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Depressive symptoms among metabolically healthy and unhealthy overweight/obese individuals: a comparative study

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Abstract

Background: Although a growing body of evidence suggests an association between obesity and depressive disorder, the association remains inconclusive. Metabolically healthy obese (MHO) phenotype, defined by favorable lipid profile, and normal insulin sensitivity, blood pressure, may be considered as a possible explanation for these inconsistencies. Accordingly, this study aimed to compare depression score among metabolic unhealthy obese (MUO) and age- and sex-matched healthy controls.

Methods: In this comparative study including 157 Iranian adults, we assigned participants into three groups (non-obese metabolic healthy group, MHO and MUO) according to the BMI cutoff and MetS criteria. Depressive symptoms were assessed by Beck Depression Inventory. Analysis was done using SPSS version 14.0. All variables are expressed as means± SD. One-way ANOVA and multiple linear regression were used for data analysis.

Results: After adjustment for sex, marital status and educational level, MUO participants had significantly higher Beck depression score (p= 0.036) compared to MHO and non-obese metabolic healthy groups. After adjustment for demographic variables, there was a significant association between waist circumference (β = 0.142, p=0.023), BMI (β= 0.347, p= 0.037), FBS (β= 0.096, p< 0.001), and the number of MetS components (β= 1.71, p= 0.002) with depression score.

Conclusion: MHO was a benign phenotype in relation to depression.

Keywords: Depressive symptom, MetS, Obesity

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Introduction

Mood disorders, particularly depression, represent a major concern in obese subjects (1-3). Although available evidence suggests that obesity is likely to have important impacts on the occurrence of major depression (1,2), the results of these studies were inconsistent (2,4), and not all obese persons have depressive symptoms (4). A subset of obese individuals who are free of unfavorable metabolic profiles so-called "metabolically healthy obesity" (MHO) may be considered as a possible explanation for these inconsistencies (5,6). MHO subject is characterized by normal insulin sensitivity, blood pressure, and favorable lipid and inflammatory profiles, despite excess body fat (7,8).

To our knowledge, only few studies examined the

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↑What is "already known" in this topic:
Depression, represent a major concern in obese subjects, however not all obese persons have depressive symptoms. Metabolically healthy obese (MHO) phenotype, subjects with favorable lipid profile, and normal insulin sensitivity, blood pressure, may be considered as a possible explanation for these inconsistencies.

→What this article adds:
In obese subjects, metabolic profile status rather than obesity is associated with risk of depression.

relation between mood disorder and MHO phenotype (6, 9-11). A pooled analysis study reported that MHO and MUO subjects had a mildly increased risk of depression-related symptoms compared to all non-obese subjects (10). Furthermore, data from Hamer et al. suggested an elevated risk for depressive symptoms among MUO, but not among MHO individuals, after a 2-year follow-up (6). However further work is required to confirm these findings.

The present study aimed to compare the depression status, between metabolic unhealthy obese (MUO) subjects with age and sex-matched healthy controls.

Methods

Study design and subject recruitment

One hundred fifty-seven adult subjects (20-55 years) participated in this cross-sectional study. The participants were divided into three groups: metabolically unhealthy overweight/obese (MUO), metabolically healthy overweight/obese (MHO) and non-obese metabolically healthy participants. The MUO, MetS patients were recruited from patients referred to the Endocrinology Center of Tehran University of Medical Sciences. The metabolically healthy groups (MHO and non-obese metabolically healthy) were age- and gender-matched to the MUO, made up of 64 weight-matched overweight/obese subjects without MetS, the "metabolically healthy obese" (MHO) and 40 non-obese metabolically healthy. MetS was diagnosed according to the National Cholesterol Education program – Adult Treatment Panel III (NCEP-ATP III) criteria (12) .

Inclusion criteria were having a BMI≥25 for the overweight/obese subjects and a BMI of 20–25 for the normal weight participants, age range 20-55 years and provided written consent of participation. Having any history of neurological (e.g., concussion, stroke, tumor, neuroinflammatory diseases) and medical conditions (e.g., cancer, chronic inflammatory or autoimmune diseases, heart diseases, diabetes mellitus, infections) as well as regular intake of medication and considered as exclusion criteria. Other non-pathological exclusion criteria included pregnancy, breastfeeding, post-menopause, smoking, professional athlete, having a special diet for any reason prescribed by the clinic dietitian, taking nutritional supplements and uncontrolled thyroid disorder. The study was approved by the ethics committee of Iran University of Medical Sciences (Ethic Number: 93-02-27-24976).

Assessment and measurement

Participants' body weight was measured in light clothing and without shoes (in kilograms −kg) using calibrate scale (Model 700, USA). Standing height was measured to nearest 1 mm using a Seca stadiometer (Model 700, USA) while subjects were barefoot, and their shoulders were in a normal position. Body Mass Index (BMI) of each participant was calculated as body weight divided by height squared (kg/m2) to the nearest 0.01kg and 0.1 cm. Waist circumference (13) was measured between the lower rib margin and the iliac crest using a flexible tape measure after normal expiration. Blood pressure was measured twice separately over a 5-min interval by a professional nurse. The average of 2 measurements was considered as blood pressure value. Levels of TG, HDL-c, and FBS were evaluated from yearly patients' medical chart records. The Beck Depression Inventory (BDI) (14) was used to assess depressive symptoms.

Statistical analysis

Analysis was done using SPSS version 14.0 for Windows (Chicago, Illinois, USA). All variables are expressed as means ± SD. Comparisons between the three groups were carried out using the one-way ANOVA. If the result of the ANOVA test was significant, LSD test was used to identify which pairs of means were statistically different. Multiple linear regression was used for assessing the association between MetS components and Beck depression score. For all analyses, a two tailed $p<0.05$ was considered statistically significant.

Results

A total of 157 participants attended in the present study. Demographic and clinical characteristics of the study population are shown in Table 1. Most subjects in all

Table 1. General characteristics, MetS parameters and Beck depression score of subjects based on study groups

	MUO[1] (n=53)	MHO[2] (n=64)	Non-obese metabolic healthy group (n=40)	p*
	SD± mean	SD± mean	SD± mean	
Age (year)	37.98±5.84	35.91±6.53	35.91±6.26	0.148
Weight (kg)	91.47±13.34[a]	89.09±12.76[a]	70.45±6.95[b]	<0.001
Height (cm)	171.48±7.56	172.63±6.93	172.65±6.23	0.659
WC (cm)	105.63±8.83[a]	100.07±11.55[b]	87.78±6.87[c]	<0.001
BMI (kg/m^2)	31.03±4.00[a]	29.85±3.52[a]	23.62±1.50[b]	<0.001
SBP	125.21±12.39[a]	116.31±11.41[b]	114.13±10.50[b]	<0.001
DBP	82.94±8.78[a]	77.08±8.85[b]	75.78±7.69[b]	<0.001
FBS	114.34±37.30[a]	97.03±18.77[b]	95.85±7.47[b]	<0.001
TG	270.92±202.38[a]	126.18±80.75[b]	122.60±73.87[b]	<0.001
HDL	50.90±8.27[a]	54.89±6.25[b]	55.47±9.25[b]	0.007
Number of MetS components	3.39±0.56[a]	1.06±0.79[b]	0.87±0.60[b]	<0.001
Beck depression score*	13.62±10.24[a]	9.53±8.04[b]	9.10±9.28[b]	0.036

1: Metabolically unhealthy obese, 2: metabolically healthy obese
Values are analyzed by one–way ANOVA, values are mean ± SD.
Dissimilar values (a, b, c) of each row are significantly different.
* Values are analyzed by ANCOVA; values are mean ± SD, adjusted for sex, marital status and educational level.

Table 2. Multiple linear regression for assessing the association between MetS components with Beck depression score

	Model 1[a]		Model 2[b]	
variables	β	p	β	p
Age (year)	0.117	0.327		
Gender	2.14	0,367		
Marital status	0.578	0.728		
Educational status	0.341	0.57		
Weight (kg)	0.080	0.118	0.088	0.091
Waist circumference (cm)	0.144	0.022	0.142	0.023
BMI (kg/m^2)	0.374	0.025	0.347	0.037
SBP	0.010	0.866	0.027	0.655
DBP	0.032	0.704	0.050	0.544
FBS	0.095	0.001	0.096	<0.001
TG	0.003	0.540	0.002	0.722
HDL	-0.133	0.153	-0.138	0.139
Number of MetS component	1.87	0.001	1.71	0.002

[a] Crude model
[b] Adjusted for sex, age, marital status, and educational level.

groups were men. In terms of age, sex, and marital status, there were no statistically significant differences between the three groups.

After adjustment for sex, marital status, and educational level, MUO patients had a significantly higher Beck depression score than MHO and non-obese subjects (p=0.036) (Table 1).

Linear regression analysis was used to assess the association between MetS components and depression score in all participants (Table 2). There was a significant association between WC (p=0.022), BMI (p=0.025), FBS (p=0.001) and number of MetS components (p=0.001). In a second model including adjustment for demographic variables (age, sex, marital status and educational level), there was a significant association between WC (p=0.023), BMI (p=0.037), FBS (p<0.001), number of MetS components (p=0.002) and depression.

Discussion

The present study aimed to compare the depression status, between metabolic unhealthy obese (MUO) subjects with age- and sex-matched healthy controls. Although a recent meta-analysis suggests that obesity is associated with an increased risk of depressive symptoms (2), literature are inconsistent (4, 15, 16). One of the interesting findings of the current research was that the simultaneous presence of obesity and MetS in a person, compared with the presence of obesity without MetS, was associated with a higher depression score. The current study shows that MUO subjects had a higher Beck depression score than MHO and metabolically healthy non-obese subjects (Table 1) .Accordingly, the obesity and depression seems to be dependent in the metabolic profile status. Evidence supporting this finding comes from several studies that report MUO to have higher odds of depression compared to MHO (6,9,11). However, to our knowledge, few studies have examined the risk of depression associated with MHO phenotype (9,10). Several factors, especially metabolic factors need to be evaluated related to depression in obesity subtypes.

Another key finding of the current report is that FBS, WC, and the number of MetS components were significant moderators of the relationship between the depression score and obesity subtypes. Elevated depression score in MUO increased almost linearly with increasing number of MetS components co-occurring with obesity. These findings remained consistent after adjusting for demographic variables including age, sex, educational level, and marital status. Previous analysis introduced WC and FBS as strong mediators of the association between depression and obesity phenotypes (6,17). A more specific delineation of other moderators such as adipocytokine is warranted to understand the link between depression and obesity phenotypes better. In the current study TG, HDL-c and BP relationship with Beck depression (Table 2) was not significant. However, this finding was supported by a similar study conducted by Hamer et al. with a large sample size (3851 men and women) (6). Furthermore, as mention earlier in this manuscript, limited number of studies investigated the relation between metabolically unhealthy obese and depressive symptoms (6, 9-11), makes it difficult to discuss. However, according to previous studies, individual components of the metabolic syndrome including impaired glycaemic control and waist circumference appear to be particularly important in driving the association (6, 17), which was also observed in this study.

Several physiological mechanisms have been proposed as explanations for the increased risk of depression among MUO adults. For example, one of the driving factors might be disturbances in the hypothalamic-pituitary-adrenal axis, particularly in the regulation of cortisol, which is, in turn, contributes to glucose dysregulation, and insulin resistance and the cascade of events in the metabolic syndrome (18-20). Hypothalamic-pituitary-adrenal axis disturbances have been associated with the depressive symptom (21). Furthermore, in obese adolescents, depression may be explained by biochemical changes directly caused by disturbances in metabolic abnormalities, such as enlarged cerebrospinal fluid space and reduced white matter volume (22).

This study had some limitations. We did not assess metabolically unhealthy non-obese individual. In addition, the observational nature of these studies may not provide definite information to ascertain a cause and effect. Accordingly, further studies are needed to establish the

relation between metabolic profile status and symptoms of depression.

Conclusion

We demonstrated that in obese subjects, metabolic profile status rather than obesity is associated with a higher risk of depression. The obesity and depression link seems to be dependent on metabolic profile status.

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None of the authors has any competing interest. And no financial competing interest in relation to the work described (Ethic Number: 93-02-27-24976).

Conflict of Interests

The authors declare that they have no competing interests.

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