patients in the age group of 25 to 34 years old were associated with higher levels of both anxiety and depression compared with patients older than 65. The age group of 35 to 44 years old also demonstrated higher levels of anxiety than patients older than 65. Similarly, evidence from Singapore

primary care populations indicates that younger adults report higher levels of anxiety and depression,^[34] whereas a global meta-analysis demonstrates a significant burden among elderly populations,^[35] highlighting age as an important consideration for clinicians.

Regarding gender, the findings indicate that being male was significantly associated with lower anxiety and depression levels compared with female patients, consistent with a previous study^[36] indicating that females are at higher risk for these disorders. Therefore, clinicians should remember that being female is associated with an increased risk of anxiety and depressive symptoms, and this should be routinely assessed.

Furthermore, our study's univariate analysis found a significant association between anxiety and obesity (i.e., a body mass index [BMI] of 30 or more), but we found no significant link between BMI and depression. Previous population-based studies have similarly reported associations between obesity and anxiety,^[37,38] whereas cross-sectional research has demonstrated a U-shaped association between BMI and depression, suggesting elevated risk at both extremes of BMI.^[39] Therefore, clinicians should consider routine mental health screening for individuals with elevated BMI.

Our findings suggest that being Saudi was significantly associated with lower levels of depression, and no association was observed between nationality and anxiety levels. Limited research has examined this relationship within Saudi Arabia, though a study during the COVID-19 pandemic similarly

reported lower depression and anxiety levels among Saudi nationals compared with non-Saudis.^[40] To understand these patterns better, further Saudi longitudinal and stratified clinical trials are needed.

Regarding relationships, the univariate analysis results indicate that married participants exhibited lower depression levels than single patients; however, no association was found between marital status and anxiety. A large cross-sectional study^[41] also found that single individuals experienced higher depression levels than their married counterparts, although the association with anxiety remains unclear. As such, clinicians should consider social support systems, including relationship status, when assessing depression. For single patients, additional screening and supportive interventions may be beneficial to address potential vulnerabilities to depressive symptoms.

Regarding education, our univariate analysis indicates that higher educational levels, such as postgraduate education, were associated with lower levels of both anxiety and depression than lower educational levels, such as primary school. This finding is supported by a study^[36] that identified lower educational attainment as a significant risk factor for increased levels of depression and anxiety. The alignment between our results and the literature reinforces the protective role of higher education regarding mental health outcomes, reflecting the need to support educational aspects further.

We also examined work status. Being retired was significantly associated with lower levels of both anxiety and depression compared with being employed. However, we found that being unemployed is associated with higher levels of depression. Previous studies support these findings, showing that unemployment negatively affects mental health and that retirement may have protective effects.^[36,40] Reduced work-related stress may explain the lower anxiety and depression levels among retirees, whereas financial insecurity, loss of social identity, and social stigma likely contribute to higher depression among the unemployed.^[40] Therefore, clinicians should assess employment status and offer support if needed. Supporting those experiencing high job stress is another key element.

Another aspect we assessed was monthly income. Our findings reveal that higher monthly income was significantly associated with lower anxiety and depression levels. This finding is supported by cross-sectional studies^[36,40] that similarly reported that higher income was associated with reduced risk of anxiety and depression, whereas individuals with lower income were more likely to develop both depression and anxiety. These consistent results across studies highlight the potential protective effect of financial stability on mental health. Integrating financial counseling into patients' care may help address underlying stressors and improve psychological outcomes.

Regarding lifestyle, our study found a significant association between regular exercise and lower levels of both anxiety and depression. This is supported by previous researches showing that exercise interventions improve depression^[42] and anxiety, as well as quality of life across diverse populations.^[43,44] Therefore, exercise and its positive effect on mental health should be emphasized to patients.

Furthermore, our study's results indicate a significant association between sleep problems and both anxiety and depression. This finding is supported by a recent review, which proposed that Rapid Eye Movement sleep instability constitutes a specific phenotype of chronic insomnia, serving as a mechanistic bridge between insomnia and mental disorders, such as depression and anxiety, through its impact on emotional regulation and processing.^[45] Moreover, a study on pregnant women sleep problems, especially in the 3rd trimester, were associated with higher rates of anxiety and depression.^[46] These findings suggest sleep disturbances may both contribute to and result from mental health issues. Therefore, promoting sleep hygiene and addressing sleep difficulties are crucial.

In addition to the earlier-mentioned findings, our multivariate analysis indicates that smoking is significantly associated with higher levels of both depression and anxiety, consistent with previous studies.^[47,48] Clinicians should routinely assess smoking status in patients presenting with depressive or anxiety symptoms, and integrating smoking-cessation support into mental health treatment plans may improve overall outcomes and reduce the burden of both conditions.

4.1. Strengths and limitations

This study has strengths and limitations. Strength-wise, first, the study focuses on a relatively underexplored area in the Saudi population. Second, it employs validated psychometric tools (GAD-7 and PHQ-9). Third, the relatively large sample size enhanced statistical power.

However, several limitations should be considered. First, conducting the study at a single center (King Khalid University Hospital) and using a convenience sampling method may limit the representativeness of the sample and introduce potential selection bias, reducing generalizability to the broader Saudi population. Second, the cross-sectional design precludes the establishment of causal relationships between AHLM use and psychiatric outcomes; future longitudinal studies are needed to clarify temporal and causal links. Third, some participants were not actively taking their prescribed medications at the time of the study, which may have attenuated associations related to medication exposure. Finally, reliance on self-reported measures in some questions may introduce recall or response bias. Despite these limitations, the study provides important preliminary insights into the mental health of patients on AHLM in Saudi Arabia and underscores the need for multicenter, longitudinal research with larger and more diverse samples to guide clinical interventions and optimize both cardiovascular and mental health outcomes.

5. Conclusion

This study investigated the association between AHLM and psychiatric symptoms, specifically anxiety and depression. The results reveal a significant association between AHLM use and depression, but no statistically significant association was found with anxiety. Factors such as sleep disturbances, smoking, and preexisting psychiatric conditions were strongly associated with increased severity of anxiety and depression. Conversely, higher income, retirement status, and regular physical activity were associated with a lower severity of these symptoms. These findings highlight the importance of monitoring psychiatric symptoms in patients prescribed AHLM, particularly those with preexisting risk factors.

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