*Original Contribution/Clinical Investigation*

# Mental health may not have a chronic low-grade inflammatory background on vascular endothelium

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## ABSTRACT

**Background:** Although sedentary lifestyle, excess weight, smoking, alcohol, chronic infection and inflammations, and cancers induced chronic low-grade inflammation on vascular endothelium may shorten human lifespan significantly, there is not enough finding about effects of the inflammatory process on mental health in the literature.

**Methods:** We studied consecutive patients between the ages of 15 and 70 years to be able to see possible consequences of under- and excess weight on mental health and to avoid debility induced weight loss in elder individuals. Patients with devastating illnesses and a history of eating disorders were excluded to avoid their possible effects on weight. History of medications for depression and current need for a psychiatric consultation for any cause according to the general physical examination findings of the Same Internist were detected.

**Results:** The study included 971 cases (554 females), totally. Prevalences of underweight, normal weight, overweight, and obesity were detected as 3.7%, 34.9%, 36.1%, and 25.2%, respectively. There were not significant differences between the four groups according to history of depression or current need for a psychiatric consultation for any cause or both ($p>0.05$ for all).

**Conclusion:** Metabolic syndrome is a chronic low-grade inflammatory process on vascular endothelium all over the body, terminating with an accelerated atherosclerosis, early aging, end-organ failures, and premature death. Although excess weight is the main determiner factor of the syndrome, neither under- nor excess weight has any adverse effect on mental health. So mental health may not have a chronic low-grade inflammatory background on vascular endothelium in general.

**Key words:** Mental health, metabolic syndrome, endothelial inflammation, body mass index

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## Introduction

Due to the prolonged survival of human beings, systemic atherosclerosis may be the major health problem in this century, and its association with physical inactivity, excess weight, smoking, and alcohol is collected under the heading of metabolic syndrome (1, 2). The syndrome is characterized by a low-grade chronic inflammatory process on vascular endothelium all over the body (3). The inflammatory process is particularly accelerated by some factors including sedentary lifestyle, excess weight, smoking, alcohol, chronic inflammation and infections, and cancers (4, 5). The syndrome can be slowed down with appropriate nonpharmaceutical approaches including lifestyle changes, diet, exercise, cessation of smoking, and withdrawal of alcohol (6). The syndrome contains reversible indicators including overweight, white coat hypertension, impaired fasting glucose, impaired glucose tolerance, hyperlipoproteinemias, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus, chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, peripheric artery disease, coronary artery disease (CAD), and stroke (7, 8). In another perspective, the metabolic syndrome may be the most important disease of human lifespan decreasing its quality and duration at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (9). The syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging, end-organ failures, and premature death for both genders. For example, CAD is the leading cause of death in developed countries. Although the absolute negative effects of excess weight on physical health (10), there are various reports about relationships between body mass index (BMI) and depression or psychiatric disorders including anxiety and somatoform disorders in the literature (11-13). We tried to understand whether or not there is a relationship between excess weight and mental health.

## Materials and Methods

Due to the prolonged survival of human beings, systemic atherosclerosis may be the major health problem in this century, and its association with physical inactivity, excess weight, smoking, and alcohol is collected under the heading of metabolic syndrome (1, 2). The syndrome is characterized by a low-grade chronic inflammatory process on vascular endothelium all over the body (3). The inflammatory process is particularly accelerated by some factors including sedentary lifestyle, excess weight, smoking, alcohol, chronic inflammation and infections, and cancers (4, 5). The syndrome can be slowed down with appropriate nonpharmaceutical approaches including lifestyle changes, diet, exercise, cessation of smoking, and withdrawal of alcohol (6). The syndrome contains reversible indicators including overweight, white coat hypertension, impaired fasting glucose, impaired glucose tolerance, hyperlipoproteinemias, alcohol, and smoking for the development of irreversible consequences including obesity, hypertension (HT), type 2 diabetes mellitus, chronic obstructive pulmonary disease, cirrhosis, chronic renal disease, peripheric artery disease, coronary artery disease (CAD), and stroke (7, 8). In another perspective, the metabolic syndrome may be the most important disease of human lifespan decreasing its quality and duration at the moment. The syndrome has become increasingly common all over the world, for instance 50 million people in the United States are affected (9). The syndrome induced accelerated atherosclerotic process all over the body may be the leading cause of early aging, end-organ failures, and premature death for both genders. For example, CAD is the leading cause of death in developed countries. Although the absolute negative effects of excess weight on physical health (10), there are various reports about relationships between body mass index (BMI) and depression or psychiatric disorders including anxiety and somatoform disorders in the literature (11-13). We tried to understand whether or not there is a relationship between excess weight and mental health.

## Results

The study included 971 cases (554 females and 417 males), totally. There were only thirty-six cases (3.7%) in the underweight group. Prevalence of the cases with normal weight, overweight, and obesity were detected as 34.9% (339 cases), 36.1% (351 cases), and 25.2% (245 cases), respectively. Mean ages of the groups showed gradual and highly significant increases from the underweight towards the obesity groups (24.4, 32.4, 43.5, and 49.1 years, respectively, $p<0.001$ nearly for all). The prominent but nonsignificant difference between the underweight and normal weight groups according to the mean age may just be due to the smaller sample size of the underweight group. So aging alone may be the main determinator factor of excess weight. Additionally, female ratios were detected as 61.1%, 51.3%, 47.0%, and 78.7% in the underweight, normal weight, overweight, and obesity groups, respectively. So there was a significant female predominance of the obesity group ($p<0.001$). On the other hand, when we compared the four groups according to history of medications for depression or current need for a psychiatric consultation for any cause, or both, there were not statistically significant differences between them ($p>0.05$ for all) (Table 1).

## Discussion

Probably obesity is found among one of the irreversible endpoints of the metabolic syndrome, since after development of obesity, nonpharmaceutical approaches provide limited benefit either to heal obesity or to prevent its complications. Overweight and obesity probably lead to a chronic low-grade inflammation on vascular endothelium that is associated with many coagulation and fibrinolytic abnormalities suggesting that excess weight may cause a prothrombotic and proinflammatory state (15). The chronic inflammatory process is characterized by lipid-induced injury, invasion of macrophages, proliferation of smooth muscle cells, endothelial dysfunction, and increased atherogenicity (16, 17). Elevation of C-reactive protein (CRP) levels in serum carries predictive power for the development of atherosclerotic end-points (18, 19), and overweight and obesity are considered as strong factors for controlling of CRP concentration in serum, because adipose tissue produces biologically active leptin, tumor necrosis factor-alpha, plasminogen activator inhibitor-1, and adiponectin. So adipose tissue is involved in the regulation of cytokines, and individuals with overweight and obesity have elevated CRP levels in serum (20, 21). On the other hand, individuals with excess weight will have an increased circulating

blood volume as well as an increased cardiac output, thought to be the result of increased oxygen demand of the extra tissue. The prolonged increase in circulating blood volume may lead to myocardial hypertrophy and decreased compliance, in addition to the common comorbidity of atherosclerosis and HT. In addition to the atherosclerosis and HT, fasting plasma glucose and serum total cholesterol levels were all elevated with the increased BMI values (22). Similarly, prevalence of CAD and ischemic stroke increased with an elevated BMI value in another study (23). On the other hand, the chronic low-grade inflammatory process may also cause genetic changes on the epithelial cells, and the systemic atherosclerotic process may decrease clearance of malignant cells by the immune system, effectively (24). Eventually, the risk of death from all causes including cardiovascular diseases and cancers increased throughout the range of moderate and severe weight excess for both genders in all age groups (25).

Although the higher BMI is associated with higher prevalence of atherosclerotic end-points, there are various reports about its association with psychiatric disorders . Some reports suggest the presence of associations between atherosclerotic consequences and psychiatric disorders, and these associations may increase the likelihood of health service utilization and length of stay in treatment programs (26). Mental health tended to be related with the BMI (27), and there was a higher prevalence of mental disorders among general practice patients showing a BMI of 30 kg/m2 or higher (28). Similarly, obesity was related with the increased rates of mental disorders in women between the ages of 18 and 25 years (29). Additionally, people with a BMI of 30 kg/m2 or higher showed higher odds for depression in a study performed among 50 to 94 year olds from Alameda County (30). In another study, obesity was associated with a 37% increase in the probability of being diagnosed with major depression in women, while with a decrease of similar magnitude in men (13). The positive association between the relative body weight and probability of major depression among adult women was additionally shown with some previous studies by using subclinical indexes of psychological well-being (31, 32). Similarly, individuals with a lifetime history of major depression were more likely to have obesity (19% versus 15%, respectively, p<0.001), and lifetime major depression was associated with higher odds of obesity in female respondents, whereas not in male respondents as a result of sex-specific multivariate analysis (33). In another study, obesity was associated with significant increases in lifetime diagnosis of major depression, bipolar disorder, and panic disorder or agoraphobia (34). Additionally, a 10-unit increase of BMI increased the risk of past-year suicide thought and attempts by 22% in females, however, reduced the risk by 26% and 55%, respectively, in males (13). An interesting finding among men may be the association between being underweight and having an increased probability of clinical depression and suicidal tendencies. The relationship between lower BMI and depression was previously demonstrated in a community sample of young

**Table 1: Characteristics of the study cases**

| Variables | Underweight | *p*-value | Normal weight | *p*-value | Overweight | *p*-value* | Obesity |
|---|---|---|---|---|---|---|---|
| Number | 36 (3.7%) | | 339 (34.9%) | | 351 (36.1%) | | 245 (25.2%) |
| ***Mean age (year)*** | ***24.4 ± 8.5 (15-61)*** | Ns† | ***32.4 ± 13.3 (15-69)*** | ***<0.001*** | ***43.5 ± 13.2 (15-70)*** | ***<0.001*** | ***49.1 ± 10.6 (19-70)*** |
| ***Female ratio*** | 61.1% | Ns | 51.3% | Ns | ***47.0%*** | ***<0.001*** | ***78.7%*** |
| Depression history | 25.0% | Ns | 26.8% | Ns | 26.4% | Ns | 25.3% |
| A psychiatric consultation need | 8.3% | Ns | 13.8% | Ns | 15.0% | Ns | 11.4% |
| Depression history and/or a psychiatric consultation need | 33.3% | Ns | 35.6% | Ns | 37.6% | Ns | 33.4% |

*Value between normal weight and obesity
†Nonsignificant (p>0.05)

males (35). When the authors analyzed weight status as a categorical variable, the underweight men were 81% more likely to have thoughts about suicide, 77% were more likely to have attempted suicide, and 25% more likely to be clinically depressed than average-weight men (13). According to the above study performed on 2,064 women aged between 18 and 25 years in Germany, obese women suffered from an anxiety disorder significantly more often (29). Eventually, according to a current review, the most rigorous clinical studies suggest those children and adolescents with major depressive disorder may be at increased risk for developing overweight , patients with bipolar disorder may have elevated rates of overweight, obesity, and abdominal obesity, and obese individuals desiring weight-loss therapy may have elevated rates of depressive and bipolar disorders (36). According to the same review, the most rigorous community studies suggest those depression patients with atypical symptoms in females is significantly more associated with overweight, obesity is associated with major depressive disorder in females, and abdominal obesity may be associated with depressive symptoms in both genders, but most overweight and obese individuals in the community do not have mood disorders (36). On the other hand, similar to our results, another survey study did not find a relationship between higher BMI and general psychopathology by using the Diagnostic and Statistical Manual for Mental Disorders IV criteria based on the Composite International Diagnostic Interview, and this study was conducted with a general population sample of 3,021 German subjects ranging from 14 to 24 years of age and controlled for eating disorders (12). There was not any significant association between the higher BMI and mood, anxiety, substance use, and somatoform disorders (12). Additionally, neither obesity nor underweight was significantly associated with any kind of general psychopathology (12). In another study, although authors found a statistically significant relationship between higher BMI and physical health, they could not between the higher BMI and psychosocial outcomes such as poorer emotional, school, or social functioning (37). Additionally, obesity was associated with significantly lower lifetime risk of substance use disorder both in males and females (34). So although the sedentary lifestyle, excess weight, smoking, alcohol, chronic infection and inflammation, and cancers induced chronic low-grade inflammatory process on vascular endothelium all over the body may shorten the human lifespan significantly, there is not any significant association between the inflammatory process and mental health in general.

In the absence of any chronic low-grade inflammatory background of mental health on vascular endothelium, our results about the effects of under- and excess weight on mental health may also be explained by the self-admiring properties of the human being. Human beings believe that their features are the best for themselves. He or she is created as the best, and he or she is actually the wonderful person in the world. Their height, weight, and intelligence are actually the optimum for themselves. Thus he or she is afraid of changing image or body compositon, actually. This property may be necessary for human beings to be able to live and fight against various stresses during their lifespan. In the absence of this property, human beings may not be able to fight against various stresses and continue to survive during their lifespan, and they may desire to terminate their lives frequently. So although the self-admiring property of human beings seem bad, it may be absolutely necessary to be able to continue his or her life in this stressful world.

As a conclusion, metabolic syndrome is a chronic low-grade inflammatory process on vascular endothelium all over the body, terminating with an accelerated atherosclerosis, early aging, end-organ failures, and premature death. Although excess weight is the main determining factor of the syndrome, neither under- nor excess weight has any adverse effect on mental health. So mental health may not have a chronic low-grade inflammatory background on vascular endothelium in general.

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