The Association Between Lipid Ratio and Depression: A Cross-Sectional Study

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Research Article

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Abstract

Background: Depression is associated with the total cholesterol, low-density cholesterol, triglycerides, and high-density cholesterol levels in the blood. However, there are only a few studies on the relationship between depression and lipid ratios. Therefore, the aim of this study was to investigate the correlation between depression and different lipid ratios.

Methods: This study was conducted using data from the Korea National Health and Nutrition Examination Survey. A total of 11,648 adult men and women aged 19 years and older, without missing data, were included in this study. Depression was diagnosed using the Patient Health Questionnaire-9. The associations between depression and total cholesterol/high-density lipoprotein cholesterol, low-density cholesterol/high-density lipoprotein cholesterol, and triglyceride/high-density lipoprotein cholesterol ratio were analyzed. A complex sample logistic regression test was used for the analysis of the odds ratios of depression.

Results: In males, the total cholesterol/high-density lipoprotein cholesterol and low-density cholesterol/high-density lipoprotein cholesterol ratios were not associated with depression. In addition, an increase in triglyceride/high-density lipoprotein cholesterol ratio by 1 was associated with a 1.041-fold higher probability of depression in males. In females, the three lipid ratios were not associated with depression.

Conclusions: Triglyceride/high-density lipoprotein cholesterol ratio is associated with depression in males. Further studies are necessary to cross-validate, explore the biological mechanism, and identify the clinical implication of this correlation.

Background

Depression is a common mental disorder that is characterized by sadness, loss of interest or pleasure, feelings of guilt or low self-esteem, trouble sleeping or eating, fatigue, and difficulty concentrating [1]. Depression is often chronic, impairs an individual's quality of life, is associated with other chronic diseases, and can lead to an increased risk of death. According to the World Health Organization, the prevalence of depression is increasing worldwide and is predicted to become the most prevalent disease by 2030 [1].

The relationship between low cholesterol levels and depression has been investigated in several previous studies. It is believed that low cholesterol levels influence depression by altering the metabolism of serotonin [2, 3] Depression causes increased food intake, increase in body weight, and decreased frequency of exercise, and it also elevates blood cortisol level, which leads to impaired glucose tolerance, high blood pressure, fat accumulation, and eventually, metabolic syndrome [3]. In addition, depression can adversely affect lipid metabolism [3]. Therefore, although a low level of low-density lipoprotein cholesterol (LDL-C) is positively correlated with depression, some studies have shown a correlation

between depression and elevated triglyceride (TG) and low high-density lipoprotein cholesterol (HDL-C) levels [4, 6].

Several studies have been conducted to analyze the relationship between depression and cholesterol levels. However, there are only a few studies on the relationship between lipid ratio and depression. Furthermore, previous studies have mainly focused on the relationship between lipid ratio, cardiovascular disease, and insulin resistance. In addition, since depression is associated with obesity and metabolic syndrome [5, 8], the association between depression and TG and HDL-C levels has been evaluated previously [6]. However, studies on the correlation between depression and the TG/HDL-C ratio are limited. Therefore, the aim of this study was to analyze the correlation between depression and three lipid ratios, total cholesterol (TC)/HDL-C, LDL-C/HDL-C, and TG/HDL-C, in a large population.

Methods

Aim, design, and setting

This large-scale cross-sectional study was conducted to analyze the association between depression and lipid ratios in a large population. In accordance with the ethical standards of the Declaration of Helsinki, this study obtained approval from the Wonkwang University Hospital's clinical trial screening committee (IRB, approval number 2021-09-001)

Participants and enrollment

This study was conducted using data from the Korea National Health and Nutrition Examination Survey (KNHANES). We analyzed the data generated in the 2016 and 2018 surveys when the Patient Health Questionnaire (PHQ)-9, which is a diagnostic tool for depression, was used. Only male and female participants aged 19 years and older and without any missing data were included. Participants who completed all nine items of the PHQ-9 were analyzed.

Anthropometric and biochemical parameters

All tests were performed by trained inspectors. Height (cm) and weight (kg) were measured using a Seca 225 machine (Seca, Hamburg, Germany) and a GL-6000-20 scale (G-tech, Seoul, Korea). Body mass index was calculated as weight (kg) divided by height (m^2) squared. Systolic blood pressure and diastolic blood pressure were measured twice or more at 10-minute intervals using a mercury sphygmomanometer (Baumanometer; WA Baum Co., Copiague, NY) wrapped around the right upper arm. Blood samples were collected after an 8-hour fasting period. Fasting blood glucose (FBG), hemoglobin A1c, TC, TG, HDL-C, LDL-C, and hemoglobin levels were measured using the Hitachi 7600 automatic analyzer (Hitachi, Tokyo, Japan).

Sociodemographic variables

The smoking and drinking history, degree of physical activity, educational level, and household income of the participants were evaluated. Regarding smoking and drinking history, participants were classified as

current smokers or non-smokers and as current drinkers or non-drinkers. An international physical activity questionnaire was used to measure the degree of physical activity. Exercising five or more times a week for 30 minutes or performing vigorous physical activity three times or more for 20 minutes or more was considered regular exercise. Activities such as slow swimming, doubles tennis, volleyball, badminton, table tennis, and light lifting were defined as appropriate physical activity. Participants were divided into four groups according to their educational background: elementary school graduate, middle school graduate, high school graduate, and college graduate or higher. Average gross household income was divided into four levels: low (less than 1 million won per month), medium-low (1 to 2 million won per month), medium (2 to 3 million won per month), and high (3 million won or more).

Screening for depression in large populations requires the use of an economical, efficient, and time-consuming tool, such as the PHQ-9 [7–9]. The PHQ-9 has the advantage of providing information on the severity of symptoms and includes a diagnostic algorithm that evaluates the presence or absence of major depressive disorder within a short period [10]. The time required for testing is relatively short, and the reliability and validity of the tool have been consistently demonstrated to be satisfactory in many studies [11, 15]. Therefore, the relationship between depression and each lipid ratio was analyzed in this study using PHQ-9 as a diagnostic tool for depression.

Statistical Analysis

Frequency analysis was performed using a complex sample plan. After categorization according to sex, we analyzed the relationship between general characteristics, blood test results, and PHQ-9 scores using a complex sample Rao–Scott adjusted chi-square test and a complex sample generalized linear model (Tables 1 and 2). Odds ratios (OR) and 95% confidence intervals were estimated by adjusting for statistically significant variables. Variables that could be affected were adjusted for age, sex, education level, household income, and drinking and smoking history. Thereafter, a complex sample logistic regression test was used for analysis (Table 3).

Table 1
Differences between depression and non-depression in male

Variable		Male(n=5,043)		
		PHQ-9<10(n=4,858)	PHQ-9≧10(n=185)	p
Age		45.96±0.31	45.92±1.28	0.972
Household income	Low	1147(24.8)	96(51)	<0.0001*
	Middle-low	1219(25.2)	42(21)	
	Middle-high	1253(25.4)	19(11.8)	
	High	1239(24.6)	28(16.2)	
Education level	Elementary	660(94.1)	49(5.9)	0.031
	Middle	490(97)	17(3)	
	High	1703(97)	60(3)	
	College	2017(97.1)	58(2.9)	
Alcohol consumption	n	1448(97.1)	55(2.9)	0.385
	y	3417(96.6)	130(3.4)	
Stress perception	n	3792(76)	60(24.4)	<0.0001*
	y	1073(24)	125(75.6)	
Smoking	n	3199(63.2)	94(45.3)	<0.0001*
	y	1665(36.8)	91(54.7)	
Height (cm)		171.55±0.13	170.76±0.49	0.118
Weight (kg)		72.5±0.2	71.96±1.15	0.647
BMI (kg/m2)		24.59±0.06	24.63±0.38	0.919
Fasting glucose (mg/dL)		102.49±0.47	109.26±3.36	0.046*
HbA1c (%)		5.67±0.02	5.77±0.08	0.278
TC (mg/dL)		191.71±0.67	191.95±3.23	0.943

Abbreviations: PHQ-9, Patient Health Questionnaire-9; BMI, body-mass index; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; Hb, Hemoglobin.

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

The P-value was determined through the complex sample Rao-Scott adjusted chi-square test and complex sample generalized linear model T test.

Variable	Male(n=5,043)		
	PHQ-9<10(n=4,858)	PHQ-9≧10(n=185)	p
HDL-C (mg/dL)	47.36±0.21	47.03±1.16	0.781
TG (mg/dL)	163.89±2.92	203.01±15.24	0.009*
LDL-C (mg/dL)	117.99±1.22	114.36±5.7	0.542
Hb (g/dL)	15.38±0.02	15.28±0.11	0.352
TC / HDL-C	4.25±0.02	4.61±0.25	0.150
LDL-C / HDL-C	2.94±0.03	3.17±0.23	0.342
TG / HDL-C	3.94±0.09	6.10±1.03	0.035*
Abbreviations: PHQ-9, Patient Health Questionnaire-9; BMI, body-mass index; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; Hb, Hemoglobin.			
Values are presented as number (%) or the mean ± standard deviation.			
The P-value was determined through the complex sample Rao-Scott adjusted chi-square test and complex sample generalized linear model T test.			

Table 2
Differences between depression and non-depression in female

Variable		Female(n=6,605)		
		PHQ-9<10(n=6,156)	PHQ-9≧10(n=449)	p
Age		47.99±0.35	48.79±1.21	0.505
Household income	Low	1436(24.3)	178(39.8)	<0.0001*
	Middle-low	1551(25.3)	125(27.2)	
	Middle-high	1551(25)	99(22.3)	
	High	1618(25.4)	47(10.8)	
Education level	Elementary	1463(89.6)	175(10.4)	<0.0001*
	Middle	619(91.4)	62(8.6)	
	High	1943(94.2)	119(5.8)	
	College	2142(95.2)	94(4.8)	
Alcohol consumption	n	3586(93.2)	275(6.8)	0.474
	y	2570(93.7)	173(6.3)	
Stress perception	n	4635(74.4)	101(20.4)	<0.0001*
	y	1520(25.6)	347(79.6)	
Smoking	n	5867(94.7)	371(80.3)	<0.0001*
	y	288(5.3)	77(19.7)	
Height (cm)		158.07±0.12	157.64±0.43	0.331
Weight (kg)		58.33±0.15	58.83±0.67	0.470
BMI (kg/m2)		23.36±0.06	23.67±0.25	0.227
Fasting glucose (mg/dL)		97.43±0.35	99.89±1.15	0.034*
HbA1c (%)		5.61±0.01	5.68±0.05	0.125
TC (mg/dL)		193.73±0.58	192.68±2.24	0.649

Abbreviations: PHQ-9, Patient Health Questionnaire-9; BMI, body-mass index; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; Hb, Hemoglobin.

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

The P-value was determined through the complex sample Rao-Scott adjusted chi-square test and complex sample generalized linear model T test.

Variable	Female(n=6,605)		
	PHQ-9<10(n=6,156)	PHQ-9≧10(n=449)	p
HDL-C (mg/dL)	54.97±0.23	54.28±0.8	0.400
TG (mg/dL)	114.29±1.38	126.75±4.82	0.011*
LDL-C (mg/dL)	118.71±1.58	114.01±4.6	0.330
Hb (g/dL)	13.1±0.02	13.09±0.07	0.912
TC / HDL-C	3.69±0.02	3.75±0.07	0.358
LDL-C / HDL-C	2.77±0.04	2.69±0.11	0.511
TG / HDL-C	2.37±0.04	2.70±0.13	0.016*
Abbreviations: PHQ-9, Patient Health Questionnaire-9; BMI, body-mass index; HbA1c, hemoglobin A1c; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; TG, triglyceride; LDL-C, low density lipoprotein cholesterol; Hb, Hemoglobin.			
Values are presented as number (%) or the mean ± standard deviation.			
The P-value was determined through the complex sample Rao-Scott adjusted chi-square test and complex sample generalized linear model T test.			

Table 3
Relationship between lipid ratio and depression

variable		Male		Female	
		PHQ-9≧10		PHQ-9≧10	
		OR	p	OR	p
Household income	Low	2.732(1.512-4.936)	.001	2.715(1.787-4.126)	<0.0001
	Middle-low	1.115(0.602-2.064)	.729	2.016(1.303-3.12)	.002
	Middle-high	0.635(0.284-1.419)	.267	1.863(1.171-2.962)	.009
	High	1		1	
Education level	Elementary	2.457(1.236-4.881)	.010	2.458(1.603-3.769)	<0.0001
	Middle	1.007(0.468-2.167)	.986	1.709(1.029-2.84)	.039
	High	0.857(0.526-1.395)	.534	1.034(0.745-1.435)	.842
	College	1		1	
Age		0.9996(0.983-1.017)	.961	1.001(0.988-1.014)	.913
Stress perception (YES)		10.41(6.88-15.751)	<0.0001	12.034(8.615-16.808)	<0.0001
Smoking (YES)		1.405(0.961-2.052)	.079	3.219(2.171-4.771)	<0.0001
Fasting glucose (mg/dL)		0.999(0.998-1.001)	.431	1.001(0.997-1.004)	.752
TG / HDL-C		1.041(1.004-1.079)	.028	0.995(0.902-1.097)	.915
Abbreviations: PHQ-9, Patient Health Questionnaire-9; HDL-C, high density lipoprotein cholesterol; TG, triglyceride					
adjusted for age, sex, education, alcohol, smoking					
The ORs and 95% CI are determined through the complex sample logistic regression test.					

Results

Participant characteristics

A total of 11,648 participants were included in this study. Of these, 5,043 were male, and 6,605 were female. Among the male participants, 4,858 (96.3%) participants had a PHQ-9 score <10, whereas 185 (3.7%) had a PHQ-9 score ≧10. Among the female participants, 6,156 (93.2%) participants had a PHQ-9 score <10, whereas 449 (6.8%) had a PHQ-9 score ≧ 10. There were significant differences in income level, stress level, smoking history, FBG level, TG level, and TG/HDL-C level between males with

depression and males without depression (Table 1). There were also significant differences in income level, education level, stress level, smoking history, FBG level, TG level, and TG/HDL-C level between females with depression and females without depression (Table 2).

Relationship between lipid ratio and depression

Factors that affect the probability of depression and the relationship between the lipid ratio and depression were analyzed after adjusting for variables. In males, the probability of depression was 10.41 times higher in those with perceived stress than in those without perceived stress. An increase in TG/HDL-C by 1 was associated with a 1.041-fold higher probability of depression. In females, the probability of depression was 12.034 times higher in those who perceived stress than in those without perceived stress, and the probability of depression in current smokers was 3.219 times higher than the probability of depression in non-smokers. In males, TG/HDL-C was correlated with the probability of depression.

Discussion

In this study, we examined the relationship between depression and three lipid ratios, namely: TC/HDL-C, LDL-C/HDL-C, and TG/HDL-C. The results showed that there is an association between TG/HDL-C and depression in men. However, TC/HDL-C and LDL-C/HDL-C were not associated with depression in both males and females.

Previous studies have mainly focused on the relationship between the abovementioned lipid ratios and cardiovascular disease and insulin resistance [12, 13, 17, 19]. However, no previous study has been conducted to analyze the association between these ratios and depression. Some previous studies have demonstrated that the TC/HDL-C ratio is an important marker of cardiovascular risk and is mainly associated with insulin resistance [12–14, 19]. As shown by the Framingham risk score, the risk of coronary artery disease increases with increase in the TG/HDL-C ratio [15]. In addition, a high TG/HDL-C ratio predicts the presence of small and dense LDL particles, and is useful for diagnosing the onset of insulin resistance and metabolic syndrome [16].

Previous studies have shown that low TC and LDL-C levels are correlated with the onset of depression [17–20]. There are some plausible explanations for this relationship. First, depression reduces a patient's appetite, leading to a low serum TC level [18]. Second, cytokine activation, which interferes with cholesterol synthesis, occurs in depression [21]. Third, low cholesterol level can reduce the availability of serotonin, making the patient more susceptible to depression [19].

A study conducted on 8,390 people using data from the National Health Survey of the United States demonstrated an association between depression and cholesterol level. Depression was diagnosed using the PHQ-9, and LDL-C levels were divided into three groups: <169 mg/dL, 169–221 mg/dL, and 222 mg/dL or higher. The results showed that compared to the middle group (169–221 mg/dL), the OR for depression was 5.13 (1.74–15.09) in the low group (<169 mg/dL) and 2.28 (1.07–4.86) in the high group

(222 mg/dL or higher), which showed a U-shaped relationship. However, LDL-C and HDL-C were not associated with moderate depression [17].

Low cholesterol levels are associated with mental health indicators. The association between low cholesterol level and depression has been consistently proven in laboratory studies. In addition, less favorable or depressive behaviors were observed in studies of animals with low cholesterol levels [22, 23]. In a previous report, patients who used cholesterol-lowering drugs long-term showed signs of depression [20]. These findings can be explained by the significant correlation between plasma serotonin and low cholesterol concentration, which has been previously reported [2, 24].

Similar to the present study, some previous studies showed that depression is associated with high TG and low HDL-C levels [25, 26]. A recent meta-analysis performed to investigate whether lipid parameters differed between healthy individuals and patients with first-episode major depressive disorder revealed that elevated TG and decreased HDL-C levels are associated with first-episode major depressive disorder [25].

The serum lipid levels of people with depression and suicidal ideation have been analyzed in a previous study using KNHANES data. The results of that study showed a significant association between high HDL-C and TG levels and depression [26]. However, that study differs from the present study in that it was conducted using KNHANES data from 2014, and depression was diagnosed as a PHQ-9 score ≥5.

The potential mediators of depression in lipids or lipoproteins and their association with the heterogeneity of symptoms have been investigated in a previous study [27]. The results indicated that melancholic features are independently associated with low HDL-C level, whereas atypical depression is independently associated with high TC and LDL-C levels [27].

The results of the present study are consistent with the findings of previous studies that suggest that depression is associated with metabolic syndrome. Research on the relationship between metabolic syndrome and depression has been actively conducted in recent years [5, 28, 29]. Several possible mechanisms may be behind this correlation between metabolic syndrome and depression. Depressed people are more likely to engage in unhealthy behaviors, such as smoking, drinking alcohol, unhealthy diet and lifestyle, and non-compliance with medical treatment, than those who are not [29]. In addition, depression causes dysregulation of the hypothalamic-pituitary-adrenal axis, which may explain its association with metabolic syndrome [30]. Furthermore, cerebrovascular disease is associated with the development of depression through disturbances in neurobiological function [31]. Since metabolic syndrome is related to the occurrence of cerebrovascular disease, metabolic syndrome can cause and exacerbate depression based on the vascular depression hypothesis [32].

The presence of depression was analyzed in this study using PHQ-9 scores. The usefulness of the PHQ-9 score as a diagnostic criterion for depression has already been verified in Korea and in other countries [7–9]. However, the score used as a diagnostic criterion varies from study to study. In the present study, a PHQ-9 score ≧10 was diagnosed as depression. In the study by Kroenke et al. [18], a cutoff of 9 points

had a high sensitivity of 95% and a specificity of 84%. However, 10 points, which is simple and easy to remember or apply in actual clinical settings, has been suggested as the optimal cutoff point [33].

The present study is meaningful because it is the first study conducted to analyze the association between lipid ratios and depression in a large population. The results of this study indicate that TC/HDL-C and LDL-C/HDL-C are not associated with depression. However, this finding may have been influenced by the sample size, design, and participants of this study. Therefore, future large-scale prospective clinical studies are needed to verify this conclusion.

This study has some limitations. First, we used data from a study in which depression and lipid levels were measured only once. Depression and cholesterol levels are likely to fluctuate over time; thus, failure to account for these fluctuations may have clouded the observed association. Second, the PHQ-9, which is a self-report questionnaire, was used to measure depression. Although individual subjectivity cannot be excluded in self-report surveys, large-scale epidemiological self-report surveys are convenient and economical; hence, they are widely used to estimate prevalence. Third, as this was a cross-sectional study, it was difficult to ascertain the relationship between low cholesterol level and depression.

Conclusions

This study is the first to examine the association between depression and three lipid ratios, namely: TC/HDL-C, LDL-C/HDL-C, and TG/HDL-C. The results showed that there is an association between TG/HDL-C and depression in males. However, TC/HDL-C and LDL-C/HDL-C were not associated with depression in both males and females. Depression is not just a psychiatric disease, but a disease that needs to be approached in terms of metabolic abnormalities as well.

Abbreviations

PHQ-9, Patient Health Questionnaire; FPG, fasting blood glucose; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; DSM-IV, Diagnostic and Statistical Manual of Mental Disorders, fourth edition

Declarations

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Conflicts of interest

The author declare that they have no conflict of interest.

Availability of data and material

Not applicable.

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Authors' contributions

A Lum Han contributed to the study conception and design. Material preparation, data collection and analysis. The first draft of the manuscript was written by A Lum Han. Author read and approved the final manuscript.

Ethics approval

This study followed the ethical standards laid out in the Declaration of Helsinki and was approved by Wonkwang University Hospital's clinical trial screening committee (IRB) (approval number: 2021-09-001).

Consent to participate

Consent was not required from all participants. We only reviewed the patient charts for this study, and we guaranteed that we would not use the information for anything other than for research purposes. Additionally, we reviewed the charts that provided only the identification numbers of participants instead of their names. This was approved by the ethics committee.

Consent for publication

Not applicable. This is because all patient information was investigated anonymously, and the manuscript did not reveal the patients' personal clinical information or their images.

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Figures

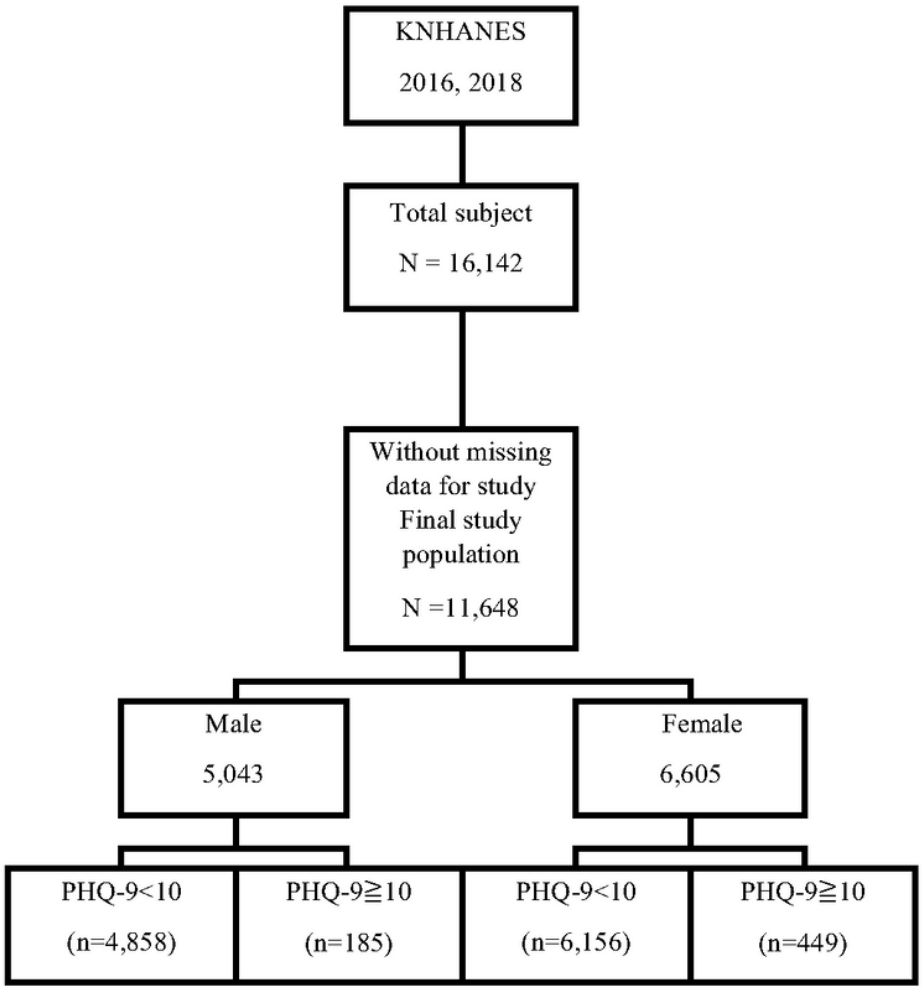

Figure 1

Flow Chart