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ORIGINAL RESEARCH

Prevalence of metabolic syndrome and its association with depression in patients with schizophrenia

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Purpose: To identify the point prevalence of metabolic syndrome in patients with schizophrenia and to evaluate the association between depressive symptoms and metabolic syndrome in patients with schizophrenia.

Patients and methods: Metabolic syndrome was assessed based on an updated definition derived from the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetes Federation criteria. The 17-item Hamilton Depression Rating Scale (HDRS-17) was used to measure depressive symptoms in 80 patients with schizophrenia. Odds ratios and 95% confidence intervals were calculated using logistic regression for the association between each depressive symptom and metabolic syndrome.

Results: The point prevalence rates of metabolic syndrome according to the modified NCEP-ATP III and International Diabetes Federation criteria were 37% and 35%, respectively. The risk of having metabolic syndrome significantly increased in those who were widowed or separated, or had longer duration of illness. Central obesity was the metabolic feature with the highest odds ratios for metabolic syndrome at 19.3. Three out of 17 items of HDRS subscales were found to be significantly associated with metabolic syndrome, including depressed mood, middle insomnia, and retardation with the odds ratios of 3.0, 3.4, and 3.6, respectively.

Conclusion: This study showed that the prevalence of metabolic syndrome in patients with schizophrenia was higher than the overall rate but was slightly lower than in the general population in the USA. Central obesity, measured by waist circumference, was found to be highly correlated with metabolic syndrome. Depressed mood, middle insomnia, and retardation were significantly associated with metabolic syndrome in patients with schizophrenia. Waist circumference and screening for depression should be done at the clinics during patient follow-up.

Keywords: mood symptoms, hypertension, dyslipidemia, hyperglycemia, central obesity

Introduction

Patients with schizophrenia suffer from two- to three-fold higher mortality rates and a shorter lifespan compared with the general population.[1] The mortality was not associated with psychotic symptoms or aggressive behavior, but was related to medical diseases.[2] One of the most common causes of death in schizophrenia was cardiovascular disease.[3] It was found that patients with schizophrenia have higher risks of coronary heart disease, hypertension, diabetes mellitus, and obesity compared with the general population.[4]

Metabolic syndrome is a constellation of metabolic abnormalities that occur together and raise the risk for cardiovascular disease and diabetes mellitus. The main features of metabolic syndrome include central obesity, hypertension,

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hypertriglyceridemia, low high-density lipoprotein (HDL), and hyperglycemia.[5,6] Each metabolic feature showed differences in predicting cardiovascular diseases.[7] Previous studies reported that central obesity, measured by waist circumference, is the key feature of metabolic syndrome as it is highly associated with other metabolic features, and is independently related with increased cardiovascular diseases risk.[8–10]

The prevalence of metabolic syndrome in patients with schizophrenia was higher than that in the general population, at 40%–60% and 27%, respectively.[11] The prevalence varies around the world and Asian people are more likely to have lower prevalence rates of metabolic syndrome compare with the Westerners due to dietary intake and lifestyle.[12,13] The prevalence of metabolic syndrome in patients with schizophrenia in Thailand was reported to be 15%–36% using the older criteria of metabolic syndrome.[14] However, in the modified criteria of metabolic syndrome, the cutoff values of waist circumference, blood pressure, and fasting blood sugar levels have been lowered.[15] Thus, the prevalence of metabolic syndrome in Thailand needs to be updated.

The increased risk of metabolic syndrome in patients with schizophrenia might be due to the disease itself (eg, negative symptoms leading to inactive lifestyle and lack of exercise), as well as external factors (eg, smoking, substance abuse, side effects from antipsychotic medication).[11,16] Depression may also raise the risk of metabolic syndrome in patients with schizophrenia. Our post hoc study found that 16% of patients with schizophrenia had depression, which was still under-recognized by psychiatrists.[17] Depression may lead to physical inactivity and increased substance abuse in patients with schizophrenia.[11] Moreover, chronic stress from depression may also activate the hypothalamic–pituitary–adrenal (HPA) axis, which leads to hypercortisolemia and metabolic changes.[18] Several studies in patients with depression found that depression increased the risk of metabolic syndrome from 1.7 to 2.8 times.[19]

Although depression has been demonstrated to be associated with metabolic syndrome, none of the previous studies have focused on this relationship in patients with schizophrenia, especially in Asia, where typical antipsychotic drugs with depressogenic effects are still commonly used. The objectives of this study were: (1) to identify the point prevalence of metabolic syndrome in patients with schizophrenia; (2) to evaluate the association of depressive symptoms and metabolic syndrome in patients with schizophrenia.

Material and methods

Sampling and data collection

We estimated the sample size required at 90% power and 5% significance to be 69 participants.[20] Therefore, after approval by the Ethics Committee, Faculty of Medicine, Chiang Mai University, 80 participants were recruited from an outpatient clinic of the Maharaj Nakorn Chiang Mai Hospital, Thailand, from January 2012 to April 2012. The inclusion criteria were Thai-speaking, aged 18 years or over, and a diagnosis of schizophrenia according to the *Diagnostic and Statistical Manual of Mental Disorders* (fourth edition text revision).[21] The exclusion criterion was having a neurological disorder that would interfere with the assessment. The details of the study were fully explained and written informed consent was obtained from all patients before the study.

Measures

Dependent variable

The metabolic syndrome was assessed based on an updated definition derived from the modified National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP III) and the International Diabetes Federation (IDF) criteria in which the waist circumferences are ethnic specific. According to the modified NCEP-ATP III, the presence of any three of the five factors is required for the diagnosis of metabolic syndrome, including central obesity (Asian origin, waist circumference ≥90 cm in males, ≥80 cm in females), elevated blood pressure (systolic blood pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg), hypertriglyceridemia (triglycerides ≥150 mg/dL), low HDL cholesterol (HDL cholesterol ≤40 mg/dL in males, ≤50 mg/dL in females), and elevated fasting blood sugar ≥100 mg/dL.[6] The IDF approach uses the same cut-off values as the modified NCEP-ATP III, but requires central obesity plus any two of the other four factors.[5,6] The prevalence of metabolic syndrome using both diagnostic criteria was reported, but only the modified NCEP-ATP III was used in all statistical analyses, as it has been recommended to identify metabolically abnormal but non-obese individuals among Thai patients with schizophrenia.[14]

Independent variable

Depressive symptoms were assessed with the 17-item Hamilton Depression Rating Scale (HDRS-17). The HDRS-17 items cover 17 symptom domains, including depressed mood, feelings of guilt, suicide, insomnia (early, middle, late), work and activities, retardation, agitation, anxiety (psychic, somatic), somatic symptoms (gastrointestinal,

general, genital), hypochondriasis, weight loss, and insight. Each item on the questionnaire is scored on a 3- or 5-point scale, depending on the item. The sum score of each item was then categorized into binary groups of 0 (depressive symptom not present) and ≥1 symptoms (depressive symptom present) for the analysis, which were defined a priori.

Statistical analysis

SPSS for Windows, version 16.0 (SPSS inc, Chicago, IL, USA) was used for analyses. The prevalence rates of metabolic syndrome were reported in percentages according to the modified NCEP-ATP III and IDF criteria. A categorical measure of metabolic syndrome (case/non-case) from the modified NCEP-ATP III was used for all analyses. Percentages for metabolic syndrome against each sociodemographic characteristic were analyzed using logistic regression models and independent *t*-test.

Odds ratios and 95% confidence intervals were calculated using logistic regression for the association between each depressive symptom and metabolic syndrome. The associations between metabolic features, the total score of HDRS-17, and metabolic syndrome were analyzed using the independent *t*-test. The statistical significance was defined as P-value < 0.05.

Results

Prevalence rates and sociodemographic characteristics

The point prevalence rates of metabolic syndrome according to the modified NCEP-ATP III and IDF criteria were 37.5% and 35%, respectively. Patients with schizophrenia who met the criteria for metabolic syndrome had an older age compared with those without metabolic syndrome at the mean age ± standard deviation (SD) of 47.9 ± 13.8 and 39.4 ± 13.3 years, respectively. Women tended to have a higher rate of metabolic syndrome compared to men, although the difference was not statistically significant. The risk of having metabolic syndrome significantly increased in those who were widowed or separated, or had longer duration of illness. However, we found no statistical difference in alcohol drinking, smoking, or Positive and Negative Syndrome Scale total score and subscores between those with and without metabolic syndrome (Table 1).

Table 1 Comparison of baseline characteristics by metabolic syndrome status

Baseline characteristics	Metabolic syndrome		*P*-value
	Yes (n = 30)	No (n = 50)	
Age group			
18–39	7 (23.3%)	27 (54.0%)	0.009
40–59	17 (56.7%)	20 (40.0%)	
≥60	6 (20.0%)	3 (6.0%)	
Sex			
Male	12 (40.0%)	22 (44.0%)	0.726
Female	18 (60.0%)	28 (56.0%)	
Marital status			
Single	15 (50.0%)	37 (74.0%)	0.003
Married	9 (30.0%)	10 (20.0%)	
Widow or separated	6 (20.0%)	3 (6.0%)	
Duration of illness (years)			
0–10	10 (33.3%)	30 (60.0%)	0.027
11–20	11 (36.7%)	15 (30.0%)	
>20	9 (30.0%)	5 (10.0%)	
Alcohol drinker			
Yes	5 (16.7%)	6 (12.0%)	0.557
No	25 (83.3%)	44 (88.0%)	
Current smoker			
Yes	4 (13.3%)	9 (18.0%)	0.584
No	26 (86.7%)	41 (82.0%)	
Current treatment			
Second-generation antipsychotics	17 (56.7%)	18 (36.0%)	0.071
First-generation antipsychotics	13 (43.3%)	32 (64.0%)	
PANSS variables (mean ± SD)			
PANSS total score	46.3 ± 13.1	45.2 ± 12.4	0.699
PANSS positive symptoms	10.7 ± 3.6	10.8 ± 4.0	0.921
PANSS negative symptoms	12.2 ± 5.0	11.5 ± 3.9	0.535
PANSS general psychopathology	23.4 ± 6.4	22.9 ± 5.9	0.691

Abbreviations: PANSS, Positive and Negative Syndrome Scale; SD, standard deviation.

Correlations between metabolic features and metabolic syndrome in patients with schizophrenia

All the metabolic features were found to be highly significantly associated with metabolic syndrome. Central obesity, high fasting blood sugar, and hypertriglyceridemia were the three metabolic features with the highest odds ratios for metabolic syndrome at 19.3, 11.4, and 10.1 respectively ($P < 0.001$) (Table 2).

Correlations between depressive symptoms and metabolic syndrome in patients with schizophrenia

Three out of 17 items of HDRS subscales were found to be significantly associated with metabolic syndrome, including depressed mood, middle insomnia, and retardation ($P < 0.05$) (Table 3). The total HDRS score was higher in patients with metabolic syndrome compared with those without metabolic syndrome, at 8.2 ± 6.7 and 6.6 ± 5.7, respectively, although the difference was not statistically significant ($P = 0.353$).

Table 2 Correlations between metabolic profiles and metabolic syndrome in patients with schizophrenia

Variables	Metabolic syndrome		Odds ratio	*P*-value
	Yes (n = 30)	No (n = 50)		
Central obesity Waist circumference ≥90 cm in male ≥80 cm in female	28 (93.3%)	21 (42.0%)	19.3 (4.1–90.2)	<0.001
High blood pressure Systolic blood pressure ≥130 mmHg or Diastolic blood pressure ≥85 mmHg	19 (63.3%)	17 (34.0%)	3.4 (1.3–8.6)	0.011
Hypertriglyceridemia (mg/dL) Triglyceride ≥150 mg/dL	16 (53.3%)	5 (10.0%)	10.1 (3.1–32.4)	<0.001
Low high-density lipoprotein (mg/dL) High-density lipoprotein ≤40 mg/dL in male ≤50 mg/dL in female	14 (46.7%)	5 (10.0%)	7.7 (2.4–24.8)	<0.001
High fasting blood sugar (mg/dL) Fasting blood sugar ≥100 mg/dL	23 (76.7%)	11 (22.0%)	11.4 (3.9–33.4)	<0.001

Abbreviations: cm, centimeter; mmHg, millimeter of mercury; mg, milligram; dL, deciliter.

Discussion

Prevalence rates of metabolic syndrome in patients with schizophrenia

The prevalence of metabolic syndrome in patients with schizophrenia from this study (39% in females, 35% in males) was slightly lower than that reported from the US Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, which found the prevalence to be 52% in females and 36% in males, but was higher than the overall rate of 32.5% from a meta-analysis by Mitchell et al.[22,23] The difference in prevalence might be explained by racial/ethnic heterogeneity, environmental factors, dietary consumption, and the criteria of metabolic syndrome used.[24] The higher prevalence of metabolic syndrome in females found in our study was in line with that reported in the CATIE study[22], although the sex difference in this study was not statistically significant.

Table 3 Correlations between depressive symptoms and metabolic syndrome in patients with schizophrenia

Variables	Metabolic syndrome		Odds ratio	*P*-value
	Yes (n = 30)	No (n = 50)		
Depressed mood	23 (76.7%)	26 (52.0%)	3.01 (1.1–8.3)	0.028
Feelings of guilt	19 (63.3%)	31 (62.0%)	1.11 (0.4–2.7)	0.905
Suicide	13 (43.3%)	15 (30.0%)	1.8 (0.7–4.6)	0.226
Insomnia early	18 (60.0%)	27 (54.0%)	1.3 (0.5–3.2)	0.600
Insomnia middle	19 (63.3%)	17 (34.0%)	3.4 (1.3–8.6)	0.011
Insomnia late	15 (50.0%)	21 (42.0%)	1.4 (0.6–3.4)	0.486
Difficulty in work and activities	19 (63.3%)	34 (68.0%)	0.8 (0.3–2.1)	0.669
Retardation	23 (76.7%)	24 (48.0%)	3.6 (1.3–9.8)	0.012
Agitation	11 (36.7%)	14 (28.0%)	1.5 (0.6–3.9)	0.418
Anxiety (psychic)	12 (40.0%)	19 (38.0%)	1.1 (0.4–2.7)	0.859
Anxiety (somatic)	23 (76.7%)	29 (58.0%)	2.4 (0.8–6.6)	0.090
Somatic symptoms (GI)	12 (40.0%)	20 (40.0%)	1.0 (0.4–2.5)	1.000
Somatic symptoms (general)	21 (70.0%)	26 (52.0%)	2.2 (0.8–5.6)	0.113
Genital symptoms	19 (63.3%)	32 (64.0%)	1.0 (0.4–2.5)	0.952
Hypochondriasis	16 (53.3%)	24 (48.0%)	1.3 (0.5–3.1)	0.644
Loss of weight	10 (33.3%)	13 (26.0%)	1.4 (0.5–3.8)	0.483
Lack of insight	16 (53.3%)	21 (42.0%)	1.6 (0.6–3.9)	0.325

Abbreviation: GI, gastrointestinal.

Metabolic features and metabolic syndrome in patients with schizophrenia

Central obesity, measured by waist circumference, was found to have the highest odds of metabolic syndrome among the metabolic features. Those with central obesity were 19 times more likely to have metabolic syndrome that those without central obesity. This finding is in line with previous studies that reported waist circumference to be one of the most predictable factors for cardiovascular disease.[8] As it is noninvasive and easy to perform, waist circumference should be measured in patients with schizophrenia at clinics during the follow-up.

Depressive symptoms and metabolic syndrome in patients with schizophrenia

To our knowledge, this is the first study to focus on the associations between depressive symptoms and metabolic syndrome in patient with schizophrenia. We found that three depressive symptoms were significantly associated with

metabolic syndrome, including depressed mood, middle insomnia, and retardation. A further CATIE schizophrenia trial, which compared subgroups with and without the metabolic syndrome, evaluated the association between depression, psychotic symptoms, quality of life, and metabolic syndrome and found no significant associations between these variables.[25] However, this study did not assess the association between each of the depressive symptoms and metabolic syndrome.

Other studies were conducted in patients with depression, not schizophrenia. Akbaraly et al 2009, using the results from the Whitehall II study in London, reported that the metabolic syndrome, especially central obesity and dyslipidemia components, was a predictive factor for depressive symptoms after a 6-year follow-up.[26] Viinamaki et al 2009, using the HDRS scale, reported that long-term depression was associated with the emergence of the metabolic syndrome in men. Nevertheless, the study used only the overall HDRS-17 score, while the depressive symptoms have not been explored.[27]

The etiologic relationships between depressed mood and metabolic syndrome in patients with schizophrenia could be described in numerous ways. First, the over-stimulation of the HPA axis leads to increased cortisol secretion and has been reported to be connected to both the development of depression and metabolic syndrome.[28,29] The disruption in HPA axis activity and relative hypercortisolemia has also been reported in patients with schizophrenia.[30]

Second, depressed mood may lead to physical inactivity and increased substance abuse in patients with schizophrenia.[11] This etiologic relationship was confirmed by our finding that psychomotor retardation was also significantly associated with metabolic syndrome. Third, antipsychotic medications with an antidopaminergic may lead to depression and increase the risk of developing metabolic syndrome in patients with schizophrenia.[31] Last, devaluation and stigma from obesity, which is commonly found in patients with the metabolic syndrome, may lower self-esteem and lead to depression.[32]

The increased risk of middle insomnia in patients with metabolic syndrome could be explained by the fact that middle insomnia is associated with obstructive sleep apnea,[33,34] and patients with metabolic syndrome are more likely to have obesity, which is a risk for obstructive sleep apnea.[35] Thus, obstructive sleep apnea might act as a mediator in the association between middle insomnia and metabolic syndrome. Moreover, a genetic study has indicated that insomnia-associated genotypic differences were found in both psychiatric disorders (eg, mood disorders, schizophrenia) and metabolic syndrome.[36] Therefore, the significant relationship between middle insomnia and metabolic syndrome in patients with schizophrenia from this study might emphasize this connection in the clinical setting.

Some limitations should be taken into account when interpreting the present findings. First, this observational cross-sectional analysis cannot provide direct evidence of causality. Potentially, complex bidirectional interrelationships may underlie the observations. Depressive symptoms might lead to metabolic syndrome, which may in turn increase the risk of depression. Second, the findings from this study might lack generalizability to patients with schizophrenia in other countries due to differences in lifestyle and race/ethnicity. Third, the small sample size of this study might lead to an insufficient power of some analyses. However, the small sample size would not explain our positive findings. Last, the use of antipsychotic medications and benzodiazepines may confound the association between some depressive symptoms (ie, retardation, insomnia) and metabolic syndrome. Further studies in drug-naive first-episode schizophrenia patients should be done in the future.

Conclusion

In conclusion, from this study, the prevalence of metabolic syndrome in patients with schizophrenia was higher than the overall rate but was slightly lower than that in the United States. Central obesity, measured by waist circumference, was found to be highly correlated with metabolic syndrome. Moreover, we found that three depressive symptoms were significantly associated with metabolic syndrome in patients with schizophrenia, including depressed mood, middle insomnia, and retardation. Therefore, to properly evaluate metabolic risk in patients with schizophrenia, waist circumference and screening for depression should be done during follow-up clinic visits.

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Disclosure

The authors have no conflicts of interest to declare.

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