Positive Association Between Body Mass Index and Hematologic Parameters, Including RBC, WBC and Platelet Count, in Korean Children and Adolescent

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Abstract

Objective: To investigate the associations between hematologic parameters and obesity in children and adolescents.

Methods: A total of 7,997 subjects (4,259 boys, 3,738 girls) aged 10–18 years was enrolled and hematologic parameters, including WBC, RBC, Hb, Hct, and platelet levels, were recorded and compared against body mass index (BMI) classified into normal-weight, overweight, and obesity groups.

Results : The obesity group had significantly higher mean levels of WBC (7.16 vs. 6.16 ($x10^3/mm^3$), $p<0.001$), RBC (4.90 vs. 4.82 ($x10^6/mm^3$), $p<0.001$), Hb (14.07 vs. 13.99 (g/dL), $p<0.05$), Hct (42.31 vs. 41.91 (%), $p<0.001$) and platelets (311.87 vs. 282.66 ($x10^3/mm^{3)}$, $p<0.001$) than the normal-weight group after adjusting for obesity and sex. BMI SDS was significantly positively associated with WBC (β=0.275, $p<0.001$), RBC (β=0.028, $p<0.001$), Hb (β=0.034, $p<0.001$), Hct (β=0.152, $p<0.001$), and platelets (β=8.372, $p<0.001$) after adjusting for age, sex, and possible socioeconomic confounders in a multiple linear regression analysis.

Conclusion: Higher BMI is associated with elevated WBC, RBC, Hb, Hct and platelet counts in children and adolescents. Because higher hematologic parameters are potential risk factors for obesity-related morbidity, more attention should be paid to evaluating and interpreting hematologic parameters in children and adolescents with obesity

Introduction

Obesity is characterized as excessive body-fat mass or body weight. Recently, obesity prevalence has sharply increased all over the world, including among children (1). Obesity is associated with chronic inflammation, which is known to contribute to atherosclerosis and metabolic syndrome (2–4). Metabolic syndrome (MS) refers to a constellation of disturbances including central obesity, glucose intolerance, hypertriglyceridemia, decreased high-density lipoprotein (HDL) cholesterol, and high blood pressure (5). MS is considered a precursor of cardiovascular disease and type-2 diabetes mellitus (T2DM) (6). Childhood obesity leads to adult obesity and metabolic syndrome (7, 8) and is associated with increased risk of cardiovascular disease and mortality (9). Therefore, prevention and early intervention for childhood obesity and related comorbidities are important challenges for public health care systems.

Obesity-induced inflammation contributes to development of insulin resistance and T2DM (4, 10), and these conditions are important contributing factors to MS (11). Inflammatory markers, including C-reactive protein, ferritin, and cytokine, are elevated in obesity (11, 12). Also, total white blood cell (WBC) count, another inflammation marker, is elevated in obesity and MS (13–15). Additionally, increased platelet count and platelet activation can occur as part of the chronic inflammation process in obesity (16, 17). Furthermore, obesity is a risk factor for high blood pressure(18), which is associated with elevated red blood cell (RBC) parameters, such as hemoglobin (Hb) and hematocrit (Hct) (19, 20). These

findings suggest that hematological parameter changes will be accompanied by increased body mass and chronic inflammation in obesity.

However, research on hematologic changes in obesity has focused on adults, and population studies of children are limited. The purpose of this study is to investigate the association between body mass index and hematologic parameter levels in children and adolescents.

Material And Methods

Data from the 2007–2018 Korea National Health and Nutrition Examination Survey (KNHANES) were analyzed in this study The survey was conducted by the Division of Chronic Disease Surveillance, Korean Centers for Disease Control and Prevention, in 3-year cycles since 1998, to assess the health and nutritional status of the noninstitutionalized civilian population of Korea (21). The KNHANES is a cross-sectional and nationally representative survey with a multistage, stratified probability sampling design. To enhance the statistical power of these analyses, data acquired from the full fourth (2007–2009), fifth (2010–2012), and sixth (2013–2015) cycles and the first and second years of the seventh cycle (2017–2018) were combined. Details of the study design have been previously reported (22).

A total of 97,622 individuals participated in the KNHANES from 2007–2017. Of these subjects, 10,734 participants aged 10–18 years were included in our preliminary analyses (Fig. 1). All subjects and their parents were interviewed at home after providing informed consent, and they underwent several examinations, including blood sampling. The hematological parameters assessed in this study were WBC, RBC, Hb, Hct, and platelet levels. Subjects with incomplete physical examination records, including incomplete anthropometric measurements and laboratory test results such as lipid profile, were excluded. Subjects with high triglyceride (TG) level ≥ 400 mg/dL were excluded (n = 17). The KNHANES database is publicly available (http://knhabes.cdc.go.kr). The 2007–2018 KNHANES study protocols were approved by the Institutional Review Board of the Korean Centers for Disease Control and Prevention. Informed consent was provided by all KNHANES subjects.

Anthropometric assessments, including height, weight, waist circumference (WC), and systolic and diastolic BP (SBP and DBP, respectively), were conducted by a trained expert. Height was measured to the nearest 0.1 cm using an electronic stadiometer (SECA, Germany). Weight was measured to the nearest 0.1 kg with an electronic scale (G-TECH, Korea). WC was measured to the nearest 0.1 cm using a calibrated measuring tape (SECA). SBP and DBP were measured three times to the nearest 1 mmHg using a standard mercury sphygmomanometer. The standard deviation scores (SDSs) for height, weight, WC, and body mass index (BMI) were calculated using age- and sex-specific least mean square parameters based on the 2017 growth reference values for Korean children and adolescents, developed by the Korean Pediatric Society and the Korea Centers for Disease Control and Prevention (23). The subjects were categorized into three groups according to BMI: normal weight (NW; BMI < 85th percentile), overweight (OW; BMI ≥ 85th percentile and < 95th percentile), and obesity (OB; BMI ≥ 95th percentile).

Lifestyle-related behaviors, such as alcohol consumption, smoking, household income, and residence, were assessed using a questionnaire. Information about alcohol consumption (drinkers vs. nondrinkers) and smoking status (smokers vs. nonsmokers) was collected from subjects 12 years and older using a self-administered questionnaire. Physical activity was divided into two groups (yes or no), and subjects were included in the "yes" group if they performed intense physical activity for ≥ 20 min/day and ≥ 3 days/week, if they performed moderate physical activity for ≥ 30 min/day and ≥ 5 days/week, or if they walked for ≥ 30 min/day and ≥ 5 days/week.

Questionnaires on household income and area of residence (urban vs. rural) were administered by trained interviewers. Diagnoses of HTN, diabetes, and dyslipidemia were included in the questionnaire.

Statistical analyses

R version 3.5.1 (The R Foundation for Statistical Computing, Vienna, Austria) was used for statistical analysis. Continuous variables are expressed as means and standard deviations (SDs). Categorical variables are presented as numbers and percentages (%). The differences were analyzed using analysis of variance for continuous variables and the chi-square test for categorical variables. The adjusted means and standard errors (SEs) of hematologic indices of WBC, RBC, platelets, Hb, and Hct were determined for each of the three BMI groups using analysis of covariance (ANCOVA) after adjustment for possible confounders. In ANCOVA model 1, the adjusted means and SEs of hematologic indices were estimated after controlling for age and sex. In ANCOVA models 2 and 3, the adjusted means and SEs of hematologic indices were estimated after controlling for age in boys and girls. The pairwise differences between BMI groups were tested for significance using *post hoc* tests with Bonferroni correction in each ANCOVA model. To evaluate the correlations of hematologic parameters and BMI SDS, Pearson's correlation coefficient analysis was performed. Age and sex adjustments were conducted in the correlation analysis. To evaluate BMI SDS and hematologic indices, multiple linear regression was performed among the three groups. Multiple linear regression analyses were conducted after adjusting for age, sex, alcohol consumption, smoking, physical activity, rural residence, household income, diagnosis of T2DM, hypertension, and dyslipidemia among all participants. The corresponding standardized regression coefficient (β) and SE were estimated. *P*-values < 0.05 were considered to indicate statistical significance.

Results

A total of 7,997 subjects was included in the final analyses. Among them, 4,259 (53.26%) were boys, and 3,738 were girls. The subjects were categorized into three groups according to BMI: 6,421 (80.29%) in the NW group, 782 (9.78%) in the OW group, and 794 (9.93%) in the OB group. Among 4,259 boys, 3,350 (78.66%) were NW, 443 (10.40%) were OW, and 466 (10.94%) were OB. Among 3,738 girls, 3,071 (82.16%) were NW, 339 (9.07%) were OW, and 328 (8.77%) were OB.

Clinical characteristics of the study population according to obesity

Table 1 shows the clinical characteristics of the study population according to obesity. Mean SDSs for height, weight, BMI, and WC were significantly different among subgroups ($p < 0.001$ for both), as were mean SBP and DBP ($p < 0.001$ for both). Hematologic parameters differed among subgroups, and subjects with obesity tended to have higher means for hematologic parameters and for serum concentrations of glucose, total cholesterol, TGs, low-density lipoprotein cholesterol (LDL-C), and lower high-density lipoprotein cholesterol (HDL-C). The proportion of subjects who drank alcohol was highest in the obesity group.

Table 1
Clinical characteristics of the study population according to weight (*N* = 7,997)

	Normal weight	Overweight	Obesity	*P*
Total, n (%)	6,421 (80.29%)	782 (9.78%)	794 (9.93%)	
Boys, n (%)	3,350 (52.17%)	443(56.65%)	466 (58.69%)	< 0.001
Age (years)	14.33 ± 2.51	14.24 ± 2.51	14.78 ± 2.54	< 0.001
Height SDS	0.17 ± 1.03	0.47 ± 1.04	0.53 ± 1.11	< 0.001
Weight SDS	-0.31 ± 0.89	1.29 ± 0.49	2.20 ± 0.74	< 0.001
BMI SDS (kg/m^2)	-0.59 ± 0.88	0.86 ± 0.45	1.64 ± 0.75	< 0.001
WC SDS	-0.49 ± 0.85	1.32 ± 0.18	2.40 ± 0.67	< 0.001
SBP (mmHg)	105.65 ± 9.77	109.94 ± 10.28	113.68 ± 10.95	< 0.001
DBP (mmHg)	65.59 ± 8.91	66.88 ± 8.88	69.07 ± 9.19	< 0.001
WBC (x10^3/mm^3)	6.16 ± 1.49	6.65 ± 1.58	7.16 ± 1.65	< 0.001
RBC (x10^6/mm^3)	4.81 ± 0.39	4.89 ± 0.40	4.93 ± 0.41	< 0.001
Hemoglobin (g/dL)	13.97 ± 1.23	14.07 ± 1.22	14.19 ± 1.30	< 0.001
Hematocrit (%)	41.86 ± 3.40	42.28 ± 3.42	42.65 ± 3.53	< 0.001
Platelets (x10^3/mm^3)	282.96 ± 58.58	296.81 ± 59.92	309.03 ± 63.53	< 0.001
Glucose (mg/dL)	90.01 ± 7.39	91.83 ± 11.05	92.45 ± 12.16	< 0.001
T-C (mg/dL)	158.25 ± 26.27	163.00 ± 28.46	169.35 ± 29.50	< 0.001
HDL-C (mg/dL)	52.16 ± 9.94	47.68 ± 8.63	44.99 ± 8.37	< 0.001
TG (mg/dL)	79.29 ± 41.79	99.34 ± 54.29	112.75 ± 58.76	< 0.001
LDL-C (mg/dL)	90.24 ± 22.42	95.46 ± 25.07	101.81 ± 25.63	< 0.001
Alcohol drinker	1564 (24.36%)	188 (24.04%)	237 (29.85%)	0.003
Smoker	718 (11.18%)	88 (11.25%)	106 (13.35%)	0.191
Household income ≤ 1st quartile	687 (10.70%)	82 (10.49%)	95 (11.96%)	0.531
Rural residence	985 (15.34%)	113 (14.45%)	125 (15.74%)	0.757

SDS, standard deviation score; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; RBC, red blood cell; T-C, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus

	Normal weight	Overweight	Obesity	*P*
Physical activity	2368 (36.88%)	279 (35.68%)	316 (39.80%)	0.194
Diagnosis of hypertension	1 (0.02%)	1 (0.13%)	1 (0.13%)	0.124
Diagnosis of T2DM	0 (0%)	0 (0%)	0 (0%)	> 0.999
Diagnosis of dyslipidemia	0 (0%)	0 (0%)	0 (0%)	> 0.999

SDS, standard deviation score; BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; RBC, red blood cell; T-C, total cholesterol; HDL-C, high-density lipoprotein cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein cholesterol; T2DM, type 2 diabetes mellitus

Mean hematologic parameters according to sex and obesity are shown in Fig. 2. Mean WBC increased significantly in boys and girls across NW, OW, and OB groups (Table 2). In both sexes, the OB group showed significantly higher mean RBC and Hct than the NW group. Mean Hb was significantly higher in the OB group than the NW group in boys but not in girls. Mean platelet counts for the OW and OB groups were significantly higher than in the NW group for both sexes.

Table 2
Means for white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels according to sex and obesity

	Boys			**Girls**		
	NW	OW	OB	NW	OW	OB
	n = 3350	*n* = 443	*n* = 466	*n* = 3071	*n* = 339	*n* = 328
WBC ($x10^3/mm^3$)	6.13 ± 1.45	6.68 ± 1.53[a]	7.13 ± 1.60[b,c]	6.18 ± 1.53	6.61 ± 1.64[a]	7.22 ± 1.71[b,c]
RBC ($x10^6/mm^3$)	5.02 ± 0.34	5.10 ± 0.34[a]	5.13 ± 0.33[c]	4.59 ± 0.31	4.62 ± 0.30	4.63 ± 0.31[c]
Hemoglobin (g/dL)	14.60 ± 1.11	14.64 ± 1.15	14.79 ± 1.20[c]	13.28 ± 0.96	13.33 ± 0.85	13.34 ± 0.92
Hematocrit (%)	43.43 ± 3.30	43.73 ± 3.38	44.18 ± 3.34[c]	40.15 ± 2.60	40.38 ± 2.42	40.49 ± 2.50[c]
Platelet ($x10^3/mm^3$)	278.59 ± 58.48	295.33 ± 61.62[a]	302.91 ± 61.66[c]	287.73 ± 58.32	298.74 ± 57.65[a]	317.73 ± 65.21[b,c]
Data are presented as means ± standard deviations (SD).						
NW, underweight and normal weight; OW, overweight; OB, obesity; WBC, white blood cell; RBC, red blood cell						
Bonferroni's *post-hoc* test after adjustment for age among girls.						
[a]: $P < 0.05$ between normal weight group versus overweight group after Bonferroni's *post-hoc* test.						
[b]: $P < 0.05$ between overweight group versus obesity group after Bonferroni's *post-hoc* test.						
[c]: $P < 0.05$ between normal weight group versus obesity group after Bonferroni's *post-hoc* test.						

Adjusted hematologic parameters according to sex and obesity

The adjusted means for hematologic parameters were significantly different according to obesity (Table 3**)**. Subjects with obesity had higher adjusted mean levels for WBC (7.16 vs. 6.16 ($x10^3/mm^3$)), RBC (4.90 vs. 4.82 ($x10^6/mm^3$)), Hct (42.31 vs. 41.91 (%)), and platelet (311.87 vs. 282.66 $x10^3/mm^3$) levels ($p < 0.001$ for all) than did normal weight subjects. Likewise, girls with obesity had higher adjusted mean levels for WBC, RBC, Hct, and platelets ($p < 0.001$ for all) than did normal weight girls. Although Hb level was significantly different among the three groups, the statistical difference was lost in post-hoc

tests of total subjects and just girls. Boys with obesity had higher adjusted mean levels of WBC, RBC, Hb, Hct, and platelets than did normal weight boys ($p < 0.001$ for all).

Table 3
Adjusted means for white blood cell, red blood cell, hemoglobin, hematocrit, and platelet levels according to sex and obesity

All participants[1] (*N* = 7,997)	**Normal weight**	**Overweight**	**Obesity**	***P* for trend**
	***n* = 6,421**	***n* = 782**	***n* = 794**	
WBC (x10^3/mm^3)	6.16 ± 0.02	6.66 ± 0.05[a]	7.16 ± 0.05[b,c]	< 0.001
RBC (x10^6/mm^3)	4.82 ± 0.01	4.88 ± 0.01[a]	4.90 ± 0.01 [c]	< 0.001
Hemoglobin (g/dL)	13.99 ± 0.01	14.04 ± 0.04	14.07 ± 0.04	0.016
Hematocrit (%)	41.91 ± 0.04	42.21 ± 0.10[a]	42.31 ± 0.10 [c]	< 0.001
Platelets (x10^3/mm^3)	282.66 ± 0.72	296.38 ± 2.05[a]	311.87 ± 2.04[b,c]	< 0.001
Boys[2]				
(*n* = 4,259)	*n* = 3,350	*n* = 443	*n* = 466	
WBC (x10^3/mm^3)	6.13 ± 0.03	6.69 ± 0.07[a]	7.12 ± 0.07[b,c]	< 0.001
RBC (x10^6/mm^3)	5.02 ± 0.01	5.11 ± 0.01[a]	5.12 ± 0.01 [c]	< 0.001
Hemoglobin (g/dL)	14.60 ± 0.01	14.72 ± 0.04[a]	14.72 ± 0.04 [c]	< 0.001
Hematocrit (%)	43.43 ± 0.04	43.96 ± 0.12[a]	44.00 ± 0.12 [c]	< 0.001
Platelets (x10^3/mm^3)	278.64 ± 0.97	293.21 ± 2.66[a]	304.58 ± 2.59[b,c]	< 0.001
Girls[3]				
(*n* = 3,738)	*n* = 3,071	*n* = 339	*n* = 328	
WBC (x10^3/mm^3)	6.18 ± 0.03	6.61 ± 0.08[a]	7.20 ± 0.09[b,c]	< 0.001
RBC (x10^6/mm^3)	4.59 ± 0.01	4.62 ± 0.02	4.66 ± 0.02 [c]	< 0.001
Hemoglobin (g/dL)	13.27 ± 0.02	13.34 ± 0.05	13.39 ± 0.05	0.015
Hematocrit (%)	40.14 ± 0.05	40.39 ± 0.14	40.59 ± 0.14 [c]	< 0.001
Platelets (x10^3/mm^3)	287.47 ± 1.05	298.90 ± 3.17[a]	319.95 ± 3.23[b,c]	< 0.001
Data are presented as means ± standard errors (SE).				
WBC, white blood cell; RBC, red blood cell				
Model 1: Statistical analysis was conducted according to obesity using analysis of covariance with Bonferroni's *post-hoc* test after adjustment for age and sex among all participants.				

All participants[1] (*N* = 7,997)	Normal weight	Overweight	Obesity	*P* for trend
	n = 6,421	*n* = 782	*n* = 794	
Model 2: Statistical analysis was conducted according to obesity using analysis of covariance with Bonferroni's *post-hoc* test after adjustment for age among boys.				
Model 3: Statistical analysis was conducted according to obesity using analysis of covariance with Bonferroni's *post-hoc* test after adjustment for age among girls.				
[a]: *P* < 0.05 between normal weight group versus overweight group after Bonferroni's *post-hoc* test.				
[b]: *P* < 0.05 between overweight group versus obesity group after Bonferroni's *post-hoc* test.				
[c]: *P* < 0.05 between normal weight group versus obesity group after Bonferroni's *post-hoc* test.				

Correlations between BMI SDS and hematologic indices

The unadjusted and adjusted correlations between BMI SDS and hematologic parameters are presented in Table 4. BMI SDS was positively correlated with WBC (r = 0.222), RBC (r = 0.109), Hb (r = 0.042), Hct (r = 0.067), and platelets (r = 0.180) after adjusting for age and sex (p < 0.001 for all). The correlation between BMI SDS and Hb level was not significant for girls in the unadjusted model but was after adjusting for age. In fact, after adjustment for age, BMI SDS was positively correlated with hematologic indices in both sexes. In girls, the Pearson's coefficients between BMI SDS and RBC, Hb, and Hct were more than twice as low as those in boys.

Table 4
Unadjusted and adjusted correlations between body mass index (BMI) standard deviation score and white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels

All Participants (*N* = 7,997)	r[1]	*P*	r[2]	*P*
WBC (x10^3/mm^3)	0.223	< 0.001	0.222	< 0.001
RBC (x10^6/mm^3)	0.096	< 0.001	0.109	< 0.001
Hemoglobin (g/dL)	0.044	< 0.001	0.042	< 0.001
Hematocrit (%)	0.067	< 0.001	0.067	< 0.001
Platelets (x10^3/mm^3)	0.169	< 0.001	0.180	< 0.001
Boys (*n* = 4,259)	r[3]	*P*	r[4]	*P*
WBC (x10^3/mm^3)	0.239	< 0.001	0.240	< 0.001
RBC (x10^6/mm^3)	0.157	< 0.001	0.180	< 0.001
Hemoglobin (g/dL)	0.070	< 0.001	0.111	< 0.001
Hematocrit (%)	0.090	< 0.001	0.137	< 0.001
Platelets (x10^3/mm^3)	0.175	< 0.001	0.177	< 0.001
Girls (*n* = 3,738)	r[5]	*P*	r[6]	*P*
WBC (x10^3/mm^3)	0.206	< 0.001	0.202	< 0.001
RBC (x10^6/mm^3)	0.047	0.004	0.078	< 0.001
Hemoglobin (g/dL)	0.014	0.383	0.033	0.043
Hematocrit (%)	0.042	0.009	0.054	< 0.001
Platelets (x10^3/mm^3)	0.164	< 0.001	0.176	< 0.001

WBC, white blood cell; RBC, red blood cell

[1]: Pearson's correlation analyses were conducted between body mass index (BMI) standard deviation score (SDS) and white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels with no adjustment for all participants.

[2]: Pearson's correlation analyses were conducted between BMI SDS and WBC, RBC, hemoglobin, hematocrit, and platelet levels after adjustment for age and sex for all participants.

[3]: Pearson's correlation analyses were conducted between BMI SDS and WBC, RBC, hemoglobin, hematocrit, and platelet levels with no adjustment in boys.

All Participants (*N* = 7,997)	r[1]	*P*	r[2]	*P*
[4]: Pearson's correlation analyses were conducted between BMI SDS and WBC, RBC, hemoglobin, hematocrit, and platelet levels after adjustment for age in boys.				
[5]: Pearson's correlation analyses were conducted between BMI SDS and WBC, RBC, hemoglobin, hematocrit, and platelet levels with no adjustments.				
[6]: Pearson's correlation analyses were conducted between BMI SDS and WBC, RBC, hemoglobin, hematocrit, and platelet levels after adjustment for age in girls.				

Multiple linear regression analyses between the three BMI groups and hematologic parameters

Table 5 shows that BMI SDS was significantly positively associated with hematologic parameters among all participants after adjusting for age, sex, alcohol consumption, smoking, physical activity, rural residence, household income, diagnosis of T2DM, hypertension, and dyslipidemia. BMI SDS was associated with WBC (β = 0.275), RBC (β = 0.028), Hb (β = 0.034), Hct (β = 0.152), and platelet (β = 8.372) levels ($p < 0.001$ for all). In boys, BMI SDS was associated with WBC (β = 0.279,), RBC (β = 0.043), Hb (β = 0.073), Hct (β = 0.267), and platelets (β = 7.658) ($p < 0.001$ for all). In girls, BMI SDS was associated with WBC (β = 0.270, $p < 0.001$), RBC (β = 0.019, $p < 0.001$), Hb (β = 0.027, $p = 0.038$), Hct (β = 0.118, $p < 0.001$), and platelets (β = 8.715, $p < 0.001$). In girls, the regression coefficients between BMI SDS and RBC, Hb, and Hct was more than twice as low as those in boys.

Table 5
Multiple regression between body mass index (BMI) standard deviation score and white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels

All Participants[1] (***N*** **= 7,997)**	**β**	**SE**	***P***
WBC (x10^3/mm^3)	0.275	0.013	< 0.001
RBC (x10^6/mm^3)	0.028	0.003	< 0.001
Hemoglobin (g/dL)	0.034	0.009	< 0.001
Hematocrit (%)	0.152	0.025	< 0.001
Platelet (x10^3/mm^3)	8.372	0.510	< 0.001
Boys[2] (*n* = 4,259)			
WBC (x10^3/mm^3)	0.279	0.017	< 0.001
RBC (x10^6/mm^3)	0.043	0.004	< 0.001
Hemoglobin (g/dL)	0.073	0.010	< 0.001
Hematocrit (%)	0.267	0.030	< 0.001
Platelet (x10^3/mm^3)	7.658	0.657	< 0.001
Girls[3] (*n* = 3,738)			
WBC (x10^3/mm^3)	0.270	0.021	< 0.001
RBC (x10^6/mm^3)	0.019	0.004	< 0.001
Hemoglobin (g/dL)	0.027	0.013	0.038
Hematocrit (%)	0.118	0.035	< 0.001
Platelet (x10^3/mm^3)	8.715	0.798	< 0.001

WBC, white blood cell; RBC, red blood cell

[1]: Multiple linear regression analysis was conducted between body mass index (BMI) standard deviation score (SDS) (as independent variables) and white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels (as dependent variables) after adjustment for age, sex, alcohol consumption, smoking, physical activity, rural residence, household income, type 2 diabetes mellitus (T2DM), hypertension, and dyslipidemia for all participants.

[2]: Multiple linear regression analysis was conducted between BMI SDS (as independent variables) and WBC, RBC, hemoglobin, hematocrit, and platelet levels (as dependent variables) after adjustment for age, sex, alcohol consumption, smoking, physical activity, rural residence, household income, T2DM, hypertension, and dyslipidemia among boys.

All Participants[1] (*N* = 7,997)	β	SE	*P*

[3]: Multiple linear regression analysis was conducted between BMI SDS (as independent variables) and WBC, RBC, hemoglobin, hematocrit, and platelet levels (as dependent variables) after adjustment for age, sex, alcohol consumption, smoking, physical activity, rural residence, household income, diagnosis of T2DM, hypertension and dyslipidemia among girls

Discussion

This study investigated the relationship between body mass index and hematologic parameters in Korean children and adolescents. Children with obesity have increased body fat mass, blood pressure, glucose, LDL-C, and blood cell counts, including WBC, RBC, and platelets. In particular, BMI SDS is positively and independently associated with hematologic parameters after adjusting for cofounding variables. To our knowledge, this is the largest population-based study of Korean children and adolescents.

It is well known that chronic inflammation around adipocytes plays an important role in obesity-related diseases (4). Because WBC count increases inflammatory status, it is reasonable to assume that WBCs are elevated in patients with obesity. One of the most plausible explanations is that adipose tissue produces IL- 6, a pro- inflammatory cytokine that plays a role in bone marrow granulopoiesis, WBC proliferation, and differentiation (24, 25). In our study, WBC increased by 0.275 ($x10^3/mm^{3)}$ in children with every 1-point increase in BMI SDS. The elevated WBC count, according to obesity degree, is consistent with previous results (26, 27). Meanwhile, relative elevation of WBC is associated with carotid atherosclerosis and impaired glucose tolerance (28). Tong *et al.* reported that patients with higher WBC counts had adverse metabolic profiles and elevated WBC counts, even when their levels were within normal range, and these elevations were associated with macrovascular and microvascular complications in T2DM (29). Furthermore, Anna *et al.* observed a significant decrease in WBC count after bariatric surgery and emphasized the importance of weight loss to reduce WBC count in morbid obesity (26).

Our findings are consistent with those of previous studies that found mean WBC count and MS prevalence increased with increasing degree of obesity in both boys and girls (13, 30). In Colombian children, WBC count was associated with truncal adiposity (12). Increased WBC count was associated with early glucose metabolism derangement and preclinical signs of liver, vascular, and cardiac damage in Italian children (31). Park *et al.* reported that higher WBC count was positively associated with increased risk of insulin resistance in Korean children and adolescents (32). Lee *et al.* suggested that elevated WBC count can be a surrogate marker for MS in Korean children and adolescents (13). Therefore, because it is inexpensive, WBC count has been suggested as an effective tool for identifying children with obesity at risk of potential complications (31, 32).

Red cell indices, including RBC count, Hb and Hct, were positively associated with BMI SDS in our study, which was consistent with previous studies. Mărginean *et al.* (33) reported significantly higher erythrocyte levels in children with obesity than controls, but there was no significant difference in Hb level.

Additionally, several studies suggest that RBC is significantly correlated with MS (34, 35), and that Hb is significantly associated with high blood pressure (36). The mechanism of increased RBC cell indices in obesity is not known. Rather, there have been reports of more frequent iron deficiency anemia in subjects with obesity/overweight compared with normal weight subjects (37). This is believed to be largely related to an obesity-induced chronic inflammatory state and the influence of hepcidin. Bekri *et al.* (38) reported that hepcidin, which is a proinflammatory adipokine, reduces iron bioavailability by controlling the ferroportin-1 exporter, resulting in severe iron deficiency anemia in obesity. Although iron status, nutritional habits, and anemia incidence were not analyzed according to BMI subgroup, BMI SDS was independently associated with RBC indices.

Meanwhile, changes in RBC indices show gender differences. Kim *et al.* (39) reported that the total numbers of RBC increased significantly in male MS subjects but not in females. All RBC indices increased according to BMI SDS in our study, but the degree of increase differed between boys and girls: RBC count increased by 0.043 ($x10^6/mm^3$) in boys and 0.019 ($x10^6/mm^3$) in girls with every 1-point increase in BMI SDS. The increased RBC count in boys was more than twice as high as that in girls. Similar patterns were found in the analyses of Hb and Hct. Obesity is a chronic hypoxia state that causes adipose tissue dysfunction, inflammation, and insulin resistance(40). Chronic hypoxia can contribute to increased production of red and white blood cells. Additionally, ferritin, one of the inflammatory markers, increases in obesity (11), and might be linked to changes in RBC indices. Although adolescent girls typically have more body fat and less muscle than boys, they lose blood and iron periodically due to menstruation. Consequently, the increase in RBC according to increased BMI SDS might be relatively small in girls compared with boys.

Thrombocytosis is thought to reflect the presence of an inflammatory process, and platelet activation plays an important role in accelerating atherothrombosis (17). Lim *et al.* (41) reported that a higher platelet count was associated with increased prevalence and risk of metabolic syndrome in children and adolescents. In our study, platelet count increased by 8.372 ($x10^3/mm^3$) with every 1-point increase in BMI SDS: by 8.715 ($x10^3/mm^3$) in girls and 7.658 ($x10^3/mm^3$) in boys. Platelet count increments also seem to be influenced by gender. Dorit *et al. (16)* reported that females with obesity had significantly elevated platelet counts compared with normal weight females, but no significant platelet count elevation was observed in males. Additionally, Charles *et al.* (42) reported a positive association between obesity and WBC or platelet counts among female officers, but not among male officers. In our study, BMI SDS was positively associated with hematologic parameters, but we also found evidence of sexual dimorphism, especially in red blood cell and platelet levels. Although it was a natural result, the adjusted mean RBC indices in boys was higher than in girls for all subgroups, as was that in RBC indices according to BMI SDS. In contrast, mean platelet count was higher in girls than in boys in all subgroups, with a larger increase in platelet count according to increased BMI SDS in girls. How gender differences affect blood cell composition and how they affect the risk of obesity complication is not well understood. Gender differences remain controversial, and further studies should be conducted.

This study has several limitations. First, this is a cross-sectional study, so it cannot identify causal relationships between obesity and hematologic parameters. Second, our study was conducted in children and adolescents between the ages of 10 and 18 years, so there were no data for children younger than 10 years. Third, pubertal status was not classified or analyzed; thus, the effect of puberty on hematologic changes was not considered. Fourth, we could not determine the mechanism of the relationships between BMI SDS and changes in hematologic indices. With regard to the links between BMI SDS and hematologic parameters, our results might not be appliable to general populations in specific environments, especially for contexts of severe obesity and malnutrition. Several studies showed that children with overweight or obesity have an elevated risk for iron deficiency anemia (43, 44). Nevertheless, this study showed that BMI SDS is an independent factor associated with hematological parameters in a relatively large number of children and adolescents. Our findings provide insights into estimating hematologic changes in children and adolescents with obesity and how to manage them.

In conclusion, this nationally representative population-based study showed that higher BMI is independently associated with high hematologic parameters including WBC, RBC, Hb, Hct, and platelet count in children and adolescents. Our results suggest that obesity is related to changes in the blood system, which might be a potential risk factor for obesity-related disease. When interpreting complete blood count in children and adolescents, it is important to consider its relevance to BMI and recognize that there are differences between boys and girls.

Declarations

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The authors have no conflicts of interest to declare.

Author contribution

Dr Jeong drafted the initial manuscript, and reviewed and revised the manuscript.

Dr Shim conceptualized and designed the study, coordinated and supervised data collection, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Figures

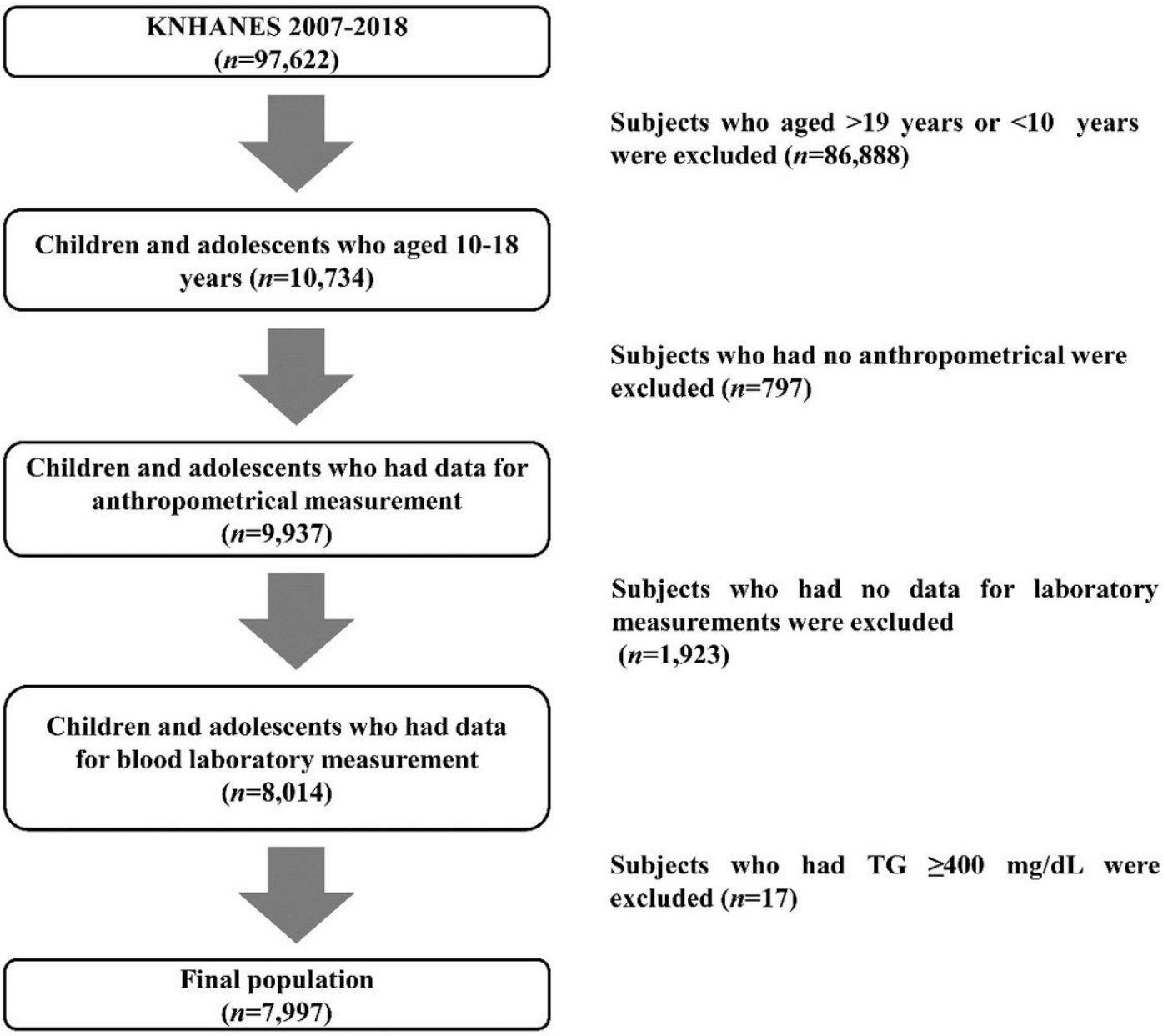

Figure 1

Flow chart of study population.

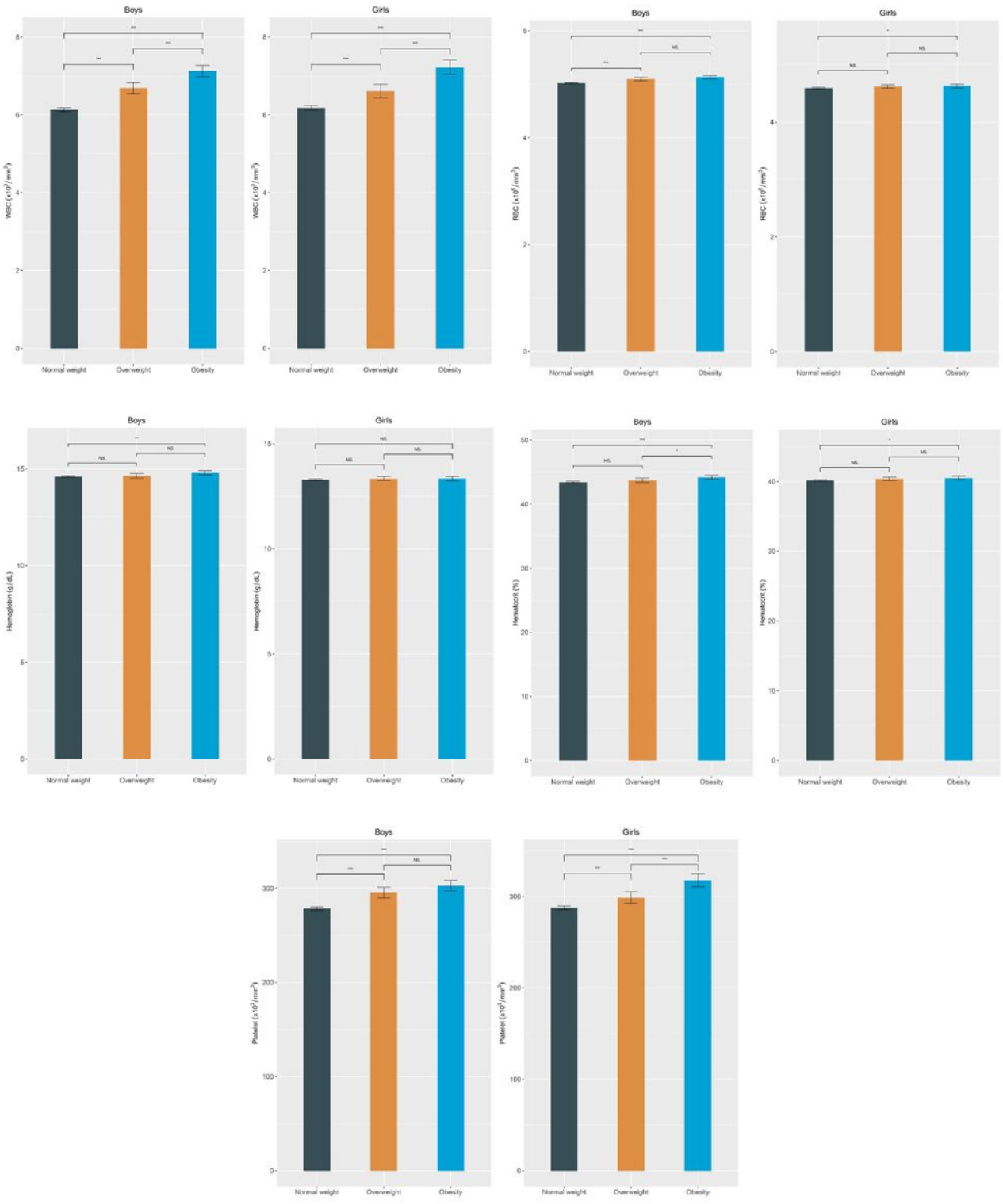

Figure 2

Means for white blood cell (WBC), red blood cell (RBC), hemoglobin, hematocrit, and platelet levels according to sex and obesity