



# Is There A Relationship Between the Components of Metabolic Syndrome and Depression?

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ARTICLE INFO	ABSTRACT
<p><i>Article type:</i> Research Paper</p>	<p><b>Introduction:</b> Metabolic syndrome is characterized by at least three out of five main criteria, including high waist circumference, hypertension, high level of triglyceride, low level of high-density lipoprotein, and elevated fasting blood glucose. The International Diabetes Federation has estimated the prevalence of metabolic syndrome at 25% across the world. Metabolic syndrome is more prevalent in the individuals with depression, as well as other psychiatric disorders. However, the current findings in this regard are conflicting. The present study aimed to evaluate the associations between the criteria of metabolic syndrome and depression as the most common psychiatric disorder.</p> <p><b>Methods:</b> This cross-sectional study was conducted on 130 participants aged 18-65 years. Metabolic syndrome was assessed based on the criteria of the International Diabetes Federation, and depression was evaluated based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV).</p> <p><b>Results:</b> After the adjustment of the important confounders (physical activity, calorie intake, history of depression, depression score, menopausal status, body mass index, and dietary patterns), the waist circumference was observed to be significantly higher in the patients with depression compared to the other subjects.</p> <p><b>Conclusion:</b> According to the results, visceral obesity may lead to depression and vice versa. Therefore, it is recommended that further investigation be conducted in this regard in order to confirm this association.</p>
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## Introduction

The prevalence of metabolic syndrome has increased from 1988 to 2012 in various socio demographic groups. By 2012, more than one-third of the adults in the United States (34.2%) corresponded with the definition and criteria of metabolic syndrome, which have been agreed upon by several international organizations. The International Diabetes Federation has reported the prevalence rate of metabolic syndrome to be 25% across the

world. The major causes of the spread of this disorder are the increased consumption of high-calorie, low-fiber fast foods and decreased physical activity (1).

Depression is considered to be the most common psychological disorder (2). The population of the patients with depression has been estimated at 322 million globally (3). As a result, the motto of the World Health Day in 2017 was "Depression: Let's talk." (4).

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Moreover, depression in adults has been associated with high morbidity and mortality, the increased risk of various diseases (5-8), and low personal satisfaction (9).

Recently, metabolic syndrome has become more prevalent among psychiatric patients (10). Metabolic syndrome is characterized by at least three of five main criteria, including high waist circumference, hypertension, high level of triglyceride, low level of high-density lipoprotein (HDL) and cholesterol, and elevated fasting plasma glucose. These issues are correlated with cardiovascular diseases and diabetes type II (11, 12).

Previous studies have indicated that metabolic syndrome is prevalent in severely depressed patients, while other findings have denoted bilateral relation between depression and metabolic syndrome (13, 14). Due to the controversy regarding this issue (14, 15), extensive research is required to clarify the association between the criteria of metabolic syndrome and depression.

The present study aimed to assess the correlations between the criteria of metabolic syndrome and depression.

## Material and methods

### Subjects and Study Design

This cross-sectional study was conducted on 130 participants at Imam Hossein and Baharloo psychiatric clinics in Tehran, Iran. The participants were enrolled for the measurement of metabolic syndrome markers and diagnosis of depression. Depressed patients were diagnosed with major depressive disorder by psychiatrists based on the criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) and had no history of depression within the past year.

The inclusion criteria of the study were the age of 18-65 years and residence in Tehran, Iran. The exclusion criteria were as follows: 1) diagnosis of cognitive impairment or other psychotic disorders by a psychiatrist; 2) severe depression or inability to cooperate and complete the questionnaire; 3) receiving antidepressants or treatment for depression; 4) hormonal disorders (e.g., Addison's disease, Cushing's disease, hyperthyroidism, hypothyroidism, and hyperparathyroidism); 5) chronic diseases

(e.g., cancer, heart disease, diabetes, stroke, fibromyalgia, kidney or liver failure, multiple sclerosis, and Parkinson's disease); 6) chronic infections (e.g., HIV, mononucleosis, tuberculosis, viral hepatitis, and pneumonia) within the past two weeks; 7) alcohol/drug addiction at the time of the study or withdrawal within the past three months; 8) body mass index (BMI) of  $\geq 40$  kg/m<sup>2</sup> and 9) pregnancy and lactation at the time of the study or within the past year.

After explaining the objectives of the research, written informed consent was obtained from the participants. The study protocol was approved by the Ethics Committee of Tehran University of Medical Sciences, Iran.

### Assessment of Covariates

A demographic questionnaire was used to collect data, as well as some confounders. After 10 minutes of relaxation, systolic and diastolic blood pressure was measured with the subjects seated after 10 minutes relaxation in chairs with no exposure to stress using a standard mercury sphygmomanometer. Waist circumference was also measured in all the participants. These covariates were considered as the criteria for metabolic syndrome. In addition, depression was diagnosed based on the 4th edition of the DSM-IV criteria (16), which have been standardized for the Iranian population (17).

Based on the metabolic equivalent task hours per day (MET-h/day), a classified physical activity questionnaire was utilized consisting of nine activity levels (from rest/sleep [MET=0.9] to vigorous physical activity [MET $\geq$ 6]). The questionnaire has been designed in Europe and was validated using the daily physical activity questionnaire and the Computer Science Application (CSA) Accelerometer (Model 7164 Ambulatory Monitor) (18). Kelishadi et al. have confirmed the validity and reliability of the questionnaire for the Iranian population (19).

In order to measure fasting blood glucose and lipid profile (i.e., metabolic syndrome criteria), blood samples (5 ml) were collected from the subjects who had been fasting for 12 hours (7-10 AM). Glucose and lipid profile, including triglyceride (TG), HDL, very low-

density lipoprotein, and total cholesterol, were assayed using enzymatic methods (Pars Azmouk, Iran) and an automatic Selecta E device (Vitalab, Netherlands). Since the highest TG concentration in our participants was lower than 400mg/dl, the concentration of low-density lipoprotein (LDL) was calculated using the Friedewald formula, as follows (20):

$$LDL \text{ Cholesterol (mg/dl)} = Total \text{ Cholesterol} - HDL \text{ Cholesterol} - 0.2 \text{ TG}$$

Insulin was assayed with caution using the radiation survey (Diasource, Belgium) and the antibodies labeled with a gamma counter (model: Gen II, Factory Genesis, USA). Insulin sensitivity was measured based on the following formula (21):

$$QUICKI \text{ Index: } 1 / (\log [\text{insulin}]) (\mu\text{U/ml}) + \log (\text{glucose}) (\text{mg/dl})$$

### Statistical Analysis

The sample size was calculated for all the criteria of metabolic syndrome, and the final sample size was determined based on the largest possible sample size and practical conditions of the researcher.

Data analysis was performed in SPSS version 20 (Chicago, IL) using the Kolmogorov-Smirnov test to assess the normality of the covariates and t-test or Mann-Whitney U test to compare the covariates between the two groups based on normality. In addition, simple logistic regression was applied to investigate the correlation between depression and metabolic syndrome criteria with an estimated odds ratio (OR). The goodness of fit (GOS) for logistic regression was examined using logical confidence intervals and Hosmer-Lemeshow test.

### Results

No significant differences were observed between the study groups in terms of quantitative factors, such as age, height, weight, BMI, and frequency of weekly tobacco use and smoking. However, patients with depression had significantly lower physical activity compared to the control group ( $P < 0.01$ ). In addition, total energy intake was significantly higher in the patients with depression compared to the controls ( $P < 0.05$ ) (Table 1).

**Table 1.** Comparison of Variables between Patients with and without Depression

variables	Depressed (Mean±SE)	Non-depressed (Mean±SE)	P value
Age (year)	35.85±1.04	35.69±0.72	0.8
Height(cm)	162.8±0.79	163.4±0.59	0.5
Weight(kg)	69.7±1.3	70.1±0.96	0.8
BMI(kg/m <sup>2</sup> )	26.4±0.49	26.4±0.37	0.9
Smoking Habits (frequency per week)	8.2±2.8	8.2±2.8	0.09
Tobacco Use (frequency per week)	0.4±0.22	0.08±0.02	0.1
Physical Activity(MET-h/day)	36.9±0.52	38.6±0.33	0.007
Total Energy Intake(kcal/day)	2887±112	2634±69.9	0.04

P-value: simple logistic regression

In current research, we assessed the association between depression and the criteria of metabolic syndrome. According to the findings, none of the variables of metabolic syndrome were significant in the study groups (Table 2). However, after the adjustment of the confounders (physical activity, calorie intake, history of depression, depression score,

menopausal status, BMI, and dietary patterns), waist circumference was observed to be significantly higher in the patients with depression compared to the controls ( $P = 0.009$ ). In other words, waist circumference was associated with depression independent of the confounders.

**Table 2.** Relation between Depression and Criteria of Metabolic Syndrome before and after Adjustment of Confounders

Criteria of Metabolic Syndrome and Other Variables	Depressed (Mean±SE)	Non-depressed (Mean±SE)	P-value <sup>a</sup>	P-value <sup>b</sup>	P-value <sup>c</sup>	OR(95%CI)
Waist Circumference (cm)	89.1±1.2	88.2±0.9	0.5	-	0.009	1.49(1.12-2.007)
Systolic Blood Pressure (mmHg)	100.6±1.6	104.9±1.2	-	0.056	0.6	0.99(0.94-1.04)
Diastolic Blood Pressure (mmHg)	64±14	66±12	-	0.36	0.8	0.99(0.93-1.06)
Fasting Blood Glucose(mg/dl)	92±599	9371±12	-	0.4	0.2	2.03(0.67-6.10)
Triglyceride(mg/dl)	101±46	98±52	0.4	-	0.9	0.99(0.97-1.02)
HDLc (mg/dl)	48.5±1.4	48.7±1.2	0.7	-	0.8	1.14(0.39-3.36)

Total Cholesterol(mg/dl)	179±4.5	177.7±4.6	0.1	-	0.5	0.72(0.23-2.25)
LDLc (mg/dl)	112.5±3.8	108.7±3.7	0.5	-	0.8	1.13(0.39-3.2)
Insulin (µIU/ml)	13.2±9	13.9±9	-	0.7	0.6	0.95(0.74-1.21)
Insulin Sensitivity	0.33±0.024	0.33±0.023	0.5	-	0.3	0.22(0.01-4.7)

P<sub>value</sub><sup>a</sup>: t-test; P<sub>value</sub><sup>b</sup>: Mann-Whitney U test; P<sub>value</sub><sup>c</sup>: multiple logistic regression after adjusting confounders (physical activity, daily calorie intake, dietary patterns, history of depression, depression score, menopausal status, and BMI)

## Discussion and Conclusion

The present study aimed to assess the correlations between depression and the criteria of metabolic syndrome, including waist circumference, HDL-C, LDL-C, TG, fasting blood sugar, systolic and diastolic blood pressure, and insulin sensitivity. According to the obtained results, only waist circumference was significantly higher in the patients with depression compared to the controls, while this association was masked by the presence of the confounders before adjustment. After adjusting some important confounders (e.g., physical activity, daily calorie intake, dietary patterns, history of depression, and depression score), the difference was revealed. Therefore, it could be concluded that waist circumference is associated with depression independent of these confounders.

Consistent with our findings, the study by Ra and Kim (22) indicated that depression was significantly associated with high waist circumference among women after the adjustment of the covariates (education level, family income, high alcohol consumption, eating out, obesity, menopause, and use of antidepressants). Therefore, it could be inferred that the association of waist circumference and depression does not depend on the mentioned confounders.

In another research in this regard, Hiles et al. reported a positive correlation between depression and antidepressant use with waist circumference. In the mentioned prospective study, the association between depression and the components of metabolic syndrome was not considered significant after the discontinuation of antidepressants. Furthermore, the discontinuation of antidepressants led to the reduction of the waist circumference in the patients with depression after four years (23). This finding could be attributed to the high activity of the parasympathetic nervous system, which is associated with worsening of metabolic control (24).

In a bidirectional prospective study (23), the

severity of depression was reported to be associated with increased waist circumference. However, the criteria of metabolic syndrome did not lead to depression. This could be due to an unhealthy lifestyle, especially smoking habits and alcohol consumption, which often persist in the patients with depression despite the resolution of the other symptoms.

According to Kahl et al. (25), Dunbar et al. (26), and Pan et al. (14), metabolic syndrome is more prevalent in the patients with depression compared to normal individuals. Moreover, the results of a large, population-based study of Mexican-Americans indicated high rates of metabolic syndrome (46%) and depression (29%) (27).

In the present study, no associations were observed between depression and the other criteria of metabolic syndrome. This could be due to the fact that all the patients had only recently been diagnosed with depression and used no antidepressants. Considering that antidepressants cause metabolic disturbances, this outcome was expected. This finding is consistent with the study by Herva et al. (29), which showed no correlations between metabolic syndrome and depression after adjusting BMI and demographic indicators. Therefore, it could be concluded that waist circumference is a significantly different criterion between depressed and healthy individuals and could be proposed for the screening of the components of metabolic syndrome in the patients with depression (28).

Owing to the cross-sectional design of the current research, the obtained data could lead to the understanding of the differences in the metabolic syndrome criteria in depressed and healthy individuals. The correlations between the criteria of metabolic syndrome and depression were assessed before and after the adjustment of some confounders and risk factors of depression. The adjusted confounders were similar to the confounders in the previous studies in this regard (15, 29), with the exception of dietary patterns, which should be taken into account (30). It is also noteworthy

that the patients in the present study had only recently been diagnosed with depression and used no antidepressants. Therefore, this factor was statistically controlled rather than adjusted. Additionally, the inclusion and exclusion criteria of the study were determined with utmost precision.

One of the limitations of the current research was that we could not realize the temporal association between depression and metabolic syndrome.

### Conflict of interest

None declared.

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