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Relationship between Metabolic Syndrome and Depression Using Patient Health Questionnaire-9: 2016 Korea National Health and Nutrition Examination Survey Result Analysis

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Background: The purpose of this study was to investigate the relationship between metabolic syndrome and depressive symptoms by administering the nine-item depression module from the Patient Health Questionnaire-9 (PHQ-9) to participants from the general population of Korea.
Methods: In total, 8,150 adults participated in the 1st year of the 7th Korea National Health and Nutrition Examination Survey, which was conducted in 2016. Of them, 5,556 participants underwent tests pertaining to the criteria for metabolic syndrome and responded to PHQ-9; 2,594 respondents were excluded. Analysis of covariance was performed to analyze the relationship between the presence of metabolic syndrome and the PHQ-9 score after adjusting for the effects of demographic and hematologic characteristics and underlying diseases.
Results: The total PHQ-9 score (mean=2.98) was significantly higher in participants with metabolic syndrome than in those without it (mean=2.59) (p=0.002). Among the individual PHQ-9 items, changes in sleep, thoughts of suicide or self-harm, and depressive mood showed the greatest differences.
Conclusion: The PHQ-9 scores in Korea were higher in adults with metabolic syndrome, suggesting an association between metabolic syndrome and depressive symptoms.

Keywords Depression; Metabolic syndrome; Patient Health Questionnaire-9

INTRODUCTION

Metabolic syndrome is a multifactorial syndrome defined by abdominal obesity, increased triglycerides, decreased high-density lipoprotein (HDL) cholesterol, increased fasting blood sugar, and increased blood pressure [1]. Metabolic syndrome increases the risk of heart attack and stroke, and of death from related diseases, such as diabetes and hypertension [2]. In Korea, the prevalence of metabolic syndrome has been increas-

ing steadily, particularly with westernization of the diet [3,4]. Cardiovascular disease was the second leading cause of death in Korea after malignant neoplasm in 2010 [5]. Cerebrovascular disease (53.2/100,000 deaths) and heart disease (46.9/100,000 deaths) ranked second and third, respectively. Diabetes mellitus was ranked fifth (20.7/100,000 deaths) and hypertension was tenth (9.6/100,000 deaths) [5].

Depressive symptom is the most common mental illness in Korean society, and early detection and inter-

vention is very important because depressive symptom accounts for a substantial proportion of all cases of sudden suicide, as well as dysfunction and disorder in activities of daily living [6]. According to the Korea Mental Health Survey of 2011, the lifetime and annual prevalence rates of major depressive disorder were 6.7% and 3.0%, respectively [7]. However, according to the World Health Organization, only 42% of patients with major depressive disorder visiting primary care clinics are diagnosed by doctors [8].

The Patient Health Questionnaire-9 (PHQ-9) is a 9-item depressive symptom screening tool based on the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition [9]. The PHQ-9 has excellent sensitivity (88%) and specificity (88%) compared with the Zung Self-Rating Depressive symptom Scale and the Beck Depressive symptom Scale, which are widely used in domestic and overseas primary care. The PHQ-9 is a reliable and valid instrument to measure the severity of depressive symptom [10,11]. Although the PHQ-9 is not a structured diagnostic tool, it is considered suitable for use in clinical situations where doctors cannot spend much time with patients, because the number of items is smaller than existing depressive symptom screening tools and only a short time is required for the examination [12].

The possibility that major depressive symptom is related to metabolic syndrome has been raised repeatedly [13]. Studies using the US National Health and Nutrition Survey data have shown that PHQ-9 scores are associated with metabolic syndrome and C-reactive protein levels [14]. However, these associations vary by race and country, where the PHQ-9 is appropriate for use in the United States and Europe, but has been shown to be inadequate in Japan [15,16]. A previous study using Korea National Health and Nutrition Examination Survey (KNHANES) data showed that depressive symptom was associated with metabolic syndrome, but an instrument specifically designed to diagnose depressive symptom, such as the PHQ-9, was not used [17].

Objectives

The purpose of this study was to investigate the relationship between metabolic syndrome and depressive symptom, as indexed by the PHQ-9, in the general population of Korea through analysis of the 2016 KNHANES data. A secondary purpose was to examine the extent to which the individual PHQ-9 items are associated with metabolic syndrome.

MATERIALS AND METHODS

The KNHANES, based on the National Health Promotion Act, investigates the health-related behaviors of the Korean populace, as well as chronic disease status and aspects of food and nutrition. The KNHANES was conducted every 3 years from 1998 to 2005, and yearly in the period 2007 to 2009. This study used raw data from the first year of the 7th KNHANES, conducted in 2016.

The survey was conducted with approval from the Institutional Review Board (IRB) of the Korea Centers for Disease Control and Prevention (KCDC) until 2014, and IRB deliberations were exempted under the revision of the Bioethics Act from 2015. A written consent form is set out in the distribution data.

The results will be disseminated via press releases, statistical publications, and raw data releases until December of next year. The KCDC only provides anonymized data that cannot be identified, and the data can be downloaded from the KNHANES website.

Weights were used during analysis of the KNHANES survey data, and inclusion errors, unequal extraction rates, and non-responses errors were corrected according to the number of households surveyed and by taking into account differences in population size between the design of the sampling methods and data inspection. Accordingly, the representativeness and accuracy of the health behavior, chronic illness, and food and nutritional status data of the Korean population were enhanced.

In the 2016 KNHANES, there were 10,806 respondents, of whom 8,150 participated in this study. Thus, the participation rate was 75.4%. A health questionnaire, health examination, and nutrition survey were applied in the KNHANES. In this study, only the health questionnaire and health examination results were included. Health data were gathered through interviews, self-report surveys, and health examinations including anthropometric measurements, blood pressure and pulse measurements, and blood and urine tests [18].

1. Subjects

Inclusion criteria were age ≥19 and ≤80 years among

2016 KNHANES subjects who had undergone measurements relevant to the criteria for metabolic syndrome, and who completed the PHQ-9. If any data pertinent to the diagnostic criteria for metabolic syndrome were missing, or if the subject had missing data on the PHQ-9 questionnaire, they were excluded. Ultimately, 5,556 subjects were included.

2. Measurements

1) Metabolic syndrome

The National Cholesterol Education Program-Third Adult Treatment Panel (NCEP ATP III), which was introduced in 2001 and is widely used, informed our diagnostic criteria for metabolic syndrome [1,19]. The NCEP ATP III definition of metabolic syndrome includes the following: 1) increased waist circumference (>102 cm [>90 cm for Asians] for men, >88 cm [>85 cm for Asians] for women); 2) elevated triglycerides (≥150 mg/dL); 3) low HDL cholesterol (<40 mg/dL in men, <50 mg/dL in women); 4) hypertension (≥130 mmHg systolic blood pressure or ≥85 mmHg diastolic blood pressure); and 5) high fasting glucose level (≥100 mg/dL) or receiving treatment for diabetes mellitus. Metabolic syndrome was diagnosed when three or more of these five criteria were met [20,21].

2) Depressive symptom

A standardized Korean language version of the PHQ-9 was used. In accordance with existing Korean studies, the cut-off value for depressive symptom was 9 [12], but the total PHQ-9 score was considered the primary measure.

3) Covariates

The demographic characteristics assessed included age, sex, marital status, employment status, income level, education level, and drinking, smoking, and exercise status. Mean income was calculated at the individual and household level. Education level was categorized as university graduate or below university level. The subjects indicated whether they drank more than one drink per month in the past year, and whether they had smoked more than five packs of cigarettes in their lifetime. The subjects had to perform at least 75 minutes' worth of aerobic exercise at least once per week to be considered to engage in exercise.

Aspartate transaminase (AST), alanine transaminase (ALT), blood urea nitrogen (BUN) creatinine, and high-sensitivity C-reactive protein levels were analyzed in addition to the blood parameters directly relevant to the diagnosis of metabolic syndrome.

Stroke, myocardial infarction, angina, thyroid disease, chronic kidney disease, liver cirrhosis, and cancer were considered as relevant underlying diseases.

Statistically significant covariates were those deemed to potentially affect metabolic syndrome status (present vs. absent).

3. Statistical analyses

Continuous variables, such as serum levels of markers of interest and hematological characteristics, were evaluated using the independent sample t-test. Discrete

Table 1. Demographic characteristics of subjects with and without metabolic syndrome

Demographic characteristics	Total sample (n=5,556)	Metabolic syndrome		Statistical coefficient (t/χ²)	p–value
		Yes (n=1,542)	No (n=4,014)		
Age (y)	50.65±16.63	57.57±14.61	48.00±16.60	21.040	<0.001
Male	2,406 (43.3)	764 (49.5)	1,642 (40.9)	33.866	<0.001
Married	4,681 (84.3)	1,430 (92.7)	3,251 (81.0)	115.823	<0.001
Employed	3,323 (59.8)	880 (57.1)	2,443 (60.9)	6.668	0.010
Above average income (individual)	2,792 (50.3)	720 (46.7)	2,072 (51.6)	10.817	0.001
Above average income (household)	3,142 (56.6)	713 (46.2)	2,429 (60.5)	92.386	<0.001
College or above	2,040 (36.7)	404 (26.2)	1,636 (40.8)	101.607	<0.001
Drinking alcohol (monthly)	3,014 (54.2)	778 (50.5)	2,236 (55.7)	12.377	<0.001
Smoking (lifetime)	2,087 (37.6)	695 (45.1)	1,392 (34.7)	51.304	<0.001
Exercise	2,490 (44.8)	584 (37.9)	1,906 (47.5)	41.608	<0.001

Values are presented as mean±standard deviation or number (%).

variables, such as sex and disease status, were evaluated using the chi-square test. As the PHQ-9 results were treated as a continuous variable, confounders were controlled for by analysis of covariance. A two-tailed p-value <0.05 was considered significant. All statistical analyses were performed using IBM SPSS Statistics ver. 23.0 software (IBM Co., Armonk, NY, USA).

RESULTS

1. Demographic characteristics

Table 1 shows the major demographic characteristics of subjects with and without metabolic syndrome.

Subjects with metabolic syndrome were older (t=21.040, p<0.001), more likely to be male (χ^2=33.866, p<0.001), more likely to be married (χ^2=115.823, p<0.001), and less likely to be employed (χ^2=6.668, p=0.010). Those with metabolic syndrome also had a lower average income level, both at the individual (χ^2=10.817, p=0.001) and household level (χ^2=92.386, p<0.001), and a lower level of education (χ^2=101.607, p<0.001). Metabolic syndrome sufferers also showed

a lower incidence of monthly drinking (χ^2=12.377, p<0.001), but a higher incidence of lifetime smoking (χ^2=51.304, p<0.001); they were also less likely to engage in exercise (χ^2=41.608, p<0.001).

Given their significance, all of the above demographic characteristics were treated as covariates.

2. Hematological findings

Table 2 shows the hematological results of subjects with and without metabolic syndrome.

The levels of AST, ALT, BUN, creatinine, and high-sensitivity C-reactive protein were significantly higher in the group with metabolic syndrome than in those without metabolic syndrome. Therefore, all of these parameters were included as covariates.

3. Underlying diseases

Table 3 shows the results regarding underlying diseases in subjects with and without metabolic syndrome. Data on liver, colon, breast, cervical, lung, thyroid, and other cancers were integrated.

The prevalence of all underlying diseases, includ-

Table 2. Hematological findings of subjects with and without metabolic syndrome

Hematological findings	Total sample (n=5,556)	Metabolic syndrome		Statistical coefficient (t)	p–value
		Yes (n=1,542)	No (n=4,014)		
AST (IU/L)	22.73±16.14	26.30±22.22	21.36±12.82	8.22	<0.001
ALT (IU/L)	22.05±17.37	28.45±19.72	19.59±15.70	15.82	<0.001
BUN (mg/dL)	14.48±4.72	15.31±5.18	14.17±4.50	7.61	<0.001
Creatinine (mg/dL)	0.83±0.28	0.88±0.34	0.81±0.26	6.98	<0.001
hsCRP (mg/L)	1.29±2.33	1.65±2.46	1.14±2.26	7.08	<0.001

Values are presented as mean±standard deviation.
AST, aspartate transaminase; ALT, alanine transaminase; BUN, blood urea nitrogen; hsCRP, high–sensitivity C–reactive protein.

Table 3. Underlying diseases of subjects with and without metabolic syndrome

Underlying diseases	Total sample (n=5,556)	Metabolic syndrome		Statistical coefficient (χ^2)	p–value
		Yes (n=1,542)	No (n=4,014)		
Stroke	83 (1.5)	47 (3.0)	36 (0.9)	35.031	<0.001
Myocardial infarction and angina	143 (2.6)	66 (4.3)	77 (1.9)	24.783	<0.001
Thyroid disease	108 (1.9)	32 (2.1)	76 (1.9)	0.193	0.660
Chronic kidney disease	17 (0.3)	9 (0.6)	8 (0.2)	5.395	0.020
Liver cirrhosis	9 (0.2)	5 (0.3)	4 (0.1)	3.475	0.062
Cancer	90 (1.6)	27 (1.8)	63 (1.6)	0.230	0.631

Values are presented as number (%).

ing stroke, myocardial infarction and angina, thyroid disease, chronic kidney disease, liver cirrhosis, and cancer, was higher when metabolic syndrome was present. However, significant differences between subjects with and without metabolic disease were found only for stroke, myocardial infarction and angina, and chronic kidney disease rates; these diseases were thus included as covariates.

4. Metabolic syndrome and the PHQ-9

The total PHQ-9 score was treated as a dependent variable, with metabolic syndrome considered an independent variable. The confounding variables controlled for included all demographic characteristics, all hematological findings, and diseases including stroke, myocardial infarction and angina, and chronic kidney disease. The PHQ-9 scores by metabolic syndrome status are shown in Table 4. The mean total PHQ-9 score of subjects with metabolic syndrome (2.98 points) was significantly higher than that of subjects without metabolic syndrome (2.59 points) (p=0.002), even after adjusting for covariates (p=0.002).

Table 5 compares the scores on individual PHQ-9 items between subjects with and without metabolic syndrome.

DISCUSSION

This study analyzed KNHANES raw data to investigate the association between metabolic syndrome and the PHQ-9 depressive symptom scale in Korean adults. The results were adjusted for confounding variables.

The total PHQ-9 score was significantly higher in those with metabolic syndrome, even after adjusting for

Table 4. Mean total PHQ-9 scores of subjects with and without metabolic syndrome

	Total sample (n=5,556)	Metabolic syndrome		Statistical coefficient (t)	p-value	Adjusted p-value[a]
		Yes (n=1,542)	No (n=4,014)			
PHQ-9 total score	2.70±3.80	2.98±4.32	2.59±3.58	3.132	0.002	0.002

Values are presented as mean±standard deviation.

PHQ-9, Patient Health Questionnaire-9.

[a]Adjusted for the effects of demographic characteristics (age, sex, marriage, employment, income, education, alcohol consumption, smoking, and exercise), hematological findings (levels of aspartate transaminase, alanine transaminase, blood urea nitrogen, creatinine, and high-sensitivity C-reactive protein), and underlying diseases (stroke, myocardial infarction and angina, and chronic kidney disease).

Table 5. Scores on individual PHQ-9 items of subjects with and without metabolic syndrome

Individual PHQ-9 items	Total sample (n=5,556)	Metabolic syndrome		Difference between means	Adjusted p-value[a]
		Yes (n=1,542)	No (n=4,014)		
Item 1. Loss of interest	0.37±0.76	0.36±0.81	0.37±0.74	−0.01	<0.001
Item 2. Depressive mood	0.27±0.65	0.32±0.75	0.26±0.60	0.06	0.001
Item 3. Change of sleep	0.59±0.94	0.65±1.03	0.56±0.91	0.09	0.001
Item 4. Decreased energy	0.67±0.93	0.67±0.96	0.67±0.91	0.00	<0.001
Item 5. Change of appetite	0.31±0.72	0.32±0.75	0.30±0.70	0.02	0.001
Item 6. Self-blame	0.19±0.57	0.22±0.64	0.18±0.54	0.04	0.001
Item 7. Decreased concentration	0.14±0.52	0.17±0.60	0.12±0.48	0.05	0.001
Item 8. Psychomotor change	0.07±0.37	0.11±0.46	0.06±0.33	0.05	0.001
Item 9. Suicide or self-harm	0.10±0.43	0.16±0.55	0.08±0.37	0.08	0.002

Values are presented as mean±standard deviation.

PHQ-9, Patient Health Questionnaire-9.

[a]Adjusted for the effects of demographic characteristics (age, sex, marriage, employment, income, education, alcohol consumption, smoking, and exercise), hematologic findings (level of aspartate transaminase, alanine transaminase, blood urea nitrogen, creatinine, and high-sensitivity C-reactive protein), and underlying diseases (stroke, myocardial infarction and angina, chronic kidney disease).

demographic and hematological characteristics, as well as underlying diseases (Table 4). These results support the findings of previous studies that assessed the association of metabolic syndrome with a depressive episode in Koreans [17], and of international studies on metabolic syndrome status according to PHQ-9 score [15].

This study utilized reliable data representative of the general Korean population, rather than being limited to those with mental illnesses, and included a large sample size.

However, the data were not generated by professional psychiatric evaluations; therefore, they have certain inherent limitations. For example, a more systematic instrument, such as the Alcohol Use Disorder Identification Test, could have been applied to assess drinking, and depressive symptom could also have been assessed using measures, such as the Beck Depressive symptom Inventory or the Hamilton Depressive symptom Scale. The monthly drinking rate was lower among subjects with metabolic syndrome, presumably due to the limitations in the survey method. However, the most significant shortcoming was that, although the statistical significance of certain group differences was high, the difference in the total PHQ-9 score between those with and without metabolic syndrome was not clinically meaningful and no causality could be inferred.

The results of the investigation of individual PHQ-9 item scores were interesting (Table 5). Among the items, mean differences between subjects with and without metabolic syndrome were highest for changes in sleep (0.09 points), thoughts of suicide or self-harm (0.08 points), and depressive mood (0.06 points).

Subsequent research will likely reveal more about the effect of metabolic syndrome on mental health, if depressive symptoms are considered in detail and other psychiatric symptoms are also evaluated.

CONCLUSION

In this study of the general adult population of Korea, the mean PHQ-9 score was higher in subjects with versus without metabolic syndrome. This suggests a link between metabolic syndrome and depressive symptom. Further studies that address the limitations of this study could support an integrated approach to physical health in the context of prevention and treatment of depressive symptom.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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