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Prevalence of emotional states (depression, anxiety, and stress) and its association with lipid accumulation product in adults: A sex-specific analysis of the Tehran Lipid and Glucose Study

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Abstract

Introduction:

Depression, anxiety, and stress represent major global contributors to psychological morbidity, yet their associations with central adiposity have been insufficiently explored beyond traditional anthropometric indices. This study examined the association between lipid accumulation product (LAP) and emotional distress in a large urban population.

Methods

This cross-sectional analysis included 7,054 adults from Phase 7 of the Tehran Lipid and Glucose Study (2018–2021). LAP was calculated using sex-specific formulas incorporating waist circumference and triglyceride levels. Emotional states were measured using the validated 21-item Depression, Anxiety, and Stress Scale (DASS-21). Linear regression models evaluated the associations of LAP (continuous and tertiles) with emotional outcomes, with analyses stratified by sex. Models were adjusted for demographic, lifestyle, and clinical factors.

Results

Higher LAP was significantly associated with elevated anxiety (β = 0.005, P = 0.009) and stress scores (β = 0.007, P = 0.004) in fully adjusted models. Participants in the highest LAP tertile exhibited higher anxiety (β = 0.452, P = 0.021) and stress scores (β = 0.714, P = 0.038) than those in the lowest tertile. The association with depressive symptoms was weaker but remained significant in the continuous analysis (β = 0.004, P = 0.038). Sex-specific analyses showed significant positive associations between LAP and both anxiety and stress among women, with no comparable associations in men.

Conclusions

LAP is positively associated with anxiety and stress, with a modest association with depressive symptoms, particularly among women. These findings highlight the relevance of visceral adiposity as a correlate of psychological distress and support incorporating metabolic and mental health assessments into preventive strategies.

Clinical Trial Number:

Not Applicable

Introduction

Depression and anxiety are among the most prevalent mental health disorders worldwide and are major contributors to disability and reduced quality of life (QoL). These conditions impose a substantial global burden of non-communicable diseases (NCDs), particularly in low- and middle-income countries (LMICs) (1, 2). The public health burden of mental disorders is also growing in Middle-Eastern populations, as a nationwide Iranian survey

reported that the prevalence of depression, anxiety, and stress was 44%, 42%, and 40%, respectively (3–5). Findings from previous phases of the Tehran Lipid and Glucose Study (TLGS) also showed high levels of these symptoms, with women consistently reporting significantly higher mean scores of depression, anxiety, and stress than men (4).

A growing body of evidence suggests a potential association between psychological disorders and cardiometabolic abnormalities (6, 7). However, most population-based investigations have focused primarily on emerging metabolic markers in relation to depressive symptoms, while anxiety and stress have received considerably less attention (8, 9). Sex differences may also influence these associations, as depression and anxiety are generally more prevalent among women, who exhibit distinct patterns of fat distribution and metabolic responses compared with men (9–11).

Obesity has been associated with mental health disorders—particularly depression—through shared neuroendocrine and inflammatory pathways (8, 12). Traditionally, adiposity has been assessed using anthropometric indices such as body mass index (BMI). However, BMI does not adequately capture variations in fat distribution and may underestimate cardiometabolic risk (13). In contrast, the Lipid Accumulation Product (LAP), a sex-specific index derived from waist circumference (WC) and triglyceride (TG) levels, provides a more accurate representation of central adiposity and has demonstrated superiority over BMI in predicting cardiovascular risk (14).

Most existing evidence on psychological distress and metabolic indices originates from high-income countries (15), whereas comparable studies from LMICs and Middle Eastern populations—each with unique socioeconomic and dietary characteristics—remain limited. Understanding such associations in these settings can help improve early risk identification and guide targeted interventions. Therefore, the present study aims to examine the association between emotional states (depression, anxiety, and stress) and LAP in a representative sample of Iranian urban adults.

Materials and Methods

Study Design and Participants

The present study was embedded within the TLGS, a large population-based cohort designed to investigate NCDs among a representative sample of residents in Tehran. For this cohort, three of the twenty health centers in district 13 were selected. Comprehensive descriptions of the TLGS design and methodology have been published previously (16, 17). The TLGS includes two major components: an initial cross-sectional survey conducted between 1999 and 2001 to assess the prevalence of NCD–related risk factors, followed by a prospective follow-up phase carried out every three years through 2021 to monitor changes in lipid and glucose profiles and the development of vascular outcomes among healthy participants.

In the current analysis, data on 7,187 participants with completed Depression, Anxiety and Stress Scale (DASS) assessments in the Phase 7 (2018–2021) were initially available. Of these, 98 individuals were excluded due to missing TG or WC data, and 35 participants with a history of cancer were removed. The final analytic sample consisted of 7,054 participants (Fig. 1).

Data Collection and Measurements

Trained interviewers collected information on participants' sociodemographic characteristics using a validated questionnaire (16, 17). Educational level was categorized into three groups based on years of schooling: (1) illiterate or primary education (< 6 years), (2) secondary school or diploma (6–12 years), and (3) academic education (> 12 years). Marital status was recorded as married or unmarried, with the latter including single, divorced, and widowed individuals. Employment status was classified as employed or unemployed, and smoking status was defined as current smokers (daily or occasional), ex-smokers, and non-smokers. Physical activity was assessed using the validated Iranian version of the Modifiable Activity Questionnaire (MAQ) (18) Total activity, expressed in MET-minutes per week, was calculated from the frequency and duration of leisure-time and occupational activities. Participants were grouped into low activity (≤ 600 MET-min/week) and moderate-to-high activity (> 600 MET-min/week).

Anthropometric assessments followed standardized procedures. Weight was measured with a digital scale (Seca 707) while participants wore light clothing and no shoes, and height was recorded using a stadiometer. BMI was calculated as weight divided by height squared. Blood pressure was measured with a calibrated mercury sphygmomanometer after 15 minutes of seated rest, and two readings taken 5 minutes apart were averaged. Fasting blood samples were collected between 7:00 and 9:00 AM after 12–14 hours of fasting. Fasting plasma glucose (FPG), total cholesterol (TC), and high-density lipoprotein cholesterol (HDL-C) were measured using enzymatic colorimetric methods (Pars Azmoon, Iran). HDL-C was determined after precipitation of apolipoprotein B–containing lipoproteins, and low-density lipoprotein cholesterol (LDL-C) was calculated using the Friedewald equation.

A documented history of cardiovascular disease (CVD), including coronary heart disease and cerebrovascular events, was obtained. Type 2 diabetes was defined as FPG ≥ 126 mg/dL or currently under glucose-lowering medications (19), and hypertension as mean SBP ≥ 140 mmHg, mean DBP ≥ 90 mmHg, or under active antihypertensive treatment (20). Chronic kidney disease (CKD) was defined according to K/DOQI guidelines as structural or functional kidney impairment or an estimated glomerular filtration rate (GFR) ≤ 60 mL/min/1.73 m² for at least three months (21). Family history was defined as the presence of diabetes, hypertension, or cardiovascular disease in first-degree relatives.

Main Exposure: LAP

The main exposure was LAP, an index that combines WC with fasting TG levels to capture central lipid excess and related metabolic risk. LAP was calculated using sex-specific formulas derived from minimal reference waist measurements (8, 14): for men, (WC in cm − 65) × TG (mmol/L), and for women, (WC in cm − 58) × TG (mmol/L).

WC was assessed by trained personnel using standardized anthropometric techniques, with the measuring tape placed at the intersection of the right iliac crest level and the mid-axillary line in upright position. Fasting TG concentrations were obtained from venous samples collected after overnight fasting and analyzed using validated enzymatic assays. By integrating both abdominal size and circulating TG, LAP provides a sensitive indicator of visceral fat accumulation and cardiometabolic burden.

Outcome: emotional states (depression, anxiety, and stress)

The emotional state of participants, specifically their levels of depression, anxiety, and stress experienced over the preceding week, was assessed using the validated Persian version of the short-form DASS-21 (22, 23). This self-

report questionnaire consists of three distinct sections, each with seven items. Participants indicate their level of agreement with each statement on a 4-point scale, ranging from 0 (not at all) to 3 (most of the time). The total score for each emotional domain (depression, anxiety, and stress) is determined by summing the scores of the seven items within that domain and then doubling the sum. These scores are then interpreted within established ranges to classify the severity of emotional distress. For depression, scores of 0–9 are considered normal, 10–13 indicate mild distress, 14–20 suggest moderate distress, 21–27 denote severe distress, and scores of 28 or higher represent extremely severe distress. For anxiety, the ranges are normal 0–7, mild 8–9, moderate 10–14, severe 15–19, and extremely severe 20+. Similarly, stress is categorized as normal (0–14), mild (15–18), moderate (19–25), severe (26–33), and extremely severe (34+). Higher scores in each category signify a greater intensity of the measured emotional state (24).

Statistical Analysis

Continuous variables were presented as means and standard deviations (SD), and categorical variables were summarized as frequencies and percentages. LAP was categorized into tertiles. Differences in various characteristics across these LAP tertiles and sex were compared using t-test and one-way ANOVA for continuous variables and the chi-square test for categorical variables. The prevalence of depression, anxiety, and stress was calculated for the participants. To examine the association between LAP tertiles and emotional state scores (DASS domains), linear regression models were performed. Both simple (unadjusted) and multiple (adjusted) linear regression analyses were conducted. Beta coefficients (β) and standard errors (SE) were reported for these associations. All statistical analyses were stratified by sex. The analyses were performed using STATA software, version 14. A $P < 0.05$ was considered statistically significant for all analyses.

Results

The total cohort of 7,054 participants (45.80% male, 54.20% female) showed statistically significant sex-based differences across numerous variables. While age and marital status showed no significant variation between males and females, educational attainment, employment status,12 and smoking habits displayed significant disparities ($P < 0.001$). Females were more likely to have higher educational levels and be non-smokers, whereas males were more frequently employed. Physical activity levels also differed significantly, with a higher proportion of males engaging in moderate to high-intensity activity. Anthropometric indices, including BMI, WC, SBP and DBP, and all measured blood parameters (FPG, TC, TG, LDL-C, and HDL-C), showed significant sex-specific differences ($P < 0.001$ for most, $P = 0.046$ for LDL-C). Notably, males had higher SBP, TG, and lower HDL-C, while females had higher BMI, WC, and LDL-C. Comorbidities such as CVD, hypertension, and CKD were more prevalent in females, while family history of type 2 diabetes was significantly more common in females as well ($P < 0.001$ for most).

Participants were categorized into three tertiles based on their LAP. A clear trend of increasing age, BMI, WC, blood pressure (both systolic and diastolic), FPG, TC, TG, and LDL-C was observed from Tertile 1 to Tertile 3, with corresponding decreases in HDL-C and physical activity (all $P < 0.001$). Higher LAP tertiles were also associated with a higher prevalence of comorbidities, including CVD, type 2 diabetes, hypertension, and CKD (all $P < 0.001$). Educational attainment generally increased with higher LAP tertiles, while the proportion of unmarried individuals and current/ex-smokers showed a significant trend across the tertiles, though unemployment status did not significantly differ. Although the proportion of males increased slightly with higher LAP tertiles ($P < 0.001$), females constituted a majority in Tertile 1 and showed a decreasing trend. Family history of type 2 diabetes and hypertension also showed a significant increase in higher LAP tertiles (Table 1).

Table 1
Demographic and Clinical Characteristics of Participants by Sex and LAP Tertile

Variables	Total (n = 7,054)	Male (n = 3,231)	Female (n = 3,823)	P-value*	Tertile 1 (n = 2,356)	Tertile 2 (n = 2,347)	Tertile 3 (n = 2,351)	P-value*
Age (year)†	46.45 (14.46)	46.39 (15.23)	46.50 (13.77)	0.730**	41.01 (15.11)	48.50 (13.78)	49.85 (12.78)	**< 0.001***
Sex								
Male	3231 (45.80)	-	-	-	1007 (42.74)	1079 (45.97)	1145 (48.70)	**< 0.001**
Female	3823 (54.20)	-	-		1349 (57.26)	1268 (54.03)	1206 (51.30)	
Educational level								
Illiterate/primary	2917 (41.36)	1426 (44.13)	1491 (39.01)	**< 0.001**	1172 (49.75)	938 (39.98)	807 (34.33)	**< 0.001**
Secondary/diploma	3508 (49.74)	1622 (50.20)	1886 (49.35)		1052 (44.65)	1196 (50.98)	1260 (53.59)	
Academic	628 (8.36)	183 (5.66)	445 (11.64)		132 (5.60)	212 (9.04)	284 (12.08)	
Marital status								
Married	5239 (74.27)	2418 (74.84)	2821 (73.79)	0.316	1457 (61.84)	1857 (79.12)	1925 (81.88)	**< 0.001**
Unmarried	1815 (25.73)	813 (25.16)	1002 (26.21)		899 (38.16)	490 (20.88)	426 (18.12)	
Job status								
Employed	3150 (44.69)	2327 (72.07)	823 (21.55)	**< 0.001**	1079 (45.86)	1016 (43.33)	1055 (44.89)	0.212
Unemployed	3898 (55.31)	902 (27.93)	2996 (78.45)		1274 (54.14)	1329 (56.67)	1295 (55.11)	
Smoking status								
Current smoker	1125 (16.04)	909 (28.28)	216 (5.68)	**< 0.001**	375 (16.02)	370 (15.88)	380 (16.21)	0.063
Ex-smoker	635 (9.05)	529 (16.46)	106 (2.79)		181 (7.73)	216 (9.27)	238 (10.15)	
Non-smoker	5255 (74.91)	1776 (55.26)	3479 (91.53)		1785 (76.25)	1744 (74.85)	1726 (73.63)	
Leisure time physical activity								

†Mean (standard deviation); **LAP**: Lipid Accumulation Product; **Unmarried**: Single, divorce, widow; **Unemployed**: Student, housewife, other; **LDL-C**: Low-Density Lipoprotein Cholesterol; **HDL-C**: High-Density Lipoprotein Cholesterol; *Based on Chi-square; **Based on T-test; ***Based on One-way ANOVA

Variables	Total (n = 7,054)	Male (n = 3,231)	Female (n = 3,823)	P-value*	Tertile 1 (n = 2,356)	Tertile 2 (n = 2,347)	Tertile 3 (n = 2,351)	P-value*
Low (≤ 600 MET min/week)	5127 (72.69)	2202 (68.15)	2925 (76.53)	**< 0.001**	1613 (68.49)	1689 (71.96)	1825 (77.63)	**< 0.001**
Moderate/high (> 600 MET min/week)	1926 (27.31)	1029 (31.85)	897 (23.47)		742 (31.51)	658 (28.04)	526 (22.37)	
Anthropometric indices†								
Body mass index, kg/m^2	27.78 (4.89)	27.48 (4.54)	28.04 (5.15)	**< 0.001****	24.17 (3.57)	28.11 (3.73)	31.08 (4.59)	**< 0.001*****
Waist circumference, cm	94.24 (11.81)	96.41 (11.36)	92.40 (11.87)	**< 0.001****	84.14 (8.83)	95.50 (7.91)	103.09 (9.80)	**< 0.001*****
Blood pressure†								
Systolic, mmHg	112.50 (15.37)	117.02 (14.51)	108.68 (15.04)	**< 0.001****	106.53 (14.44)	113.67 (14.98)	117.33 (14.68)	**< 0.001*****
Diastolic, mmHg	75.39 (9.38)	78.32 (9.40)	72.92 (8.63)	**< 0.001****	71.72 (8.68)	75.88 (8.89)	78.59 (9.29)	**< 0.001*****
Blood glucose†								
Fasting plasma glucose, mg/dl	99.45 (26.51)	101.14 (27.80)	98.02 (25.27)	**< 0.001****	92.33 (18.75)	98.76 (22.83)	107.28 (33.52)	**< 0.001*****
Lipid profile†								
Total cholesterol, mg/dl	182.82 (39.16)	180.36 (39.23)	184.90 (38.99)	**< 0.001****	166.47 (33.10)	182.81 (36.76)	199.22 (40.24)	**< 0.001*****
Triglyceride, mg/dl	142.77 (92.64)	157.31 (99.32)	130.49 (84.68)	**< 0.001****	79.86 (25.27)	125.05 (32.59)	223.51 (115.12)	**< 0.001*****
LDL-C, mg/dl	107.74 (32.29)	106.89 (32.33)	108.44 (32.26)	**0.046****	98.54 (27.97)	110.49 (31.93)	114.57 (34.65)	**< 0.001*****
HDL-C, mg/dl	46.93 (11.15)	42.67 (9.79)	50.53 (10.96)	**< 0.001****	51.94 (10.37)	47.28 (10.11)	41.54 (10.46)	**< 0.001*****
Comorbidities (yes)								
Cardiovascular disease	1167 (16.54)	501 (15.51)	666 (17.42)	**0.031**	327 (13.88)	404 (17.21)	436 (18.55)	**< 0.001**
Type 2 diabetes	787 (11.16)	357 (11.05)	430 (11.25)	0.792	127 (5.39)	249 (10.61)	411 (17.48)	**< 0.001**

†Mean (standard deviation); **LAP**: Lipid Accumulation Product; **Unmarried**: Single, divorce, widow; **Unemployed**: Student, housewife, other; **LDL-C**: Low-Density Lipoprotein Cholesterol; **HDL-C**: High-Density Lipoprotein Cholesterol; *Based on Chi-square; **Based on T-test; ***Based on One-way ANOVA

Variables	Total (n = 7,054)	Male (n = 3,231)	Female (n = 3,823)	P-value*	Tertile 1 (n = 2,356)	Tertile 2 (n = 2,347)	Tertile 3 (n = 2,351)	P-value*
Hypertension	1275 (18.12)	650 (20.17)	625 (16.39)	**< 0.001**	200 (8.50)	431 (18.39)	644 (27.52)	**< 0.001**
Chronic kidney disease	1778 (25.21)	567 (17.55)	1211 (31.68)	**< 0.001**	375 (15.92)	644 (27.44)	759 (32.28)	**< 0.001**
Family history (yes)								
Cardiovascular disease	261 (3.72)	110 (3.42)	151 (3.97)	0.226	71 (3.03)	101 (4.33)	89 (3.80)	0.062
Type 2 diabetes	1053 (15.23)	366 (11.64)	687 (18.21)	**< 0.001**	269 (11.69)	389 (16.83)	395 (17.16)	**< 0.001**
Hypertension	1363 (20.00)	446 (15.51)	917 (24.51)	**< 0.001**	416 (18.25)	481 (21.10)	466 (20.66)	**0.035**

†Mean (standard deviation); **LAP**: Lipid Accumulation Product; **Unmarried**: Single, divorce, widow; **Unemployed**: Student, housewife, other; **LDL-C**: Low-Density Lipoprotein Cholesterol; **HDL-C**: High-Density Lipoprotein Cholesterol; *Based on Chi-square; **Based on T-test; ***Based on One-way ANOVA

Prevalence of the emotional states (depression, anxiety and stress) by Sex

Among participants, 66.02% experienced moderate depression, 15.81% severe, and 18.17% extremely severe. Females reported slightly higher rates of moderate (61.55% vs. 71.31% in males) and extremely severe depression (21.71% vs. 13.99% in males), while males had a slightly higher rate of severe depression (14.7% vs. 16.74% in females) ($P < 0.001$). Anxiety levels were predominantly in the severe (26.69%) and extremely severe (60.86%) categories. Females reported higher rates of extremely severe anxiety (66.54% vs. 54.15% in males), while males had higher rates of severe anxiety (30.4% vs. 23.55% in females) ($P < 0.001$). Stress levels were distributed across moderate (22.54%), severe (29.23%), and extremely severe (31.6%) categories. Females showed a higher prevalence of extremely severe stress (35.99% vs. 26.4% in males), whereas males had slightly higher rates of moderate (23.83% vs. 21.45% in females) and severe stress (30.27% vs. 28.35% in females) ($P < 0.001$). In summary, all participants reported significant levels of emotional states. While females generally showed higher rates of extremely severe symptoms in all three categories, males showed slightly higher rates in the severe categories for anxiety and stress, and moderate depression (Fig. 2).

Prevalence of emotional states (depression, anxiety and stress) by LAP Tertile

When examining the impact of LAP tertiles on emotional state outcomes, there was no significant difference in the prevalence of depression across the three LAP tertiles for any category (normal, mild, moderate, severe, extremely severe) ($P = 0.623$ for continuous score). A significant association was found between LAP tertiles and anxiety ($P = 0.002$ for continuous score). While the prevalence of normal and mild anxiety mood remained zero, there was a trend of increasing extremely severe anxiety from Tertile 1 (58.87%) to Tertile 3 (63.40%). Moderate and severe anxiety showed slight decreases in Tertile 3 compared to Tertile 1 and 2. No significant difference was observed in

the prevalence of stress across the LAP tertiles (P = 0.463 for continuous score). However, there was a noticeable increase in the “normal” stress category from Tertile 1 (4.12%) to Tertile 3 (6.21%) **(**Table 2**)**.

Table 2
Prevalence of Depression, Anxiety and Stress in Participants by LAP Tertile

DASS Domain		Tertile 1 (n = 2,356)	Tertile 2 (n = 2,347)	Tertile 3 (n = 2,351)	P-value*
Depression	Continuous†	20.61 (8.04)	20.62 (7.90)	20.81 (8.15)	0.623**
	Normal	0 (0.00)	0 (0.00)	0 (0.00)	0.423
	Mild	0 (0.00)	0 (0.00)	0 (0.00)	
	Moderate	1559 (66.17)	1548 (65.96)	1550 (65.93)	
	Severe	389 (16.51)	374 (15.94)	352 (14.97)	
	Extremely Severe	408 (17.32)	425 (18.11)	449 (19.10)	
Anxiety	Continuous†	22.30 (7.43)	22.65 (7.59)	23.08 (7.83)	**0.002****
	Normal	0 (0.00)	0 (0.00)	0 (0.00)	**0.015**
	Mild	0 (0.00)	0 (0.00)	0 (0.00)	
	Moderate	314 (13.33)	281 (11.98)	283 (12.04)	
	Severe	655 (27.80)	650 (27.71)	577 (24.55)	
	Extremely Severe	1387 (58.87)	1415 (60.32)	1490 (63.40)	
Stress	Continuous†	28.77 (9.45)	28.70 (9.56)	29.03 (9.58)	0.463**
	Normal	97 (4.12)	106 (4.52)	146 (6.21)	**< 0.001**
	Mild	266 (11.29)	320 (13.63)	238 (10.12)	
	Moderate	571 (24.24)	498 (21.22)	521 (22.16)	
	Severe	693 (29.41)	702 (29.91)	667 (28.37)	
	Extremely Severe	729 (30.94)	721 (30.72)	779 (33.13)	

Data are presented as frequency (percent); †Mean (standard deviation); **LAP**: Lipid Accumulation Product; *Based on Chi-square test; **Based on One-way ANOVA

Association between LAP Tertile and DASS Domain

In the total population, a significant positive association was observed between LAP and anxiety scores in the fully adjusted model. For each one-unit increase in LAP, anxiety scores increased by 0.005 units on average (β = 0.005, P = 0.009). When comparing participants in the highest LAP tertile (Tertile 3) to those in the lowest tertile (reference), anxiety scores were 0.452 units higher on average (P = 0.021). Similarly, participants in Tertile 2 showed a significant increase of 0.296 units in anxiety scores compared to the reference group (β = 0.296, P = 0.034). A significant positive association was also found between LAP and stress scores in the total population.

Each one-unit increase in LAP was associated with a 0.007-unit increase in stress scores (P = 0.004). Participants in Tertile 3 had stress scores that were 0.714 units higher on average compared to those in Tertile 1 (β = 0.714, P = 0.038), while those in Tertile 2 showed a significant increase of 0.420 units (β = 0.420, P = 0.049). For depression scores, the continuous LAP variable showed a significant positive association (β = 0.004, P = 0.038), though the categorical comparisons between tertiles did not reach statistical significance.

When stratified by sex, notable differences emerged. In males, no significant associations were found between LAP tertiles and any of the DASS domains in the fully adjusted model. In contrast, females demonstrated several significant positive associations. Each one-unit increase in LAP was associated with a 0.009-unit increase in anxiety scores (P = 0.002). Female participants in Tertile 3 had anxiety scores that were 1.157 units higher on average compared to those in Tertile 1 (β = 1.157, P = 0.005), while those in Tertile 2 showed a significant increase of 0.492 units (β = 0.492, P = 0.044). For stress, a significant positive association was observed with the continuous LAP variable (β = 0.010, P = 0.004). Females in Tertile 3 had stress scores that were 1.371 units higher on average compared to the reference group (β = 1.371, P = 0.006), and those in Tertile 2 showed a significant increase of 0.829 units (β = 0.829, P = 0.049). For depression in females, the continuous LAP variable showed a significant positive association (β = 0.006, P = 0.047), though the categorical comparisons between tertiles did not reach statistical significance. Overall, these findings suggest that higher LAP levels are significantly associated with increased anxiety and stress scores, particularly among female participants, while the association with depression is weaker and primarily evident in the continuous analysis (Table 3).

Table 3
Association between LAP Tertile and DASS Domain using Linear Regression

Sex	DASS Domain		Model I		Model II		Model III	
			β (SE)	P-value	β (SE)	P-value	β (SE)	P-value
Total	**Depression**	**Continuous**	0.003 (0.002)	0.074	0.004 (0.002)	**0.035**	0.004 (0.002)	**0.038**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.011 (0.234)	0.960	0.128 (0.236)	0.587	0.105 (0.253)	0.676
		Tertile 3	0.202 (0.234)	0.386	0.204 (0.240)	0.395	0.164 (0.289)	0.570
	Anxiety	**Continuous**	0.007 (0.001)	**< 0.001**	0.008 (0.001)	**< 0.001**	0.005 (0.002)	**0.009**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.348 (0.222)	0.117	0.508 (0.224)	**0.023**	0.296 (0.237)	**0.034**
		Tertile 3	0.779 (0.222)	**< 0.001**	0.901 (0.227)	**< 0.001**	0.452 (0.271)	**0.021**
	Stress	**Continuous**	0.005 (0.002)	**0.028**	0.009 (0.002)	**< 0.001**	0.007 (0.002)	**0.004**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.066 (0.277)	0.810	0.537 (0.281)	**0.038**	0.420 (0.300)	**0.049**
		Tertile 3	0.259 (0.277)	0.351	0.925 (0.286)	**0.001**	0.714 (0.344)	**0.038**
Male	**Depression**	**Continuous**	0.0001 (0.002)	0.945	0.001 (0.002)	0.587	0.003 (0.003)	0.311
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	-0.167 (0.312)	0.592	0.031 (0.315)	0.919	0.095 (0.340)	0.780
		Tertile 3	-0.292 (0.307)	0.342	-0.157 (0.314)	0.616	-0.079 (0.382)	0.835
	Anxiety	**Continuous**	0.003 (0.002)	0.177	0.002 (0.002)	0.292	0.0005 (0.002)	0.866
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.162 (0.291)	0.578	0.218 (0.296)	0.460	0.064 (0.317)	0.838

LAP: Lipid Accumulation Product; **DASS**: Depression, Anxiety and Stress Scale; **β**: Regression Coefficient; **SE**: Standard Error; **Model I**: Unadjusted; **Model II**: Adjusted for age, sex, educational level, marital status, and physical activity; **Model III**: Adjusted for Model II and body mass index and comorbidities

		Tertile 3	0.103 (0.287)	0.719	0.018 (0.294)	0.950	-0.324 (0.355)	0.362
	Stress	**Continuous**	0.006 (0.003)	**0.049**	0.007 (0.003)	**0.041**	0.004 (0.004)	0.263
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	-0.193 (0.397)	0.625	0.187 (0.401)	0.641	-0.044 (0.432)	0.917
		Tertile 3	0.271 (0.391)	0.488	0.450 (0.399)	0.260	0.029 (0.485)	0.952
Female	**Depression**	**Continuous**	0.008 (0.002)	**0.004**	0.006 (0.002)	**0.027**	0.006 (0.003)	**0.047**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.259 (0.336)	0.441	0.210 (0.349)	0.548	0.152 (0.369)	0.680
		Tertile 3	0.858 (0.341)	**0.012**	0.534 (0.372)	0.152	0.452 (0.435)	0.298
	Anxiety	**Continuous**	0.013 (0.002)	**< 0.001**	0.012 (0.002)	**< 0.001**	0.009 (0.003)	**0.002**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.630 (0.318)	**0.047**	0.733 (0.332)	**0.028**	0.492 (0.347)	**0.044**
		Tertile 3	1.659 (0.322)	**< 0.001**	1.664 (0.354)	**< 0.001**	1.157 (0.409)	**0.005**
	Stress	**Continuous**	0.006 (0.003)	**0.045**	0.011 (0.003)	**0.001**	0.010 (0.003)	**0.004**
		Tertile 1	Ref.		Ref.		Ref.	
		Tertile 2	0.166 (0.383)	0.663	0.887 (0.400)	**0.027**	0.829 (0.421)	**0.049**
		Tertile 3	0.492 (0.388)	0.205	1.462 (0.426)	**0.001**	1.371 (0.496)	**0.006**

LAP: Lipid Accumulation Product; **DASS**: Depression, Anxiety and Stress Scale; **β**: Regression Coefficient; **SE**: Standard Error; **Model I**: Unadjusted; **Model II**: Adjusted for age, sex, educational level, marital status, and physical activity; **Model III**: Adjusted for Model II and body mass index and comorbidities

Discussion

The principal finding of the present study is that higher levels of LAP are associated with higher anxiety and stress scores after adjustment for major confounding factors. Although the association with depressive symptoms was weaker, it remained statistically significant when LAP was analyzed as a continuous variable. Sex-stratified analyses showed that these associations were more pronounced among women. In particular, female participants in the highest LAP tertile showed substantially higher emotional distress scores compared with those in the lowest

tertile. These sex-specific patterns suggest that the LAP index may be associated with multiple dimensions of emotional distress.

A growing body of evidence supports a bidirectional relationship between obesity and psychological disorders through several biological pathways, including chronic low-grade inflammation, dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis leading to altered cortisol secretion, and insulin resistance. Moreover, visceral adipose tissue promotes systemic inflammation by secretion of pro-inflammatory cytokines such as interleukin-6 and tumor necrosis factor-α, which is implicated in the development of depression, anxiety, and stress-related symptoms (7, 12). These mechanisms may influence neurotransmitter systems and stress responsiveness, thereby contributing to emotional disturbances. In line with this perspective, Alshehri et al. (25) proposed an energy homeostasis theory to explain the relationship between obesity and depression, demonstrating that both general obesity (BMI) and abdominal adiposity (WC) were strongly associated with atypical neurovegetative symptoms of depression. The aforementioned endocrine and inflammatory properties of visceral fat is more accurately captured by LAP than traditional anthropometric indices (14).

Our findings are broadly consistent with previous research linking indicators of central adiposity and metabolic dysfunction with psychological distress (26). For example, the “jolly fat” hypothesis has been suggested to describe the complex association between obesity and psychoneurotic symptoms such as anxiety and depression (27). Some recent studies have also reported evidence supporting this hypothesis, particularly among women in Asian populations, indicating that the relationship between adiposity and psychological health may vary across populations and obesity phenotypes (28). Furthermore, a study conducted in Iran reported a significant relationship between the abdominal volume index and symptoms of depression and anxiety (29). Moreover, two large population-based studies in the United States documented an L-shaped association between LAP and depression, suggesting that depressive symptoms increased markedly at lower-to-moderate levels of LAP (8, 30). Compared with previous investigations, the present study expands existing knowledge by simultaneously examining depression, anxiety, and stress using the DASS-21 instrument, and by demonstrating stronger associations with anxiety and stress than with depressive symptoms.

The observed sex-specific patterns are consistent with several prior studies indicating that the relationship between adiposity and psychological disorders may differ by sex. Similar to our findings, Li et al. (9) reported a stronger association between obesity and major depression among women. Likewise, Vogelzangs et al. (31) discovered that abdominal adiposity is independently related to anxiety disorders, particularly among female participants. In contrast, Gu et al. (32) observed a U-shaped association between LAP and depression among middle-aged and older men, with no comparable pattern among women. Likewise, Dai et al. (33) found that the association between LAP and depression was stronger among men in a large American sample. These inconsistencies across studies may reflect differences in population characteristics, age distribution, cultural context, or measurement approaches. Several mechanisms may contribute to the sex-specific associations observed in the present study, including sex hormone influences, differences in body fat distribution and visceral adiposity, and greater psychosocial vulnerability to stress-related neuroendocrine responses among women (9).

The present findings may have several clinical and public health implications. LAP is an easily obtainable index derived from routine clinical measurements (WC and TG) and may serve as a practical marker for identifying individuals at elevated risk of psychological distress in cardiometabolic screening settings. Integrating mental health assessment into metabolic risk evaluation could facilitate earlier detection of emotional disorders and support comprehensive lifestyle interventions targeting both metabolic and psychological health (12). This

approach may be particularly relevant in LMICs, where the burden of cardiometabolic diseases and mental health disorders is increasing and integrated preventive strategies are needed.

Several limitations should be considered when interpreting the findings. First, the cross-sectional design precludes causal inference, and the directionality of the observed associations cannot be determined. Reverse causation is possible, as psychological distress may contribute to unhealthy lifestyle behaviors—such as poor diet, physical inactivity, and sleep disturbances—which in turn may increase LAP levels (8, 34, 35). For instance, stress, a key dimension of psychological distress, is increasingly recognized for its potential role in the development of metabolic disorders (36). Second, emotional states were assessed using the self-reported DASS-21 questionnaire rather than clinical diagnostic interviews based on standardized criteria such as the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), which may introduce reporting bias. Third, although major confounders were controlled for, residual confounding from unmeasured factors—including dietary intake, sleep quality, medication use (e.g., antidepressants or lipid-lowering agents), and genetic susceptibility—cannot be completely excluded. Finally, the study population consisted of urban Iranian adults participating in the TLGS; therefore, the generalizability of the findings to other populations or rural settings should be interpreted with caution.

Conclusion

In conclusion, this study provides evidence of a positive association between the lipid accumulation product and symptoms of anxiety and stress, with a weaker association observed for depressive symptoms when LAP was analyzed as a continuous variable. These associations were more pronounced among women, suggesting potential sex-specific association between central adiposity and emotional distress. The findings highlight the importance of considering visceral adiposity markers such as LAP in the broader context of psychological well-being. Future longitudinal and interventional studies are needed to clarify causality and explore whether reducing visceral adiposity may contribute to improvements in psychological well-being. Incorporating both metabolic and mental health assessments in clinical and public health settings may help improve early identification and prevention strategies for individuals at risk.

Abbreviations

BMI
Body Mass Index
CKD
Chronic Kidney Disease
CVD
Cardiovascular Disease
DASS
Depression, Anxiety and Stress Scale
DSM-V
Diagnostic and Statistical Manual of Mental Disorders
FPG
Fasting Plasma Glucose
GFR
Glomerular Filtration Rate
HDL-C

High-Density Lipoprotein Cholesterol
HPA
Hypothalamic–Pituitary–Adrenal
LAP
Lipid Accumulation Product
LDL-C
Low-Density Lipoprotein Cholesterol
LMIC
Low- and Middle-Income Countries
MAQ
Modifiable Activity Questionnaire
NCDs
Non-Communicable Diseases
TC
Total Cholesterol
TG
Triglyceride
TLGS
Tehran Lipid and Glucose Study
WC
Waist Circumference

Declarations

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Authors' Contributions

N. I: Contribution to study concept and design, acquisition, analysis and interpretation of data, drafting of the manuscript

A. E: Contribution to study concept and design, acquisition, drafting of the manuscript

S-S. O-H: Contribution to study concept and design, acquisition, drafting of the manuscript

M. M-A: Contribution to study concept and design, acquisition, and drafting of the manuscript

F. A: Contribution to study concept and design

P. A: Contribution to study concept and design, acquisition, interpretation of data, drafting of the manuscript

All authors have read and approved the manuscript.

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Availability of data and materials

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

Ethic's approval and consent to participate

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving research study participants were approved by the Ethics Committee of Research Institute for Endocrine Sciences, Shahid Beheshti University of Medical Sciences (IR.SBMU.ENDOCRINE.REC.1405.019). Written informed consent was obtained from all subjects or their legal guardians (if indicated).

Consent to publication

Not applicable. The manuscript does not contain patient identifiable data.

Competing interests

The authors declare that they have no competing interests.

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Figures

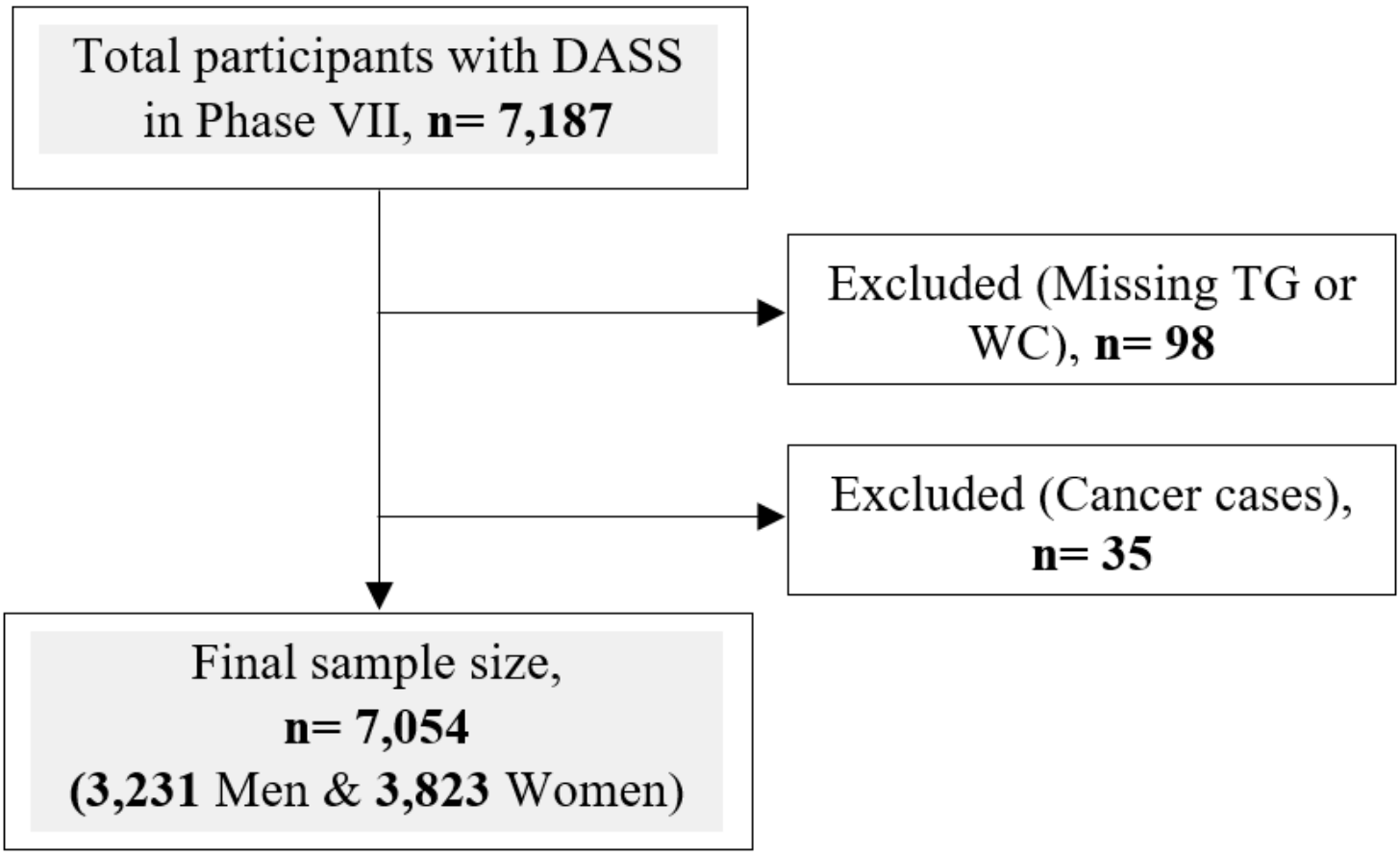


Figure 1

Flowchart of the study participants

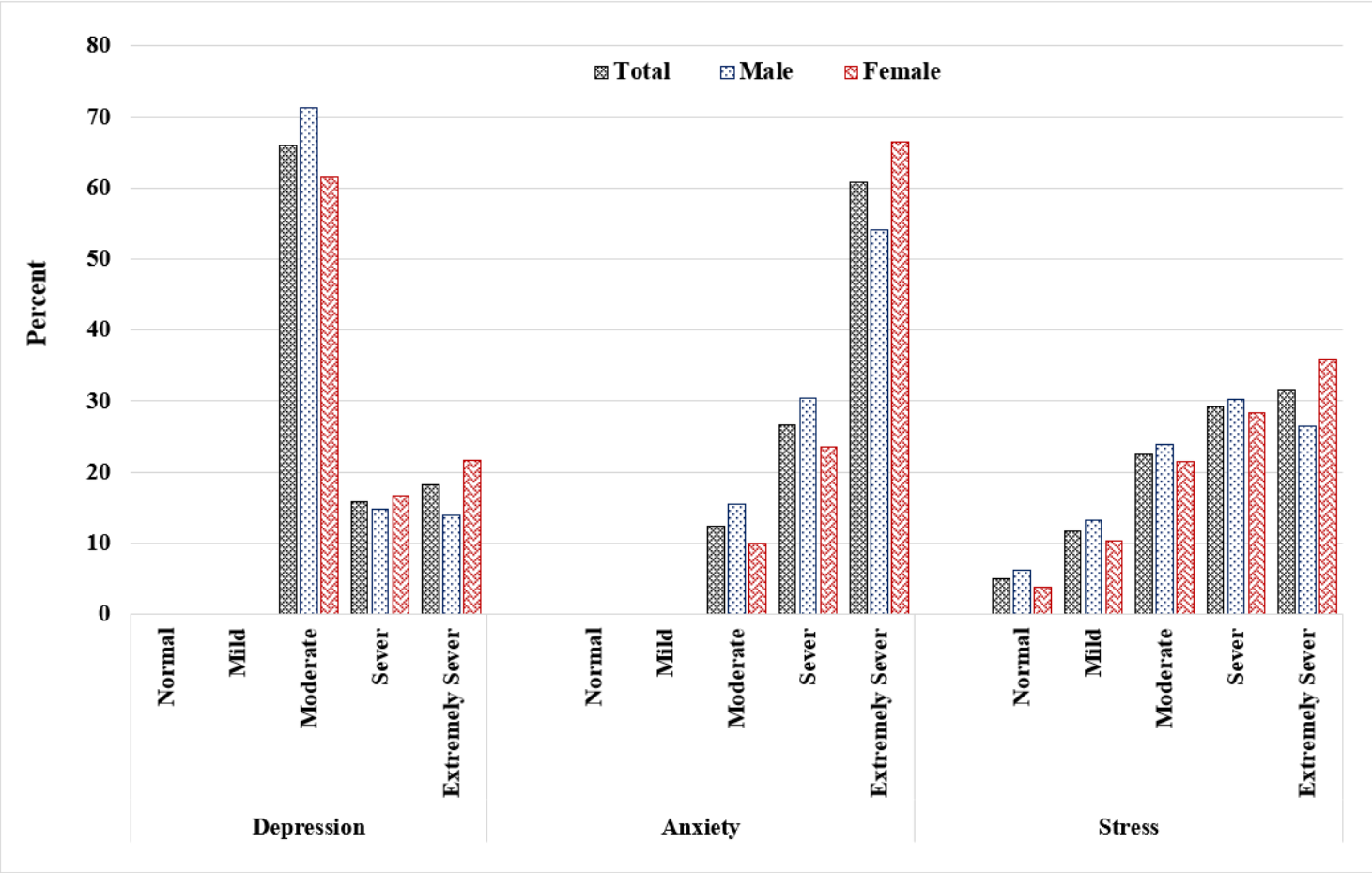


Figure 2

Prevalence of Depression, Anxiety and Stress in Participants by Sex