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Sex-related associations among anemia, body mass index, and kidney function in Koreans

A cross-sectional study with propensity analysis

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Abstract

The association between anemia and body mass index (BMI) in Koreans, considering kidney function, has not been clarified. Thus, we aimed to examine the association between anemia and BMI among Korean adults aged ≥19 years.

This retrospective cross-sectional study evaluated male and female Korean adults aged ≥19 years who participated in the 5th, 6th, and 7th Korean National Health and Nutrition Examination Surveys (KNHANES) conducted between 2010 and 2017 were used. The participants were classified as underweight, normal weight, and overweight according to their BMI. Anemia was defined as hemoglobin levels of <13 g/dL for men and <12 g/dL for women according to the World Health Organization standards. Kidney function was evaluated according to the estimated glomerular filtration rate (eGFR), with abnormal kidney function in men defined as eGFR <60 mL/min/1.73 m^2. Clinicodemographic variables were analyzed using logistic regression adjusted for weight. After propensity score matching (PSM), 6596 study participants were divided into 2 groups of 3298 participants each. Additionally, subgroup analysis by sex and kidney function was performed.

On PSM, similar distribution patterns were obtained between the anemia and non-anemia groups; significant differences in BMI; kidney function; level of hemoglobin, hematocrit, and serum creatinine; iron intake; and eGFR were also observed between these groups. Anemia and BMI showed a significant association in both crude and adjusted logistic regression models. In model 2, which was adjusted for age, sex, education level, household income, alcohol consumption, smoking status, and exercise period, underweight men with abnormal kidney function showed a significantly higher risk of anemia than did normal weight men (odds ratio [OR]: 3.27; 95% confidence interval [CI]: 1.25–8.57; $P = .016$). Meanwhile, overweight men showed a significantly lower risk of anemia than did normal weight men (OR: 0.48; 95% CI: 0.33–0.70, $P < .001$).

Anemia is associated with BMI according to sex. Compared with normal weight men, underweight men with abnormal kidney function had a significantly higher prevalence of anemia after adjusting for kidney function and sex, thus highlighting their need for careful management for anemia.

Abbreviations: BMI = body mass index, eGFR = estimated glomerular filtration rate, KNHANES = Korea National Health and Nutrition Examination Survey, OR = odds ratio, PSM = propensity score matching.

Keywords: anemia, body mass index, cross-sectional study, kidney function, propensity score matching

1. Introduction

Anemia as a major global public health issue is caused by hemoglobin deficiency, resulting in a decline in the blood's oxygen-carrying capacity.[1] Anemia occurs as a complicated and multifactorial condition. It is a complication associated with several chronic diseases. Aside from being a potential risk factor

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The datasets generated during and/or analyzed during the current study are publicly available.

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for cardiovascular disease, it is also a risk factor for chronic kidney damage.[2] Anemia affects a third of the world's population and contributes to increased morbidity and mortality.[3] Recently, anemia was estimated to be globally prevalent in 29% of pregnant women, 38% of nonpregnant women, and 43% of children, with reductions since 1995.[4] In Korea, anemia is more prevent in women than men and in older people than younger people.[5]

The association between body mass index (BMI) and anemia remains controversial. Some studies have revealed that anemia is associated with high BMI.[6–8] While the causes are believed to be inadequate iron intake and inflammation related to fat cells, a clear cause has not been identified. Conversely, some studies also showed high incidence rates of anemia in underweight people with low BMI, whereas they were relatively low in obese people.[9–11]

Anemia is a common complication that accompanies kidney function.[12,13] A US study using data from the National Health and Nutrition Examination Survey III data reported a higher incidence of anemia in participants with a $<60\,mL/min/1.73\,m^2$ glomerular filtration rate (GFR).[14,15] Anemia may occur due to various factors including iron deficiency, hemorrhage, and inflammation, and can lead to a gradual worsening of kidney function.[16,17] BMI also negatively affects the estimated glomerular filtration rate (eGFR). In many large population studies, a high BMI was found to be associated with decreasing eGFR, leading to a related decrease in kidney function.[18–22]

However, although anemia, BMI, and kidney function are closely related, there has been no study on the association between anemia and BMI, considering kidney function, in Koreans.[23] Therefore, this study aimed to examine the association between anemia and BMI according to both sex and kidney function. Towards this goal, we analyzed the data of male and female Korean adults aged ≥19 years who participated in the 5th, 6th, and the 7th Korea National Health and Nutrition Examination Survey (KNHANES) conducted from 2010 to 2017. Moreover, the analysis was performed following confounding variable correction by propensity score matching (PSM), carrying out an objective analysis of the association between anemia and BMI.

2. Materials and methods

2.1. Study design and participants

This cross-sectional study evaluated the participants of the 5th, 6th, and 7th KNHANES (2010–2017). The KNHANES has been annually conducted by the Korean Centers for Disease Control and Prevention (KCDC) since 1998 to evaluate the health and nutritional status of the country's general population. The KNHANES is a complex, layered, multiphased, probability cluster survey that uses a rolling sampling design and proportionately distributes Korea's national sample by region, sex, and age. It includes health surveys, health examinations, and dietary questionnaires.[24] The 5th, 6th, and 7th versions of the KNHANES were approved by the Institutional Review Board of the KCDC. Informed consent was obtained from all the participants at the time of the surveys.

Of the 64,759 participants in the 3 surveys, we initially evaluated 36,752 individuals aged ≥19 years who participated in surveys related to anemia symptoms. After excluding 30,156 participants with missing PSM analysis data such as age, sex, educational level, household income level, alcohol consumption, smoking, and duration of muscle-strength exercise, 6596 participants selected through PSM were included in the analysis (Fig. 1).

2.2. Ethics statement

The institutional review board of Jaseng Hospital of Korean Medicine waived the need for study approval and informed

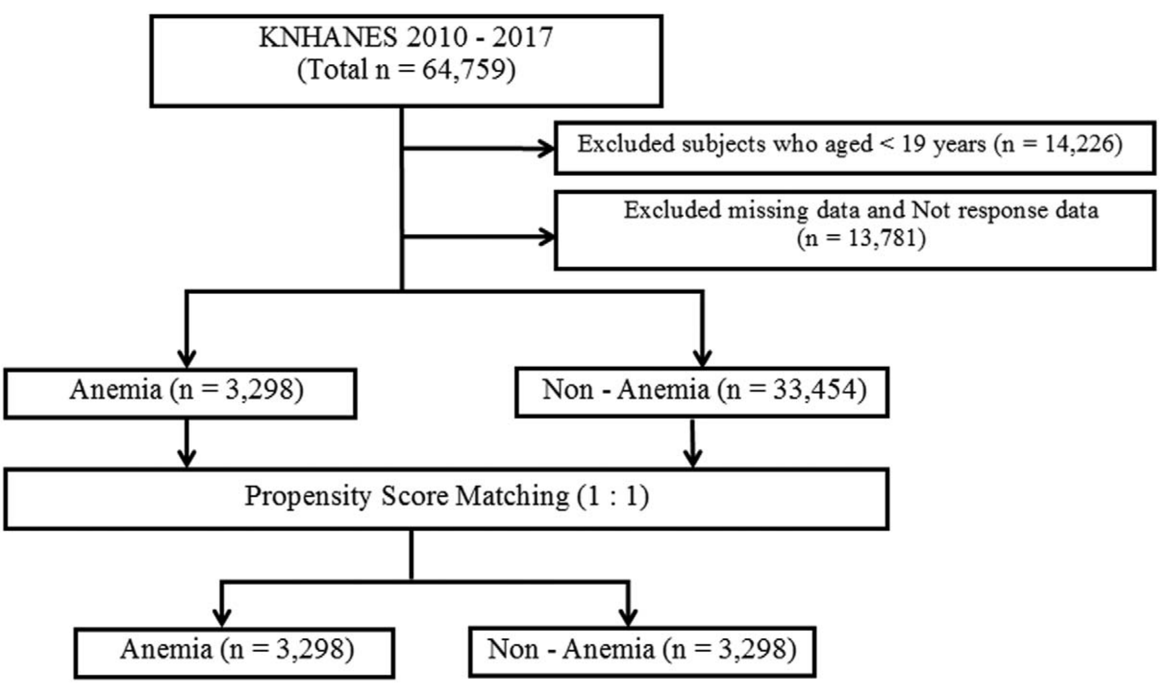

Figure 1. Participant inclusion flowchart.

consent because the study did not deal with sensitive information, but rather accessed publicly available data from the KNHANES (JASENG 2019–04–003).

2.3. Definitions of anemia, BMI, and eGFR

2.3.1. Anemia. Anemia was diagnosed according to the hemoglobin level obtained from blood examinations and was defined according to the World Health Organization (WHO) criteria as follows: men, <13 g/dL; non-pregnant women, <12 g/dL; and pregnant women, <11 g/dL.[25]

2.3.2. BMI. BMI was calculated as weight (kg)/height (cm)^2 and was set as a continuous variable obtained using body measurements. The participants were accordingly categorized according to their BMI according to the following cutoff: underweight, <18.5 kg/m^2; normal weight, 18.5–24.9 kg/m^2; and overweight, ≥25.0 kg/m^2.[26]

2.3.3. eGFR. Adult eGFR was calculated using either the Cockcroft-Gault (CG) equation or modification of diet in renal disease (MDRD) equation. Previous comparative studies on MDRD GFR and CG GFR reported that they have similar accuracies.[27–30] In general, CG is the most popular equation for assessing eGFR. It uses the serum creatinine (Cr) levels in patients who have stable serum Cr.[31] The CG eGFR is calculated as CrCl (mL/min) = ([140–age in years] × weight [kg])/(SCr [mg/dL] × 72), where CrCl is the creatinine clearance and SCr is the serum creatinine for men. For women, the result obtained is multiplied by 0.85.[32] A CG eGFR of <60 was defined as abnormal kidney function.[33]

2.3.4. Assessment of patient characteristics. The participants provided data regarding demographic and socio-economic characteristics, medical history (e.g., high blood pressure, diabetes), nutritional status, and other attributes in the health and nutritional surveys and the examinations conducted by the interviewers. Information related to anemia was extracted exclusively from the raw data in surveys and examinations. Basic characteristics such as age, sex, and BMI were analyzed. We obtained data on demographics, education levels, household income, smoking, alcohol consumption, and time spent on muscle-strength exercise from the health survey. Meanwhile, data on height, weight, BMI, hemoglobin, serum Cr, and iron ingestion were obtained from the examinations.

Education level was divided into 4 categories: elementary school or below, middle school, high school, and university and above. Household income was calculated using the square root index method of the Organization for Economic Cooperation and Development (OECD), which is widely used in Korea. Equalized personal income is calculated by dividing total household income by the square root of the number of household members.[34] It was classified into 4 levels: low, middle, middle-high, and high. Alcohol consumption was classified as "never drank at all" in the past year, "less than once a month," "one to four times a month," and "five times or more a month." Regarding smoking, those who currently smoked were categorized as smokers; those who only smoked in the past as once-smokers; and those who never smoked as never-smokers. Time spent on muscular-strengthening exercises during the past week was classified as none, 1 to 2 days, and ≥3 days. The reference values of daily iron intake for men were 10 and 9 mg/d for those aged 19 to 64 years and ≥65 years, respectively. For women, they were 14, 8, and 7 mg/d aged for those aged 19 to 49, 50 to 74, and ≥75 years, respectively. Daily intake data used in the study were obtained from individual interviews using the 24-hour recall method.

2.4. Propensity score matching

To analyze the association between anemia and BMI, we attempted to balance all potentially related variables by performing corrections for selection bias and confounding variables. We further explored this alongside its connection with kidney function level, which is a risk factor associated with anemia. PSM was performed using the IBM SPSS Statistics Version 25.0 (Windows; IBM Corp., Armonk, NY). Items with missing values were removed at this stage. In PSM, the logistic regression estimation algorithms, matching algorithm as the nearest neighbor, and 1:1 matching were used. Age, sex, education level, household income level, alcohol consumption in a year, smoking status, and time spent on muscular-strengthening exercise in 1 week were set as covariates. Anemia was set as a binary treatment indicator, and matching was conducted. Among the 6596 participants, 3298 participants with and without anemia were matched.

2.5. Statistical analysis

The KNHANES is a nationwide sample survey, applying stratification, clustering, and weights. Data analysis of the composite sample was conducted accordingly, using stratification, aggregation, and weighting variables as composite sample design elements. Continuous variables were expressed as the mean ± standard error of mean, and categorical variables, as number (%). Prior to PSM matching, chi-square test was conducted to determine the association of anemia with age, sex, education level, household income level, alcohol consumption in a year, smoking status, and exercise time in 1 week. After matching, the chi-square test was performed for each factor, in relation to anemia and followed by analysis according to sex, reflecting the characteristics of the composite sample data. Moreover, composite sample t test was performed using age; BMI; hemoglobin, hematocrit, and Cr levels; iron intake; and kidney function readings. To determine the association of anemia with each factor, odds ratios (ORs) were calculated using composite sample multiple logistic regression, and the analysis was performed with factor correction. All statistical analyses were performed using SPSS ver. 25.0 (SPSS Inc., Chicago, IL), and P values of <.05 were considered statistically significant.

3. Results

3.1. General characteristics of study participants and comparisons before and after PSM

Before PSM, 14,532 men (43.4%) and 18,922 women (56.6%) were studied, among whom 3298 and 33,454 did and did not have anemia (Fig. 1). Table 1 lists the general characteristics of the study group before and after PSM. Both pre-and post-PSM anemia groups showed significant differences in age, sex, education level, household income, alcohol consumption, smoking status, and exercise time.

After PSM, 6596 participants remained, with 3298 participants each in the non-anemia and anemia groups. After PSM, no

Table 1

Characteristics of the study population, with respect to anemia, before and after propensity score matching.

	Before propensity score matching			After propensity score matching		
Characteristics	Non-anemia (n = 33,454)	Anemia (n = 3298)	*P*-value	Non-anemia (n = 3298)	Anemia (n = 3298)	*P*-value
Age						
19–29	3938 (11.8)	242 (7.3)	<.001	252 (12.5)	242 (11.9)	.971
30–39	5678 (17.0)	588 (17.8)		589 (19.4)	588 (19.2)	
40–49	5955 (17.8)	759 (23.0)		754 (26.6)	759 (27.0)	
50–59	6822 (20.4)	383 (11.6)		379 (12.4)	383 (12.3)	
≥60	11,061 (33.1)	1326 (40.2)		1324 (29.2)	1326 (29.6)	
Sex						
Male	14,532 (43.4)	704 (21.3)	<.001	705 (18.3)	704 (18.4)	.964
Female	18,922 (56.6)	2594 (78.7)		2593 (81.7)	2594 (81.6)	
Educational level						
Elementary school or lower	7722 (23.1)	950 (28.8)	<.001	940 (22.1)	950 (23.3)	.584
Middle school	3651 (10.9)	298 (9.0)		296 (8.0)	298 (8.0)	
High school	11072 (33.1)	1080 (32.7)		1086 (37.7)	1080 (35.9)	
College or higher	11009 (32.9)	970 (29.4)		976 (32.2)	970 (32.9)	
Household income level						
Low	6161 (18.4)	802 (24.3)	<.001	799 (20.4)	802 (20.9)	.965
Low-moderate	8459 (25.3)	878 (26.6)		878 (26.9)	878 (27.1)	
Moderate-high	9225 (27.6)	859 (26.0)		860 (28.3)	859 (27.7)	
High	9609 (28.7)	759 (23.0)		761 (24.3)	759 (24.3)	
Alcohol consumption						
Never drank	9129 (27.3)	1292 (39.2)	<.001	1291 (35.0)	1292 (35.0)	.982
<1 time per month	6291 (18.8)	703 (21.3)		700 (22.5)	703 (22.7)	
1–4 times per month	10,834 (32.4)	926 (28.1)		935 (31.2)	926 (31.3)	
≥5 drinking episodes per month	7200 (21.5)	377 (11.4)		372 (11.3)	377 (11.0)	
Smoking						
Non-smoker	20,076 (60.0)	2533 (76.8)	<.001	2535 (78.6)	2533 (78.5)	.532
Ex-smoker	7013 (21.0)	540 (16.4)		533 (13.7)	540 (14.5)	
Current smoker	6365 (19.0)	225 (6.8)		230 (7.7)	225 (7.0)	
Duration of muscle-strength exercise (d/wk)						
0 day	24,955 (74.6)	2686 (81.4)	<.001	2699 (81.2)	2686 (81.1)	.962
1–2 days	3524 (10.5)	250 (7.6)		247 (8.1)	250 (8.2)	
≥3 days	4975 (14.9)	362 (11.0)		352 (10.8)	362 (10.6)	

Chi-square test was performed to determine the differences between groups with respect, to anemia. Missing values/nonresponses were excluded from the analysis. Categorical variables are presented as frequency and percentage (%), and continuous variables are presented as mean and standard deviation.

The value before propensity score matching (PSM) is N (%) and that after PSM is N (% of composite sample). *P*-value after PSM is the chi-square result of the compound sample.

significant differences were found in terms of sex, education level, household income, consumption of alcohol, smoking status, and exercise time ($P < .001$), indicating a good match. While the histogram distribution patterns differed regarding anemia before PSM, the distribution patterns between the anemia and non-anemia groups after PSM were similar and matched well (Fig. 2).

3.2. Participants characteristics by sex

The clinical characteristics of the study group after PSM are summarized in Table 2. After PSM, the 6596 participants were classified according to sex and anemia. When PSM was adjusted for age, sex, education level, household income, alcohol consumption, smoking status, and exercise time, no significant differences were found between men and women, with or without anemia (Table 2). However, when examining BMI; kidney function; average age; hemoglobin, hematocrit, and serum Cr levels; iron intake; and eGFR according to anemia, significant differences were observed between men and women after PSM. Moreover, significant differences concerning anemia were observed by sex when the patients were divided according to their BMI and eGFR (<60 mL/min/1.73 m^2 vs ≥60 mL/min/1.73 m^2) (Table 3).

3.3. Risk of anemia in relation to BMI

To identify the association between anemia and BMI, a multiple logistic regression analysis model was built for PSM using sex. As presented in Table 4, overweight participants showed a lower risk of anemia than normal-weight participants in models 1, 2, and 3, with ORs and 95% confidence intervals (CIs) of 0.72 (95% CI, 0.63–0.82), 0.70 (95% CI, 0.62–0.80), and 0.77 (95% CI, 0.68–0.88), respectively ($P < .0001$). Particularly, the risk of anemia was significantly higher in underweight (OR, 2.30; 95% CI, 1.22–4.34; $P = .01$) and overweight men (OR, 0.43; 95% CI, 0.32–0.57; $P < .0001$) than that in normal-weight men. Overweight women showed a lower risk of anemia than normal-weight women (OR, 0.81; 95% CI, 0.70–0.94; $P = .006$) in model 1. In model 2, which was adjusted for age, sex, education level, household income, alcohol consumption, smoking status, and exercise period were considered, overweight groups showed a lower risk of anemia than normal-weight groups ($P < .0001$). Compared with normal-weight men, underweight men had a

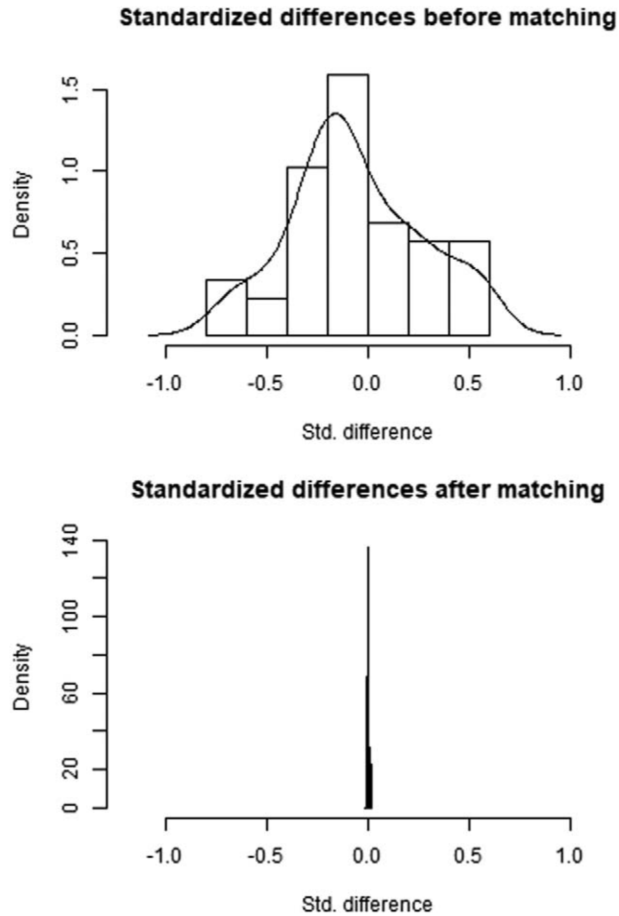

Figure 2. Distribution of the participants before and after propensity score matching, according to the presence or absence of anemia.

higher risk of anemia (OR, 2.39; 95% CI, 1.25–4.53, $P=.008$) whereas overweight men had a lower risk (OR, 0.41; 95% CI, 0.31–0.55, $P<.0001$). Overweight women were 0.80 times less likely than normal-weight women to have anemia ($P=.005$). In model 3, overweight groups had a 0.77-fold lower risk of anemia than did normal-weight groups ($P<.01$). Compared with normal-weight men, underweight men were 2.12 times more likely to have anemia ($P=.022$), whereas overweight men were 0.48 times less likely to have anemia ($P<.01$).

3.4. Association between anemia and BMI in relation to kidney function

The serum Cr level was established as an important factor related to the association between anemia and BMI, as evidenced by the significant variation between corresponding OR values in model 2 and model 3 (Table 4). Accordingly, we performed additional analysis with kidney function, as shown in Table 5. For men with normal kidney function (eGFR ≥60 mL/min/1.73 m^2) both before and after correction (models 1 and 2), the overweight group had a significantly lower risk of anemia than did the normal weight group, with an OR of 0.44 ($P<.001$). However, no significant risk was observed in the underweight group. For men with abnormal kidney function (eGFR <60 mL/min/1.73 m^2), the OR values for the underweight group were 2.94 for model 1 ($P=.010$) and 3.27 for model 2 ($P=.016$) when compared with the normal-weight group. Meanwhile, they were 0.54 for model 1 ($P=.002$) and 0.48 for model 2 ($P=.001$) for the overweight group. For women with normal kidney function (eGFR ≥60 mL/min/1.73 m^2), the overweight group had a significantly lower risk of anemia than did the normal weight group (model 1, $P=.005$). However, no significant differences were observed between the underweight and abnormal kidney function groups.

4. Discussion

The association between anemia and body mass index (BMI) in Koreans, considering kidney function, remains unclear to date. The results of this study showed a significant association between anemia and BMI. The overweight groups had a lower risk of anemia than did the normal-weight groups (OR, 0.77; 95% CI, 0.68–0.88). In the sex-stratified analysis, underweight men showed a higher risk of anemia (OR, 2.39; 95% CI, 1.25–4.53) and overweight men showed a lower risk of anemia (OR, 0.41; 95% CI, 0.31–0.55) than did normal-weight men. Specifically, for men with abnormal kidney function (eGFR <60 mL/min/1.73 m^2), the OR values of the underweight group were 2.94 and 3.27, showing a significantly higher risk of anemia than the normal weight men. The OR values of the overweight group were 0.54 and 0.48, showing a significantly lower risk of anemia than in the normal weight group.

When the participants were classified according to BMI and sex, the risk of anemia was significantly low in overweight women and high in underweight women. These results were consistent with previous studies conducted in Chinese,[10] Peruvian,[11] and Egyptian women.[11,34] Overweight and obese Chinese women were found to less likely to have anemia than normal-weight women.[10] Studies in women in Peru, Egypt, and Mexico also found a significantly lower prevalence of anemia in overweight Peruvian and Egyptian women, excluding Mexican women, than in their non-overweight counterparts.[11] Nutritional factors such as vitamin C, vitamin B12, and vitamin K, which play an important role in hemostasis, may be present in very low levels in people with low BMI, which is believed to have affected these results.[6] Moreover, the dietary intake of obese or overweight people would have delivered sufficient iron to lower the risk of anemia compared with the diet of underweight women, explaining the results.[11] Some studies in other countries reported a high prevalence of anemia in the obese.[6–8] However, other studies also reported conflicting results.[23,24] The difference in the diets of the Eastern and Western obese population, which mainly consists of fats and carbohydrates and lacks fruits and vegetables, could explain the results as this diet can cause anemia.[35,36] Conversely, while the obese population in Korea shows reduced grain consumption and increased consumption of animal meat due to the influx of Westernized eating habits, the proportion of fat intake has not exceeded 20% of the total energy consumption thus far.[37] Moreover, it has been speculated that the prevalence of anemia is low because of the adherence to a rice-centric diet as a staple food, despite the increase in the consumption of bread and fast foods.[38]

The prevalence of anemia and moderate-severe anemia vary among races. For all age groups, Blacks had the highest prevalence of anemia for both sexes. In general, the proportion of Hispanics with anemia and moderate-severe anemia is higher than that of whites and Asian.[39,40] Regarding sex, there was a significant association between anemia and BMI in both the

Table 2

Characteristics of the study population according to sex after propensity score matching.

Characteristics	Male			Female		
	Non-anemia (n=705)	Anemia (n=704)	*P*-value	Non-anemia (n=2,593)	Anemia (n=2,594)	*P*-value
Age category						
19–29	16 (5.9)	11 (4.2)	.748	236 (14.0)	231 (13.6)	.985
30–39	19 (4.7)	15 (3.8)		570 (22.7)	573 (22.6)	
40–49	33 (7.5)	34 (9.4)		721 (30.9)	725 (31.0)	
50–59	83 (17.8)	85 (19.1)		296 (11.1)	298 (10.8)	
≥60	554 (64.0)	559 (63.4)		770 (21.3)	767 (22.0)	
Educational level						
Elementary school or lower	261 (31.5)	265 (33.9)	.626	679 (20.0)	685 (20.8)	.500
Middle school	100 (12.3)	103 (13.1)		196 (7.1)	195 (6.8)	
High school	230 (36.4)	228 (36.1)		856 (38.0)	852 (35.9)	
College or higher	114 (19.8)	108 (16.8)		862 (34.9)	862 (36.5)	
Household income level						
Low	269 (34.1)	270 (34.1)	.997	530 (17.4)	532 (17.9)	.949
Low-moderate	216 (29.6)	213 (29.1)		662 (26.3)	665 (26.7)	
Moderate-high	131 (21.5)	131 (21.5)		729 (29.8)	728 (29.1)	
High	89 (14.8)	90 (15.2)		672 (26.5)	669 (26.3)	
Alcohol consumption						
Never drank	271 (35.0)	269 (35.6)	.930	1020 (35.0)	1023 (34.8)	.996
<1 time per month	77 (11.4)	81 (12.5)		623 (25.0)	622 (25.0)	
1–4 times per month	177 (27.1)	173 (26.7)		758 (32.1)	753 (32.3)	
≥5 drinking episodes per month	180 (26.4)	181 (25.1)		192 (8.0)	196 (7.8)	
Smoking						
Non-smoker	146 (23.1)	149 (23.0)	.560	2389 (91.0)	2384 (91.0)	.915
Ex-smoker	408 (51.0)	404 (54.0)		125 (5.4)	136 (5.6)	
Current smoker	151 (25.9)	151 (23.0)		79 (3.6)	74 (3.4)	
Duration of muscle-strength exercise (d/wk)						
0 day	506 (68.9)	505 (71.4)	.710	2193 (83.9)	2181 (83.3)	.888
1–2 days	51 (8.8)	50 (8.3)		196 (7.9)	200 (8.2)	
≥3 days	148 (22.3)	149 (20.3)		204 (8.2)	213 (8.5)	

Chi-square test was performed to determine the differences between groups, with respect to anemia, according to sex. Categorical variables are presented as frequency and percentage (%), and continuous variables are presented as mean and standard deviation.

Table 3

Comparison of clinical characteristics between anemia and non-anemia by sex.

Characteristics	Male			Female		
	Non-anemia	Anemia	*P*-value	Non-anemia	Anemia	*P*-value
BMI, kg/m^2	24.32 (0.17)	22.54 (0.14)	<.001	23.26 (0.09)	22.85 (0.09)	<.001**
BMI[a]						
Underweight	17 (3.1)	66 (9.1)	<.001	137 (6.3)	151 (6.4)	.033*
Normal weight	396 (52.4)	470 (66.4)		1642 (63.3)	1738 (67.2)	
Overweight	292 (44.5)	168 (24.5)		814 (30.4)	705 (26.4)	
eGFR						
eGFR < 60 mL/min/1.73 m^2	361 (41.8)	498 (61.2)	<.001	340 (9.2)	507 (15.0)	<.001**
eGFR ≥60 mL/min/1.73 m^2	344 (58.2)	206 (38.8)		2253 (90.8)	2087 (85.0)	
eGFR,[b] mL/min/1.73 m^2	68.18 (1.3)	56.7 (1.48)	<.001	91.86 (0.58)	91.01 (0.74)	<.001**
Hemoglobin, g/dL	15.1 (0.05)	11.9 (0.05)	<.001	13.37 (0.02)	10.92 (0.03)	<.001**
Hematocrit, (%)	44.96 (0.14)	36.8 (0.15)	<.001	40.44 (0.06)	34.6 (0.06)	<.001**
Serum creatinine, mg/dL	0.98 (0.01)	1.32 (0.09)	<.001	0.72 (0.002)	0.75 (0.01)	<.001**
Iron intake, mg/d	17.54 (0.6)	16.6 (0.57)	<.001	14.12 (0.29)	13.71 (0.21)	<.001**

Chi-square test or *t* test was performed to determine the differences between groups, with respect to anemia, according to sex. For BMI; hemoglobin, hematocrit, and serum creatinine levels; iron intake; and eGFR, composite sample *t* test was conducted to analyze the estimated means and standard deviations.

Categorical variables are presented as frequency and percentage (%), and continuous variables are presented as mean and standard deviation.

[a] BMI = weight (kg)/height (cm)^2. BMI was categorized into underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (≥25.0 kg/m^2).

[b] eGFR: for men: CrCl (mL/min) = ([140–age in years] × Weight [kg])/(SCr [mg/dL] × 72).

where CrCl is creatinine clearance and SCr is serum creatinine. For women, the result is multiplied by 0.85.

* *P*-value < .05.

** *P*-value < .01.

Table 4

Association between anemia and BMI according to sex.

	Model 1		Model 2		Model 3	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Total						
Normal weight	1.00		1.00		1.00	
Underweight	1.10 (0.85–1.42)	.469	1.13 (0.87–1.46)	.348	1.06 (0.82–1.38)	.639
Overweight	0.72 (0.63–0.82)	<.001	0.70 (0.62–0.80)	<.001	0.77 (0.68–0.88)	<.001
Male						
Normal weight	1.00		1.00		1.00	
Underweight	2.30 (1.22–4.34)	.01	2.39 (1.25–4.53)	.008	2.12 (1.14–4.03)	.022
Overweight	0.43 (0.32–0.57)	<.001	0.41 (0.31–0.55)	<.001	0.48 (0.36–0.65)	<.001
Female						
Normal weight	1.00		1.00		1.00	
Underweight	0.95 (0.71–1.28)	.752	0.96 (0.71–1.30)	.819	0.92 (0.68–1.25)	.620
Overweight	0.81 (0.70–0.94)	.006	0.80 (0.69–0.93)	.005	0.86 (0.74–1.01)	.067

Logistic regression analysis with complex sampling design was performed by adjusting for covariates.
BMI = weight (kg)/height (cm)^2. BMI was categorized into underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), overweight (≥25.0 kg/m^2).
Model 1: Not adjusted (crude).
Model 2: Adjusted for age, educational level, marital status, household income level, alcohol consumption, smoking, duration of muscle-strength exercise.
Model 3: Model 2 + Serum creatinine.
95% CI = 95% confidence interval; OR = odds ratio.

underweight and overweight groups. However, the risk of anemia was significantly lower in overweight women than that in underweight women. Regarding kidney function, the risk of anemia was lower in men with normal kidney function, both before and after correcting for confounding variables. In women, however, there was no significant association between anemia and normal kidney function, given the confounding factors. Among the participants with abnormal kidney function, only underweight men showed a significant prevalence of anemia, with no significant results observed in women. Although there is no clear explanation for these findings on the association between anemia and BMI depending on sex, a plausible explanation could be the difference in the pathogenicity of anemia between men and women. The most common form of anemia observed in women is iron-deficiency anemia caused by regular menstrual blood loss. Menstruating women weighing around 60 kg need to consume about 10 mg more iron than men or non-menstruating women. Meanwhile, iron-deficiency anemia in men occurs due to chronic disease or low iron intake, similar to that in postmenopausal women.[4] Thus, the association between body mass and anemia

Table 5

Association between kidney function and BMI among participants with anemia according to sex.

	Model 1		Model 2	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Male				
eGFR ≥60 mL/min/1.73 m^2				
Normal weight	1.00		1.00	
Underweight	1.02 (0.29–3.50)	.972	1.12 (0.31–4.00)	.852
Overweight	0.44 (0.29–0.68)	<.001	0.44 (0.28–0.69)	<.001
eGFR <60 mL/min/1.73 m^2				
Normal weight	1.00		1.00	
Underweight	2.94 (1.29–6.66)	.010	3.27 (1.25–8.57)	.016
Overweight	0.54 (0.37–0.79)	.002	0.48 (0.33–0.70)	<.001
Female				
eGFR ≥60 mL/min/1.73 m^2				
Normal weight	1.00		1.00	
Underweight	0.87 (0.63–1.21)	.420	0.84 (0.60–1.17)	.324
Overweight	0.79 (0.68–0.93)	.005	0.85 (0.72–1.00)	.061
eGFR <60 mL/min/1.73 m^2				
Normal weight	1.00		1.00	
Underweight	2.11 (0.97–4.57)	.058	2.15 (0.98–4.73)	.055
Overweight	1.02 (0.72–1.46)	.878	1.03 (0.71–1.50)	.841

Logistic regression analysis with complex sampling design was performed by adjusting for covariates.
eGFR ≥60 mL/min/1.73 m^2 is normal, eGFR <60 mL/min/1.73 m^2 is abnormal. BMI = weight (kg)/height (cm)^2. BMI was categorized into underweight (<18.5 kg/m^2), normal weight (18.5–24.9 kg/m^2), and overweight (≥25.0 kg/m^2).
Model 1: Not adjusted (crude).
Model 2: Adjusted for age, educational level, marital status, household income level, alcohol consumption, smoking, duration of muscle-strength exercise.
95% CI = 95% confidence interval; OR = odds ratio.

may vary depending on sex due to these differences in pathogenicity. Moreover, kidney disease is a crucial factor in anemia occurrence, and abnormal kidney function may affect the association between anemia and BMI, as evidenced by an association different from that in the case of normal kidney function.[41]

This study used data from the KNHANES that has been performed with large community groups, is rich in analytical data, and has strict quality control. Hence, the results of this study have a high potential for generalization. Moreover, this study has clinical significance because there is a strong association between anemia and BMI. Sub-analysis was performed by subdividing characteristics such as sex and kidney function, and the analysis was performed with 3 different weight groups, based on BMI. The advantage of this study was that we examined the association between anemia and BMI according to sex. Furthermore, the subgroup analysis according to kidney function stratified by sex showed the relationship between anemia according to kidney function and BMI.

However, this study also has some limitations. The amount of serum iron could change due to various factors such as menstrual volume, blood donation status, gastrointestinal disease-causing blood loss, and inflammatory disease. However, this was not reflected in the study due to the lack of relevant research data.[6] This is a cross-sectional study where only the association between anemia and BMI could be identified, thus having limitations in identifying the exact causal relationship. We performed PSM to reduce baseline differences in the comorbidities between the study groups. However, aside from kidney function, there are many other factors (e.g., hemorrhagic disease, iron deficiency, lack of folic acid, etc[42]) that can influence the pathogenesis of anemia and kidney function. These were not sufficiently considered in the study, and thus limiting the interpretation of the results. Moreover, the KNHANES data used in the present study were collected without dividing the patients according to reduced erythropoietin and iron-deficiency anemia. Hence, the relationship between BMI and kidney function depending on each type of anemia could not be identified.

In general, it is known that eGFR increases by 40% to 50% in early pregnancy compared with non-pregnancy eGFR.[43] Although pregnancy was an influencing factor for eGFR as described above, the present study mainly focused on the relationship between BMI and anemia. Thus, we did not pay attention to the pregnancy variable that can affect kidney function. This should be considered in follow-up studies.

Further studies should clarify the mechanisms that affect the correlation between anemia and BMI. Because kidney diseases were not considered in the subgroup analysis according to kidney function, this should be considered in future large-scale studies. Additionally, large-scale studies should be conducted to identify the relationship between overweight and anemia and the cause of this relationship.

5. Conclusions

This study found a strong association between anemia and BMI. In the sex-stratified analysis, overweight men and women had a lower risk of anemia than did normal-weight men and women. Moreover, underweight men had a higher risk of anemia than overweight and normal-weight men. Furthermore, among men with abnormal kidney function, those who were underweight have a particularly high risk of anemia. Collectively, these findings support that BMI is a strong independent factor that can predict the risk of anemia, especially in underweight men with abnormal kidney function. Given the high risk in this group, careful management for anemia is recommended.

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