Metabolic Syndrome and Depression: A Cross-Sectional Analysis

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Objective: To examine the prevalence of the metabolic syndrome in depressive outpatients and to identify its correlates in depression.

Method: This cross-sectional analysis was performed on 121 depressive outpatients from January 2002 through January 2004 who were diagnosed at baseline with the Structured Clinical Interview for DSM-III-R. The metabolic syndrome was diagnosed at 6-year follow-up according to the modified criteria of the National Cholesterol Education Program. The severity of depressive symptoms was assessed at follow-up with the Beck Depression Inventory and the Hamilton Rating Scale for Depression, and general psychopathology was assessed with the Symptom Checklist-90.

Results: At 6-year follow-up, the prevalence of metabolic syndrome in the study group of depressive outpatients was 36% (N = 44). The syndrome was associated with a current diagnosis of major depression and overeating, but not with age or sex.

Conclusion: The metabolic syndrome is highly prevalent among patients with a history of depression, especially those with current major depression. This may have implications for treatment. Furthermore, attention should be focused on the physical health of those suffering from depression.

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Depression is a chronic and recurrent disorder[1] associated with significant functional impairment,[2] morbidity,[3] and increased mortality, especially death by unnatural causes and cardiovascular disease.[4,5] Levels of functional impairment in depression are considered even greater than with other long-term somatic disorders, such as hypertension and diabetes, and rank close to myocardial infarction.[2] There is growing evidence that depression affects physical health.[6] The connection between depression and insulin resistance has been especially in focus in the last few years.[7–9]

The concept of the metabolic syndrome, also known as the insulin resistance syndrome, was introduced by Reaven in 1988.[10] Since then, the metabolic syndrome has been considered a cluster of metabolic abnormalities, including disturbed glucose and insulin metabolism, hypertension, dyslipidemia, and centrally distributed obesity.[11,12] The pathogenesis of the syndrome is complex and incompletely understood, but the interaction of obesity, a sedentary lifestyle, and dietary and genetic factors is known to contribute to its development.[10,13,14] The metabolic syndrome is associated with an increased risk of both type 2 diabetes mellitus (by 5- to 9-fold) and cardiovascular diseases.[15,16] It also increases cardiovascular mortality by 2- to 3-fold.[17,18]

The prevalence of the metabolic syndrome in nondiabetic adult Europeans is approximately 15%. According to a modification of the World Health Organization definition, the age-standardized prevalence of the metabolic syndrome is 15.7% for men and 14.2% for women (aged 30–89 years, median age = 57 years).[19] In a Swedish study among clinically healthy men, all aged 58 years, the prevalence of the metabolic syndrome according to World Health Organization criteria was 16%.[20]

In central-eastern Finland, similar rates for the metabolic syndrome have been found. The prevalence of the syndrome was 11% in a cohort of 1038 men aged 42 to 60 years without cardiovascular disease, diabetes, or cancer,[15] as defined by the National Cholesterol Education Program (NCEP). In a general population sample of 1355 subjects aged 40 to 45 years, the prevalence of the metabolic syndrome was 17% in men and 18% in women.[21]

Meanwhile, a cross-sectional population-based study of women aged 35 to 54 years recorded the prevalence of metabolic syndrome according to the looser criteria as 19.5% and by the standards of the more strict criteria as 6.3%.[22]

In 2005, the International Diabetes Federation (IDF) released a consensus definition of the metabolic syndrome.[23] Among U.S. adults in the National Health and Nutrition Examination Survey, the age-adjusted prevalence of the metabolic syndrome was 34.6% according to NCEP criteria and 39.1% according to IDF criteria; both sets of criteria were quite concordant in discovering the same people—the overlapping was 93% in the study by Ford.[24] The present IDF definition of metabolic syndrome is, thus, in white subjects quite similar in practice to the modified Adult Treatment Panel (ATP) III (NCEP) definition.[25]

The prevalence of the metabolic syndrome among psychiatric patients has previously been studied in association with schizophrenia,[26–28] bipolar disorder,[29] and depression.[30] In schizophrenia, the prevalence of the metabolic syndrome in Finland according to NCEP criteria was 37% in patients with a mean age of 45 years[26] and 19% among patients in their early 30s.[28] By comparison, in a Canadian study,[27] the prevalence of the metabolic syndrome in schizophrenia according to ATP III criteria was 42.6% in men (mean age = 42.7 years) and 48.5% in women (mean age = 44.5 years). Among bipolar disorder patients in Pennsylvania, the metabolic syndrome rates have been found to be 30% in a cohort with a mean age of 47 years.[29]

The relationship between major depressive disorder and the metabolic syndrome has so far been examined only in young adult men and women in the United States.[30] In this population-based study (N = 6189), women with a history of at least 1 major depressive episode were twice as likely to have the metabolic syndrome compared with those women having no lifetime history of depression. Among men, however, there was no association between history of depression and the metabolic syndrome. The prevalence of the syndrome according to NCEP criteria was 11.7% and 12.3% in depressed men and women, respectively.[30] A longitudinal study in the United States revealed that middle-aged physically healthy women with high scores for depression, anger, anxiety, and tension at baseline had an increased risk of developing the metabolic syndrome during a 7-year follow-up period.[31]

No earlier studies have assessed the prevalence of metabolic syndrome in depressive patients who have received treatment for depression. The aim of the present study was to determine the prevalence of metabolic syndrome in patients with long-term depression. Furthermore, factors associated with the metabolic syndrome were examined among the patients.

METHOD

The original sample of the longitudinal Kuopio Depression (KUDEP) Study at Kuopio University Hospital, Kuopio, Finland, consisted of 175 treatment-seeking outpatients with depression. Of these, 149 had major depression. Patients (N = 4) were excluded if they had previously been diagnosed as suffering from a central nervous system disease, a severe physical disease (recent myocardial infarction, sequelae of stroke, etc.), alcohol or drug dependence, a marked deficiency in cognitive capacity, or any other serious mental disorder such as schizophrenia or other psychosis. During the 6-year follow-up period, 43 patients (25%) withdrew from the study or their follow-up data were incomplete, and 7 died, leaving 121 study subjects in the final 6-year follow-up sample. The study subjects had received standard care during the follow-up period. Approval to conduct the study was obtained from the ethics committee of Kuopio University Hospital and the University of Kuopio. All patients gave their written informed consent before entering the study. This group comprised 46 men (38%) and 75 women (62%), with a mean age of 51.4 years (SD = 9.4). This cross-sectional analysis ran from January 2002 through January 2004.

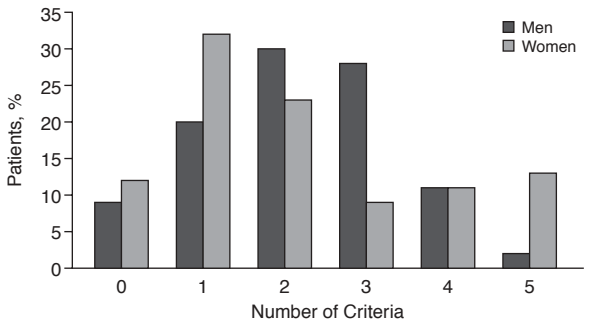
Metabolic syndrome was diagnosed at follow-up, according to the criteria of the NCEP,[32] based on the presence of 3 or more of the following: fasting plasma glucose levels ≥ 5.6 mmol/L, serum triglycerides ≥ 1.7 mmol/L, serum high-density-lipoprotein (HDL) cholesterol < 1.0 mmol/L in men and < 1.3 in women, systolic blood pressure ≥ 130 mm Hg and/or diastolic blood pressure ≥ 85 mm Hg, or waist girth > 102 cm for men and 88 cm for women. Height and body weight were measured with the patients in light clothing. Waist circumference was taken at the midpoint between the lowest rib and the iliac crest. Blood pressure was measured at 5-minute intervals after a 10-minute rest in the sitting position, and systolic and diastolic blood pressures were recorded as the mean of 3 measurements. Subjects were asked to fast for 12 hours before blood sampling.

Psychiatric diagnoses were performed at baseline and at 6-year follow-up using the Structured Clinical Interview for DSM-III-R (SCID-I).[33] This was administered by an experienced interviewer who achieved a total κ of 0.78 against a trainer experienced in SCID-I and SCID-II diagnoses. At baseline, 87 patients (72%) had major depression, 1 patient (1%) had bipolar disorder and depressive episode, and the remaining 33 patients (27%) had dysthymia or another depressive diagnosis. At baseline, patients completed a questionnaire relating to their sociodemographic background, and additional information was obtained on duration of depressive symptoms. Somatic diagnoses were verified by checking each patient's medical case records and referrals, but this was done 6 months

Table 1. Clinical Characteristics of 121 Patients With Depression 6 Years Earlier in Relation to Present Metabolic Syndrome

Variable	Metabolic Syndrome		p Value
	No (N = 77)	Yes (N = 44)	
Age, mean (SD), y	50.4 (10.0)	53.0 (8.2)	.163
Gender, % (N/N)			.376
Male	59 (27/46)	41 (19/46)	
Female	67 (50/75)	33 (25/75)	
Marital status, % (N/N)			.279
Single/divorced/widowed	58 (29/50)	42 (21/50)	
Married/cohabiting	68 (48/71)	32 (23/71)	
Education, mean (SD), y	12.2 (3.5)	11.4 (3.7)	.205
No somatic illnesses, %	60	40	.355
Current smoker, %	18	16	.751
Alcohol use, %	21	18	.730
Physical exercise, %	56	55	.951

Figure 1. Number of Fulfilled Criteria for Metabolic Syndrome Among 121 Men and Women With a History of Depression 6 Years Earlier



after the initial interviews; somatic diseases were reassessed at follow-up. At follow-up, according to SCID-I, 19 patients (15.7%) had major depression and 102 patients (84.3%) had no major depression, or depression was in remission.

At follow-up, depressive symptoms were assessed with the Beck Depression Inventory (BDI) (range 0–63).[34] A cut-off point of 12/13 was used for the BDI in assessing clinically significant depressive symptoms.[35] The depression level of each patient was also assessed separately by an investigator using the Hamilton Rating Scale for Depression (HAM-D) (range 0–52).[36] A cut-off point of 9/10 was used for assessing clinically significant depression.

The general psychopathology of patients was assessed using the Symptom Checklist-90 (SCL-90) total score (Global Severity Index, range 1–5),[37,38] which is the mean value of 9 subscales. The SCL-90 consists of a total of 90 items on 9 different subscales of psychological distress: somatization, interpersonal sensitivity, depression, anxiety, phobic anxiety, obsession-compulsion, hostility, paranoid ideation, and psychoticism, together with 7 additional items including, e.g., disturbances in appetite (poor appetite, overeating) and sleep.

In the SCL-90, these additional items, for example, overeating, are each asked by 1 question. One can choose from the following possibilities: "not at all" (1 point), "a little bit" (2 points), "moderately" (3 points), "quite a bit" (4 points), or "extremely" (5 points).

Alexithymia was assessed using the Finnish version[39] of the 20-item Toronto Alexithymia Scale (TAS-20) (range 20–100).[40,41] Each TAS-20 item was rated on a 5-point Likert scale. Higher total scores indicate more alexithymic features. A cut-off point of 60/61 was used for TAS-20. The level of psychosocial functioning was assessed by a trained interviewer using the Global Assessment of Functioning (GAF) scale (range 1–100).[42]

Life satisfaction was screened using a 4-question life satisfaction (LS) scale (range 4–20), with increasing scores indicating decreasing satisfaction.[43] The level of hopelessness was assessed using the Beck Hopelessness Scale (BHS),[44] which is a 20-item self-administered rating scale designed to measure the negative expectancies of adults concerning themselves and their future. The BHS is based on 3 dimensions of hopelessness: affective (e.g., lack of hope), motivational (giving up), and cognitive (lack of future expectations).[44] The total score of BHS ranges from 0 to 20, and higher scores indicate greater levels of hopelessness.

The interviewer also asked about current smoking (yes/no) and drinking habits. Alcohol use was defined as positive if a subject reported drinking alcohol once a week or more often. Physical exercise was defined as positive if a subject reported exercising more often than once a week.

Patients with and without the metabolic syndrome were compared using χ^2 analysis for categorical variables and the Mann-Whitney U test for continuous variables.

RESULTS

At 6-year follow-up, the prevalence of the metabolic syndrome in the study group was 36% (N = 44). Altogether, 19 men (41%) and 25 women (33%) were diagnosed as having the syndrome (p = .376). No statistically significant differences in age, marital status, education, current smoking, alcohol use, or physical exercise were detected between those with and without the metabolic syndrome (Table 1). Furthermore, there were no statistically significant differences between sexes in single criteria of the syndrome (data not shown). However, women met a higher total number of metabolic syndrome criteria than men (p = .027) (Figure 1).

The levels of different components of metabolic syndrome are summarized in Table 2. The prevalence of different components of metabolic syndrome in the sample was as follows: fasting plasma glucose level ≥ 5.6 mmol/L,

Table 2. Level of Selected Concurrent Risk Factors in Relation to Metabolic Syndrome in Patients With History of Depression 6 Years Earlier

Variable	Metabolic Syndrome[a] No (N = 77)	Yes (N = 44)	p Value
Plasma glucose, mmol/L[b]	5.5 (1.5)	6.9 (2.1)	< .001
Systolic blood pressure, mm Hg	136 (17)	147 (15)	.001
Diastolic blood pressure, mm Hg	83 (10)	89 (7)	< .001
Total cholesterol, mmol/L[c]	5.2 (1.1)	5.3 (0.9)	.771
HDL cholesterol, mmol/L	1.61 (0.47)	1.17 (0.28)	< .001
LDL cholesterol, mmol/L	3.10 (0.8)	3.17 (0.8)	.642
Triglyceride, mmol/L[d]	1.08 (0.42)	2.08 (0.98)	< .001
Waist girth, cm	89.0 (13.0)	106.8 (13.9)	< .001
Insulin, mU/L[e]	6.4 (2.6)	12.8 (8.3)	< .001
Height, cm	168 (10)	168 (7)	.963
Weight, kg	75.2 (17.3)	93.3 (16.1)	< .001
BMI, kg/m^2	25.9 (5.2)	33.0 (5.2)	< .001
Uric acid, µmol/L[f]	277.0 (98.3)	324.5 (81.2)	.001

[a]Values shown as mean (SD).
[b]To convert plasma glucose from mmol/L to mg/dL, multiply by 18.01.
[c]To convert total cholesterol, HDL cholesterol, and LDL cholesterol from mmol/L to mg/dL, multiply by 38.67.
[d]To convert triglyceride from mmol/L to mg/dL, multiply by 88.57.
[e]To convert insulin from mU/L to pmol/L, multiply by 6.0.
[f]To convert uric acid from µmol/L to mg/dL, multiply by 0.01681.
Abbreviations: BMI = body mass index, HDL = high-density lipoprotein, LDL = low-density lipoprotein.

Table 3. Present Metabolic Syndrome and Current Associated Factors in 121 Patients With History of Depression 6 Years Earlier

Variable	Metabolic Syndrome[a] No (N = 77)	Yes (N = 44)	p Value
BDI score	9.1 (9.2)	10.9 (8.1)	.100
HAM-D score	6.0 (5.8)	6.7 (5.1)	.224
TAS-20 score	44.7 (10.4)	47.1 (11.4)	.286
GAF score	72.4 (11.6)	69.2 (10.8)	.057
BHS score	4.9 (4.4)	5.5 (4.3)	.216
LS score	9.3 (3.9)	9.4 (3.4)	.619
SCL-90 scores			
GSI	1.7 (0.6)	1.8 (0.5)	.320
Depression	1.9 (0.8)	2.0 (0.7)	.416
Anxiety	1.6 (0.7)	1.7 (0.6)	.796
Phobic anxiety	1.4 (0.7)	1.4 (0.6)	.518
Obsessive-compulsive	2.0 (0.8)	2.2 (0.7)	.144
Somatization	2.0 (0.7)	2.2 (0.7)	.128
Psychoticism	1.3 (0.4)	1.4 (0.4)	.707
Paranoid ideation	1.6 (0.7)	1.6 (0.6)	.453
Anger-hostility	1.5 (0.5)	1.5 (0.4)	.680
Interpersonal sensitivity	1.7 (0.7)	1.7 (0.7)	.673
Sleep disturbances	2.1 (0.9)	2.1 (1.0)	.850
Poor appetite	1.2 (0.6)	1.3 (0.5)	.227
Overeating	1.6 (0.9)	2.3 (1.1)	< .001
Duration of depressive symptoms at baseline, y	11.2 (10.8)	9.8 (11.0)	.426
Current major depression, %	10.4	25.0	.034
BDI score ≥ 13, %	24.7	40.9	.062
HAM-D score ≥ 10, %	19.5	27.3	.322
TAS-20 score ≥ 61, %	10.3	15.9	.375

[a]Values shown as mean (SD) except where indicated as percent.
Abbreviations: BDI = Beck Depression Inventory, BHS = Beck Hopelessness Scale, GAF = Global Assessment of Functioning scale, GSI = Global Severity Index, HAM-D = Hamilton Rating Scale for Depression, LS = life satisfaction scale, SCL-90 = Symptom Checklist-90, TAS-20 = Toronto Alexithymia Scale.

48%; systolic blood pressure ≥ 130 mm Hg, 76%; diastolic blood pressure ≥ 85 mm Hg, 57%; serum HDL cholesterol < 1.0 mmol/L (in men), 23%, and < 1.3 mmol/L (in women), 37%; serum triglyceride ≥ 1.7 mmol/L, 30%; and waist girth > 102 cm (in men), 40%, and > 88 cm (in women), 46%.

Patients with the metabolic syndrome more often had current major depression compared to the patients without metabolic syndrome. Furthermore, overeating was associated with the syndrome (Table 3). However, no other statistically significant associations were recorded between measures of current mental status and the metabolic syndrome (Table 3). There was no association between duration of depressive symptoms at baseline and emergence of metabolic syndrome.

DISCUSSION

The present study recorded a high prevalence of the metabolic syndrome (36%) in patients who had earlier been treated for depression. The prevalence of the syndrome was higher than has previously been observed in general-population subjects from the same geographical area, both in men (41% vs. 11%–17%)[15,21] and in women (33% vs. 6%–20%).[21,22] Furthermore, the prevalence of the metabolic syndrome was 58% among those who were diagnosed as still suffering from major depression at the 6-year follow-up, but the size of that group was small (N = 19).

A diagnosis of current major depression was associated with the metabolic syndrome. Our results indicate that while physicians are treating patients with depression, the metabolic syndrome should also be kept in mind. We do not currently know whether the treatment of depression affects the prevalence of the metabolic syndrome, or whether better treatment could reduce its prevalence, and longitudinal studies are therefore needed.

A population-based study of 425 middle-aged healthy women revealed that the metabolic syndrome at baseline correlated with higher BDI scores and that higher BDI scores at baseline predicted an elevated risk of developing the metabolic syndrome during a 7.4-year follow-up[31]; similar studies among depressed men are lacking. Furthermore, in a cross-sectional study by Timonen et al.,[8] insulin resistance and the severity of depressive symptoms measured by the BDI were positively correlated in elderly people with impaired glucose tolerance but not in patients with normal glucose tolerance or with type 2 diabetes. All these results, together with the present study, indicate that depression and metabolic syndrome are strongly related.

Interestingly, a simple question concerning overeating was associated with the metabolic syndrome in subjects

with depression. As obesity results from excess energy intake in relation to energy expenditure, this association is to be expected. However, we observed no association between the occurrence of the metabolic syndrome and the scores for global psychopathology (SCL-90), the level of psychosocial functioning (GAF), alexithymia (TAS-20), life satisfaction (LS), or the level of hopelessness (BHS). Thus, although diagnosis of depression is an important correlate of the metabolic syndrome, other kinds of psychopathology may be unimportant.

This study detected no association between sex and the metabolic syndrome, although women met a higher total number of syndrome criteria than men. The study by Kinder et al.[30] revealed that a history of major depressive episodes, based on DSM-III-R, was associated with metabolic syndrome among women but not among men. Furthermore, the authors reported that a history of major depressive episodes in women was associated with the number of metabolic syndrome components present. Thus, our results are parallel with earlier results.

Depression may precede the emergence of the metabolic syndrome in various ways. Räikkönen et al.[31] suggested that the association between anger and metabolic syndrome may also be reciprocal in women. Longitudinal studies are required to establish a causal relationship between depression and the metabolic syndrome. The endocrine common denominator for both conditions could be linked via altered cortisol metabolism[3] or via the recently described endocannabinoid system.[45]

The metabolic syndrome, with its associated complications, is a substantial public health problem, and its prevalence is increasing as a consequence of lifestyle changes, such as a diet high in saturated fats and a lack of physical exercise.[46] However, depressed patients seem to be at high risk for cardiovascular disease and diabetes.[4,5,47] Thus, regardless of causality, more attention should be paid to the variety of risk factors in both diagnoses.

The main limitations of the present study were the small sample size and lack of a control group. We also lacked the baseline prevalence of metabolic syndrome, and therefore our study design was cross-sectional. Nevertheless, our findings suggest that it is important to assess metabolic syndrome and pay more attention to lifestyle modifications in depressed patients. The association between metabolic syndrome and current major depression underscores the need to treat major depressive disorder to remission.

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