

High-sensitivity C-reactive protein is associated with prediabetes and adiposity in Korean youth

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Introduction

- Obesity is a chronic low-grade inflammatory condition which increases the risk of cardiovascular disease.
- Elevated high-sensitivity C-reactive protein (hs-CRP) levels are associated with cardiovascular disease, type 2 diabetes, and metabolic syndrome in adults.
- This study aimed to determine the association of hs-CRP and cardiometabolic risk factors, including obesity, prediabetes, hypertension, and dyslipidemia, in the nationally representative data of Korean youth.

Methods

- This study was performed using data from the Korea National Health and Nutrition Examination Survey (KNHANES) 2015–2017.
- A total of 1,723 youths (918 boys, 53.5%) aged 10-18 years from the KNHANES(2015-2017) were included.
- Anthropometric, biochemical, physical activity and nutritional survey data were collected. Participants were classified into 3 groups according to hs-CRP tertile.
- Abdominal obesity, impaired fasting glucose, elevated triglyceride, decreased high-density lipoprotein (HDL) cholesterol and elevated blood pressure, and prediabetes (HbA1c 5.7-6.4%) were compared according to sex and hs-CRP tertile.

Results

Table 1. Clinical characteristics of study participants by tertiles of hs-CRP

Variables	Lower tertile (n = 738, 43.0%)	Mid-tertile (n = 448, 27.1%)	Upper tertile (n = 508, 29.9%)	P-value	P for trend
hs-CRP (mg/L) (range), total	0.233 ± 0.004 (0.106, 0.30)	0.409 ± 0.003 ^b (0.31, 0.50)	1.645 ± 0.081 ^b (0.51, 9.16)	<0.001	<0.001
hs-CRP (mg/L) (range), male	0.234 ± 0.005 (0.106, 0.30)	0.411 ± 0.004 ^b (0.31, 0.53)	1.664 ± 0.088 ^b (0.54, 9.16)	<0.001	<0.001
hs-CRP (mg/L) (range), Female	0.226 ± 0.005 (0.106, 0.30)	0.376 ± 0.003 ^b (0.31, 0.42)	1.350 ± 0.105 ^b (0.43, 8.86)	<0.001	<0.001
Age (yr)	14.2 ± 0.1	14.6 ± 0.1	14.7 ± 0.1 ^b	0.021	0.012
Sex, male (%)	359 (48.7%)	240 (54.0%)	309 (61.2%)	<0.001	0.007
BMI z-score	-0.49 ± 0.04	0.03 ± 0.07 ^b	0.82 ± 0.07 ^b	<0.001	<0.001
Waist circumference (cm)	67.2 ± 0.4	70.9 ± 0.4 ^b	77.4 ± 0.6 ^b	<0.001	<0.001
Obesity, n (%)	18 (2.3%)	41 (9.4%)	143 (29.2%)	<0.001	<0.001
Systolic BP (mm Hg)	107.3 ± 0.4	108.7 ± 0.5 ^a	110.4 ± 0.6 ^b	<0.001	<0.001
Diastolic BP (mm Hg)	66.2 ± 0.4	66.5 ± 0.4	67.4 ± 0.4	0.062	0.004
Fasting glucose (mg/dL)	91.1 ± 0.3	91.1 ± 0.3	92.3 ± 0.3 ^b	0.009	0.006
HbA1c (%)	5.30 ± 0.01	5.33 ± 0.01 ^a	5.38 ± 0.01 ^b	<0.001	<0.001
Insulin (mIU/L)	10.2 ± 0.4	10.9 ± 0.6	12.3 ± 0.6 ^b	0.012	0.004
HOMA-IR	2.30 ± 0.10	2.43 ± 0.15	2.79 ± 0.14 ^b	0.009	0.004
Total cholesterol (mg/dL)	162.0 ± 1.1	159.3 ± 1.4	163.3 ± 1.3	0.090	0.581
Triglyceride (mg/dL)	72.4 ± 1.5	76.1 ± 2.2	79.8 ± 1.9 ^b	0.004	0.007
HDL cholesterol (mg/dL)	52.9 ± 0.4	49.6 ± 0.5 ^b	48.7 ± 0.5 ^b	<0.001	<0.001
Alanine aminotransferase (U/L)	13.1 ± 0.4	14.3 ± 0.5	21.2 ± 1.6 ^b	<0.001	<0.001
White blood cell count (/μL)	6182 ± 59	6550 ± 67 ^b	6743 ± 78 ^b	<0.001	<0.001
Moderate-to-vigorous physical activity (min/day)	23.0 ± 2.5	24.9 ± 3.3	24.3 ± 3.1	0.880	0.687
Moderate-to-vigorous physical activity (≥ 30 min/day), n (%)	40 (8.2%)	29 (13.9%)	33 (13.8%)	0.067	0.034
Sedentary time (hour/day)	11.1 ± 0.1	11.1 ± 0.2	11.1 ± 0.2	0.941	0.738
Total energy intake (Kcal/day)	2112 ± 38	2180 ± 51	2158 ± 44	0.515	0.387
Protein intake (g/day)	76.3 ± 1.8	81.9 ± 2.6	79.2 ± 2.0	0.163	0.174
Fat intake (g/day)	59.3 ± 1.7	63.7 ± 2.1	62.7 ± 1.9	0.187	0.134
Carbohydrate intake (g/day)	316.2 ± 5.3	319.4 ± 8.1	316.6 ± 7.6	0.939	0.934
Total energy intake (≥ 120% of estimated average requirements for age and sex), n (%)	144 (21.0%)	86 (20.5%)	99 (22.1%)	0.870	0.712
Abdominal obesity, n (%)	25 (3.3%)	39 (9.0%)	140 (28.1%)	<0.001	<0.001
Impaired fasting glucose, n (%)	74 (9.5%)	46 (9.8%)	73 (13.5%)	0.093	0.049
HbA1c ≥ 5.7%, n (%)	49 (6.6%)	45 (8.8%)	70 (13.9%)	<0.001	<0.001
Elevated blood pressure, n (%)	16 (2.0%)	16 (3.3%)	30 (6.0%)	0.002	0.002
Elevated triglyceride, n (%)	46 (6.1%)	39 (8.3%)	56 (10.8%)	0.019	0.005
Low HDL cholesterol, n (%)	73 (10.8%)	75 (16.9%)	110 (21.8%)	<0.001	<0.001
Metabolic syndrome, n (%)	5 (0.6%)	7 (2.0%)	28 (5.4%)	<0.001	<0.001

- The higher hs-CRP tertile were associated with higher BMI z-scores, WC, obesity, systolic BP, fasting glucose, HbA1c, insulin levels, HOMA-IR, triglyceride level, ALT levels, and WBC counts. Moreover, the proportions of subjects with abdominal obesity, prediabetes, elevated BP, elevated triglyceride, low HDL cholesterol, and metabolic syndrome progressively increased in the higher tertile.(Table 1)

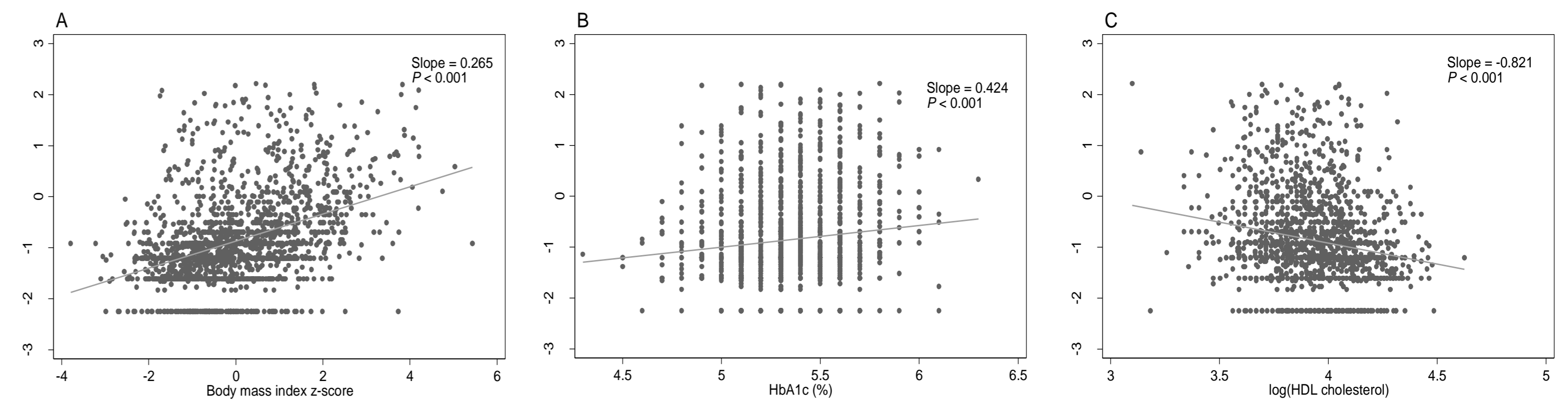


Figure 1. Association between high sensitivity C-reactive protein (hs-CRP) and body mass index z-score (A), HbA1c (B), high density lipoprotein (HDL) cholesterol (C).

Table 2. Association between hsCRP tertiles and cardiometabolic risk factors

	Lower versus Mid-tertile		Lower versus Upper tertile	
	OR (95% CI)	P value	OR (95% CI)	P value
Obesity				
Univariate	4.34 (2.28, 8.27)	<0.001	17.38 (10.10, 29.92)	<0.001
Multivariate (Model 1)	4.34 (2.27, 8.31)	<0.001	17.58 (10.12, 30.53)	<0.001
Multivariate (Model 2)	4.00 (1.82, 8.76)	0.001	12.07 (6.18, 23.57)	<0.001
Abdominal obesity				
Univariate	2.94 (1.64, 5.29)	<0.001	11.59 (7.21, 18.63)	<0.001
Multivariate (Model 1)	0.76 (0.33, 1.79)	0.534	1.09 (0.49, 2.44)	0.832
Multivariate (Model 2)	1.31 (0.41, 4.18)	0.642	1.30 (0.48, 3.54)	0.607
Impaired fasting glucose				
Univariate	1.03 (0.66, 1.60)	0.890	1.48 (1.02, 2.16)	0.040
Multivariate (Model 1)	0.92 (0.58, 1.44)	0.710	1.05 (0.67, 1.65)	0.819
Multivariate (Model 2)	1.10 (0.50, 2.42)	0.820	1.19 (0.58, 2.44)	0.629
Prediabetes (HbA1c ≥ 5.7%)				
Univariate	1.37 (0.90, 2.10)	0.145	2.29 (1.48, 3.56)	<0.001
Multivariate (Model 1)	1.36 (0.88, 2.12)	0.166	2.19 (1.35, 3.57)	0.002
Multivariate (Model 2)	1.60 (0.80, 3.18)	0.182	3.08 (1.49, 6.36)	0.002
Elevated blood pressure				
Univariate	1.65 (0.85, 3.23)	0.142	3.07 (1.54, 6.17)	0.002
Multivariate (Model 1)	1.18 (0.58, 2.43)	0.644	1.35 (0.66, 2.76)	0.417
Multivariate (Model 2)	0.62 (0.21, 1.83)	0.385	1.10 (0.44, 2.76)	0.834
Elevated triglyceride				
Univariate	1.39 (0.85, 2.27)	0.185	1.85 (1.20, 2.87)	0.006
Multivariate (Model 1)	1.14 (0.68, 1.90)	0.612	1.07 (0.64, 1.81)	0.786
Multivariate (Model 2)	0.57 (0.21, 1.53)	0.264	1.01 (0.43, 2.37)	0.981
Decreased HDL cholesterol				
Univariate	1.68 (1.16, 2.43)	0.007	2.29 (1.63, 2.43)	<0.001
Multivariate (Model 1)	1.42 (0.97, 2.09)	0.073	1.48 (0.99, 2.20)	0.054
Multivariate (Model 2)	1.85 (1.04, 3.29)	0.035	1.58 (0.87, 2.88)	0.135
Metabolic syndrome				
Univariate	3.40 (1.02, 11.39)	0.047	9.27 (3.42, 25.16)	<0.001
Multivariate (Model 1)	1.70 (0.51, 6.58)	0.440	1.70 (0.51, 5.67)	0.384
Multivariate (Model 2)	1.50 (0.22, 10.18)	0.680	2.83 (0.62, 13.03)	0.181

Model 1 adjusted for age, sex, and BMI except for BMI z-score (adjusted for age and sex)
Model 2 adjusted for age, sex, BMI, white blood cell count, moderate-to-vigorous physical activity, and daily caloric intake except for BMI z-score (adjusted for age and sex, white blood cell count, moderate-to-vigorous physical activity, and daily caloric intake).

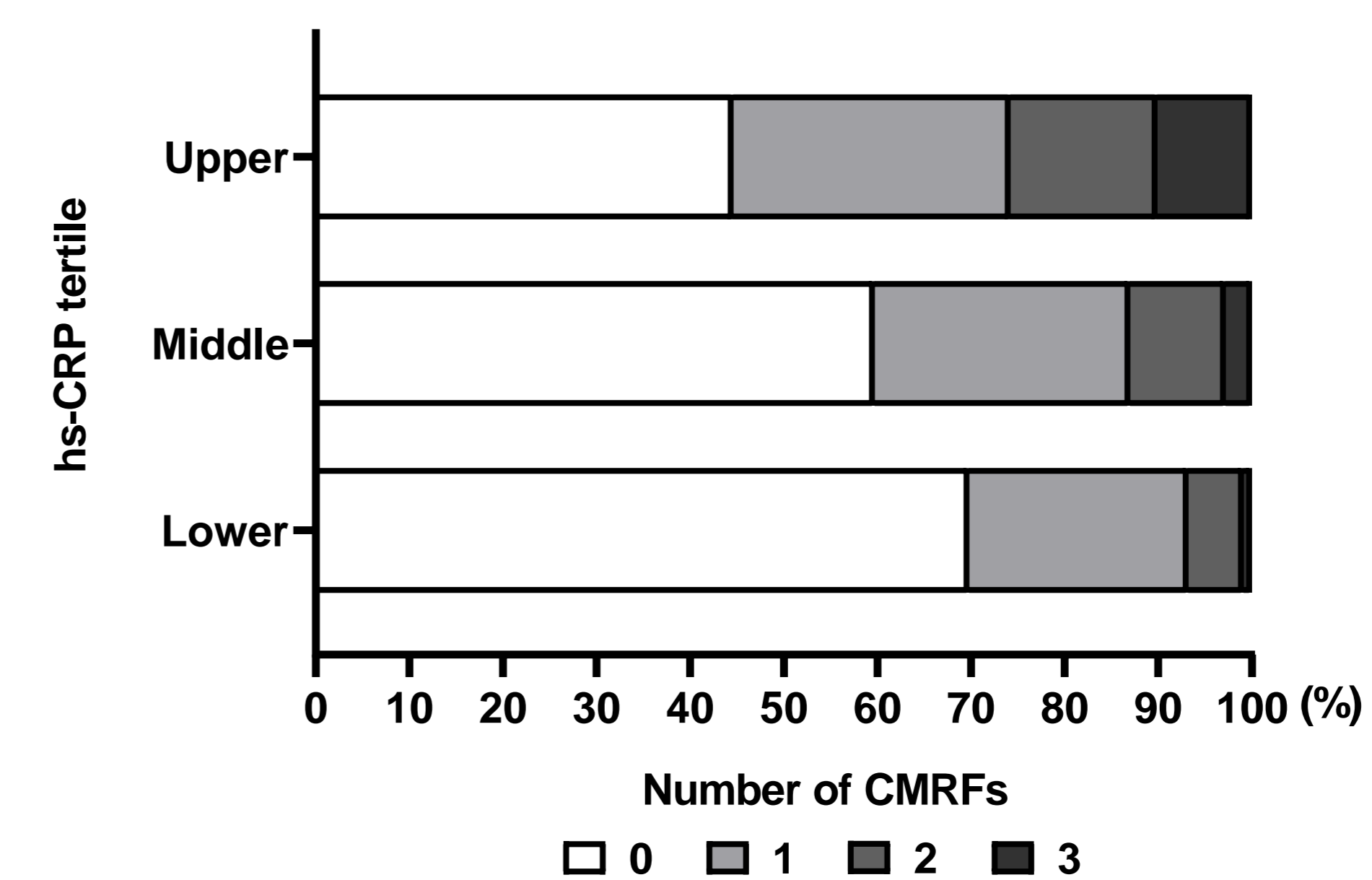


Figure 2. Proportion of participants by numbers of cardiometabolic risk factors (CMRFs) and high sensitivity C-reactive protein (hs-CRP) tertile (P < 0.001).

- BMI z-score ($\beta = 0.60$, $P < 0.001$), HbA1c ($\beta = 0.036$, $P = 0.012$), and HDL cholesterol ($\beta = -0.025$, $P = 0.029$) were significantly associated with hs-CRP.
- Obesity (OR 2.47, 95% CI 1.93–3.17) and prediabetes (OR 1.67, 95% CI 1.25–2.22) were significantly associated with hs-CRP.
- The upper tertile of hs-CRP showed significant association with obesity (OR = 12.07, $P < 0.001$) and prediabetes (OR = 3.08, $P = 0.002$).(Table 2)
- The proportion of participants with cardiometabolic risk factors was higher according to increasing hs-CRP tertile ($P < 0.001$) (Fig. 2.).

Conclusion

- Elevated hs-CRP is associated with high BMI z-score and HbA1c, and low HDL cholesterol in Korean children and adolescents. Hence, hs-CRP could be a reliable indicator for adiposity, prediabetes, and abnormal lipid metabolism in the pediatric population