



# The Association between Obesity-Insulin Resistance and Depression-Anxiety: One Center, Cross-Sectional Study

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## Abstract

**Objective:** Obesity is related to mental illnesses. Atypic body weight affects mental health as well as mental illnesses affecting weight. In this study, our aim is to investigate psychological changes in obese patients.

**Methods:** Three hundred patients were included in the study. Weight, height, and waist circumference (WC) were recorded. FBS and insulin were measured. Insulin resistance (IR) was calculated. Patients were evaluated by psychiatrist according to the Beck depression–anxiety scale.

**Results:** Two hundred and forty-nine patients had BMI of  $>30$  kg/m<sup>2</sup> (83%, group 1) and 51 people had a BMI of  $>25$  kg/m<sup>2</sup> (17%, group 2). Two hundred and thirty females had WC of  $>85$  cm and 47 males had WC of  $>104$  cm. One hundred and forty-two patients had a BMI of  $>30$  kg/m<sup>2</sup>, and 13 in the control group had depression ( $p=0.00$ ). Eighty-four patients in the obese group and 5 in the control group had anxiety. Depression and anxiety rates were significantly different according to WC s ( $p=0.015$  vs.  $p=0.001$ ); 191 patients had IR, although 91 of the patients had depression and 54 had anxiety.

**Conclusion:** Our study found an association between obesity and depression in midlife population. These results suggest that obesity may contribute to depression. Also, a positive association was found between depression and IR; the association seemed to be mediated partially by WC.

**Keywords:** Obesity, insulin resistance, depression, anxiety

## Introduction

Obesity and depression are two prevalent disorders associated with adverse consequences. They have medical and economic costs for both individuals and society. Globally, obesity has reached epidemic proportions. According to the World Health Organization (WHO) estimate, approximately 1.5 billion adults are overweight (BMI, 25–29.9 kg/m<sup>2</sup>); among them, more than 200 million men and nearly 300 million women are obese, with a BMI greater than or equal to 30 kg/m<sup>2</sup> (1). Obesity rates have increased dramatically over the last 30 years (2). This is related to social, cultural, and environmental factors. The health impact of obesity is tremendous; it increases risks for many chronic diseases and conditions, including hypertension, diabetes, hypercholesterolemia, coronary heart disease, cancers, and many others (3, 4). Obesity, particularly abdominal obesity, is associated with an increased risk of outcomes such as cardiovascular or cancer mortality (5).

Depression is a major global health problem, and it will rank second among the most common diseases by the year 2030 (6). Depressive and anxiety disorders are the most common mental disorders, with lifetime prevalence varying across countries between 4.8% and 31.0% for anxiety disorders and between 3.3% and 21.0% for depressive disorders (7, 8). Furthermore, recent prescription statistics suggest that antidepressant medications are currently among the most commonly prescribed classes of medications in outpatient medical practices (9). In addition to the broad range of obesity-related physiologic outcomes, obesity is associated with an increased number of mental disorders (i.e., depression, bipolar disorder, panic disorder, anxiety, and many others) that have a substantial impact on public health (e.g., disability, increased mortality, and reduced quality of life). The relationship between mental disorders and obesity is controversial. Atypical body weight affects mental health, just as mental illnesses affect body weight.

Meta-analyses and systemic reviews of cross-sectional studies have suggested that depression and obesity are associated with one another (10, 4). However, cross-sectional evidence does not provide detailed insight into the temporal relationship between two conditions. Several longitudinal studies were conducted, and meta-analyses suggested a reciprocal link between obesity and depression (11). In this study, our aim is to investigate psychosocial changes in obesity. We suggest that obesity is a risk factor for depression. We used waist circumference (WC) measurement and BMI to show the relationship between obesity and mental disorders. We also analyzed the relationship between depression–anxiety and insulin resistance (IR). Our second aim is to test whether or not depression and anxiety disorders are associated with the duration of obesity.

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## Methods

An outpatient obesity clinic followed 249 patients. None of them had any systemic illness, and none had taken drugs in the last 3 months that could affect body weight; a control group of 51 healthy weight volunteers was also included in the study. All patients were weighed without shoes using a digital scale their standing heights were measured using a fixed stadiometer. BMI was calculated by dividing body weight in kilograms by body height in square meters and then categorized based on the WHO cut-off points for normal weight (BMI of  $<25 \text{ kg/m}^2$ ), overweight (BMI of 25 to  $<30 \text{ kg/m}^2$ ), mild obesity (BMI of 30 to  $<35 \text{ kg/m}^2$ ), moderate obesity (BMI of 35 to  $<40 \text{ kg/m}^2$ ), and severe obesity (BMI of  $>40 \text{ kg/m}^2$ ). WC and hip circumference (HC) were measured using a flexible tape, and waist-to-hip ratio (WHR) was calculated. All patients had at least 12 h of fasting before blood sampling for biochemical analysis. Fasting blood glucose (FBG), triglyceride (TG), total cholesterol (TC), high-density cholesterol (HDL), and low-density cholesterol (LDL-C) were measured spectrophotometrically using the Abbot Aeroset 2.0 (Abbot Diagnostics USA). Insulin was measured by the electro chemiluminescence immunoassay (ECLIA) method on Roche-Hitachi E 170. IR was calculated using the homeostasis model assessment formula ( $\text{HOMA-IR} = \text{fasting insulin (mU/L)} \times \text{glucose (mmol/dL)} / 22.5$ ).

Our psychologist and psychiatrist evaluated patients according to the Beck depression–anxiety scale. The Beck Depression Inventory (BDI-I) is made up of 21 (self-reported depression) questions designed to help mental health professionals assess the mood, symptoms, and behaviors of people who are depressed. Each answer is given a score of 0–3 that indicates the severity of symptoms.

Depression can be considered to have the following two components: the affective component (e.g., mood) and the physical or “somatic” component (e.g., loss of appetite). The BDI-II reflects this and can be separated into two subscales. The purpose of subscales is to help determine the primary cause of a patient’s depression.

The affective subscale contains the following eight items: pessimism, past failures, guilty feelings, punishment feelings, self-dislike, self-criticalness, suicidal thoughts or wishes, and worthlessness. The somatic subscale consists of the remaining 13 items: sadness, loss of pleasure, crying, agitation, loss of interest, indecisiveness, loss of energy, changes in sleep patterns, irritability, change in appetite, concentration difficulties, tiredness and/or fatigue, and loss of interest in sex. The two subscales are moderately correlated at 0.57, suggesting that the physical and psychological aspects of depression are related.

The research protocol was approved by the local ethical committee at İstanbul Training and Research Hospital. All patients gave written informed consent.

### Statistical analysis

Statistical analyses were performed using the SPSS program for Windows v. 17.00. Baseline data were expressed as means  $\pm$  SD. To analyze differences between groups, we used an independent sample t-test. A value of  $p < 0.05$  was considered statistically significant.

## Results

The study included 253 females and 47 males for a total of 300 participants. Among them, 249 people had a BMI of  $>30 \text{ kg/m}^2$  (83%, Group 1) and 51 had a BMI of  $>25 \text{ kg/m}^2$  (17%, Group 2). WC data showed 230 females with a WC of  $>85 \text{ cm}$  and 47 males with a WC of  $>104 \text{ cm}$ . The mean age of patients was  $46.1 \pm 13.3$  years. Among obese patients, 32 had been obese for less than 5 years (10.7%) and 217 patients had been obese for more than 5 years (72.3%). There were no significant differences for average systolic or diastolic blood pressure, serum total cholesterol, or HDL-C levels, whereas FBG, triglyceride, and LDL-C levels had significant differences. As expected, IR was higher in the obesity group. Table 1 shows the characteristics of the patients.

Of patients with BMI greater than 30, 142 had depression, as did 13 from the control group ( $p = 0.00$ ). Eighty-four patients in the obese group and five in the control group had anxiety. There is a positive correlation between higher BMI and depression–anxiety risk.

According to BMI values, a significant difference was observed in depression and anxiety rates between the two groups ( $p = 0.001$  vs.  $0.000$ ). Depression was associated with an increase in obesity rates.

Depression and anxiety rates were significantly different according to WC ( $p = 0.015$  vs.  $0.001$ ). Rates were higher as WC increased, whereas no correlation was observed with waist-to-hip ratio (Table 2).

In the obese for less than 5 years group, 13 patients had depression; in the obese for more than 5 years group, 133 had depression. As for anxiety, it affected 11 patients in the obese for less than 5 years group and 75 patients in the obese for more than 5 years group.

In our study, females were represented more than males (230 females vs. 29 males). Of these 230 patients, 132 had depression and 79 had anxiety, whereas in our control group, 11 had depression and 2 had anxiety. Among the 29 obese male patients, 14 had depression and seven had anxiety, while in the control group, two had depression and three had anxiety.

**Table 1. Mean characteristics of the patients**

	Obese group	Control group	p
n	249	51	
BMI ( $\text{kg/m}^2$ )	$39.05 \pm 6.10$	$23.63 \pm 1.54$	0.000
WC (cm)	$112.47 \pm 13.36$	$82.71 \pm 6.13$	0.000
Waist/Hip ratio	$0.87 \pm 0.8$	$0.86 \pm 0.4$	0.167
BP systolic (mmHg)	$134.77 \pm 72.73$	$120.59 \pm 10.66$	0.167
BP diastolic (mmHg)	$80.47 \pm 8.65$	$76.67 \pm 8.92$	0.060
FBG (mg/dL)	$105.06 \pm 35.09$	$85.90 \pm 8.54$	0.000
T-Chol (mg/dL)	$196.52 \pm 40.17$	$177.76 \pm 24.89$	0.020
LDL-C (mg/dL)	$120.64 \pm 34.46$	$103.37 \pm 20.76$	0.001
HDL-C (mg/dL)	$47.65 \pm 11.16$	$47.84 \pm 6.62$	0.905
TRG (mg/dL)	$154.73 \pm 80.61$	$126.27 \pm 30.31$	0.014
Insulin (mU/L)	$16.17 \pm 12.56$	$7.49 \pm 4.01$	0.000
HOMA	$4.34 \pm 4.00$	$1.59 \pm 0.49$	0.000

BMI: body mass index; WC: waist circumference; FBG: fasting blood glucose; LDL-C: low density cholesterol; HDL-C: high-density cholesterol; HOMA: homeostatic model assessment

**Table 2. Demographic characteristics of depressive–anxiety patients**

	Depression (+) n=159	Depression (-) n=141	p	Anxiety (+) n=91	Anxiety (-) n=209	p
BMI	37.50±7.51	34.55±8.44	0.001	39.10±7.82	34.81±7.87	0.000
WC	109.15±15.30	104.43±17.92	0.015	111.79±15.57	104.82±16.80	0.001
Waist-to-hip ratio	0.87±0.08	0.87±0.7	0.627	0.87±0.9	0.87±0.6	0.413
Obesity duration<5 years, n=32	13	19		11	21	
Obesity duration>5 years, n=217	133	184		75	132	
Obese female, n=220	32	188		79	141	
Control female, n=33	11	22		2	31	
Obese male, n=29	14	15		7	22	
Control male, n=18	2	16		3	15	

BMI: body mass index; WC: waist circumference

We observed more cases of depression and anxiety in patients with IR. IR, as expressed by HOMA, was found to be  $4.34\pm 4.00$  in Group 1 vs.  $1.59\pm 0.49$  in Group 2 ( $p=0.000$ ). Of the 300 patients, 191 patients had IR; 91 of them had depression and 54 had anxiety.

We observed no relationship between lipid parameters (total cholesterol, LDL-C, HDL-C, and triglyceride) and depression and anxiety.

## Discussion

Depression symptoms are a common source of distress and dysfunction and have a great impact on a patient's quality of life. It is estimated that by the year 2020, unipolar major depression will be the second leading cause of the global disease burden (12). Obesity is a major health problem, and it has been linked to greater depression in previous studies. Obesity and depression are two prevalent disorders that are medically and economically costly to both individuals and society (13). Also, gender differences have been observed in the relationship between anthropometric measures and depressive symptoms (13, 14). According to Zhao's study, women who were either overweight or obese were 17%–31% more likely to experience current depression, 17%–53% more likely to have depression, and 9%–17% more likely to be diagnosed with anxiety at some time in their lives (15).

As previously noted, our study has a larger female population than male population. Age and sex have significant influences on obesity. One study has suggested that there might be a U-shaped association between BMI and depression; being underweight or overweight were both associated with depression compared with being normal weight (12, 16). Moreover, anxiety disorders are elevated among underweight men compared with normal weight men and women. On the other hand, mood disorders are elevated among obese women compared with normal weight women and men (17). Although there is a meta-analysis showing an 18% increased chance of obese patients having depression (8), in our study, we observed a 46% increased chance of having depression among our obese group compared with the control group. We also showed a greater increase than that shown in the meta-analysis of 18% depression among obese patients.

Most previous studies have focused on the association between obesity and depression, and various mechanisms have been proposed to explain this relationship. Some of those mechanisms

propose causal pathways leading from depression to obesity. Increased appetites lead people to eat more carbohydrates and fats; thus, weight gain is a common symptom of depression. Depression may lead to reduced physical activity in addition to increasing the risk of obesity (18). Medications used to manage mood or anxiety disorders may also lead to weight gain (19). Alternatively, some proposed mechanisms suggest a causal relationship leading from obesity to depression. In particular, emotional eating, food reward processes, and elevated brain monoamine activity may be linked to depression and obesity (20, 21). Overeating disorders may result from a dysregulation of the hypothalamic–pituitary–adrenal (HPA) axis in people with major depressive disorders; this could stimulate food intake (through the neuropeptide Y system) and reduce the efficiency of the inhibition of food intake (through the leptin system), thereby increasing food intake and body fat accumulation (15). Moreover, persistent unhealthy dietary habits may lead to increases in dyslipidemia and abdominal obesity. A biologic mechanism may be an increased activity of the sympathetic nervous system (SNS), HPA axis, and proinflammatory cytokines. Cell-mediated cytokine production is another possible mechanism for IR. Patients with depressive or anxiety disorders display higher levels of inflammation than do controls. At the same time, inflammation induces obesity through leptin resistance (22, 23). Chronic inflammation in people who are vulnerable to depression or anxiety may cause progressive dyslipidemia, abdominal obesity, and IR (22).

In a longitudinal study conducted van Reedt Dorland (22), they observed that people with more severe symptoms of depression or anxiety displayed a decline in HDL cholesterol and increased abdominal obesity over the subsequent 2 years. Zhao et al. (5) suggested that abdominal obesity is strongly correlated with depression. In our study, we noted that patients reported more depression or anxiety as their WC increased, yet no impact was spotted with varying HDL and LDL levels.

Robert et al. (24) who were working in the US with a sample of 1886 middle-aged and elderly men and women found that obesity as a baseline measurement was associated with an increased risk of depressed mood 5 years later (25). Likewise, in our study, we observed that patients reported more depression and/or anxiety as the number of years in which they have lived with obesity increased.

A meta-analysis by Luppino et al. (11) on the bidirectional association between depression and obesity found that baseline depression was associated with an increased risk of developing obesity

(OR, 1.53; 95% CI, 1.33–1.87), and baseline obesity increased the risk of occurrence of depression (OR, 1.55; 95% CI, 1.22–1.98) (24). In our study, although we included patients without known depression or anxiety, after employing the Beck depression test and observing our patients, we determined that 46% had depression and 23% had anxiety. Our results were partially explained by the reciprocal association between depression and obesity, which are both conditions related to elevated BMI levels.

In this study, we also examined the association between IR and depression among obese adults. We used HOMA indexes to measure IR and found that it was significantly related to depressive disorders. This relationship was, however, partially mediated by WC. One of the mechanisms to which depression may contribute is the disruption in glucose metabolism, central adiposity. Insulin resistant-type 2 diabetes mellitus is thought to be a result of the activation of the HPA axis and SNS. Pearson et al. (26) reported similar findings in healthy young adults. A recent meta-analysis found that the risk of depression is similar with normal and impaired glucose tolerance and undiagnosed diabetes (27). However, others have shown that depression is often present with IR (28).

Our study has several limitations. One of the main limitations was its cross-sectional design, which made it impossible to determine any causal pathway or relationship between the development of depression and obesity via the mechanisms outlined above. We were also limited by not being able to measure HPA activity such as cortisol. A long period of increased production of stress hormones from the HPA axis and SNS are involved in depression, which contributes to body fat accumulation. We observed a causal association between depression and IR that is partially mediated by increases in WC. Poor social relationships, low socioeconomic status, and multiple chronic diseases associated with obesity may have predisposed obese people to impaired mental health. Our study excluded people who had any systemic diseases, but we did not evaluate patients according to their social and economic status. The number of healthy volunteers in our study made up only 20.8% of the total number of patients; this could have been higher to facilitate and easier comparison of results.

## Conclusion

Our study found a consistent association between obesity and depression in a midlife population. Obesity may contribute to depression and may have different effects on various aspects of depression symptoms. Also, the results of this study show a significant relationship between depressive disorders and IR. The association with depression may be because of confounding by abdominal obesity. A causal association between depression and IR mediated by increases in WC among those with depression is also plausible. The effective treatment of depression can improve IR, and lifestyle programs can improve IR and reduce depressive symptoms. In clinical settings, care providers need to monitor body weight in depressive patients and mood status in obese individuals. Multidisciplinary approaches may be useful for controlling depression and IR.

**Ethics Committee Approval:** Ethics committee approval was received for this study.

**Informed Consent:** Written informed consent was obtained from patients who participated in this study.

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