Clinical Pediatric Endocrinology

Vol.33 / No.4
October 2024
pp 207–213

Original Article

Platelet and white blood cell counts correlate with leptin and body mass index in Japanese adolescents

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Highlights

- BMI-SDS was significantly correlated with WBC and platelet count.
- Platelet count was correlated with serum leptin and glucose.
- WBC count was correlated with serum leptin, insulin, HOMA-IR, and glucose.

Abstract. Obesity is associated with mild chronic inflammation, frequently observed along with increased platelet and white blood cell (WBC) levels in adults. We aimed to clarify the relationship between peripheral blood cell count, body mass index standard deviation score (BMI-SDS), and adipocytokine levels in obese adolescents. Participants included 31 patients with obesity (age: 13.1 ± 3.1 yr) and 28 normal-weight controls (age: 13.3 ± 1.9 yr). Obesity was defined as a percentage of overweight ≥ 20%; patients with type 2 diabetes were excluded. As sex differences were observed in blood cell counts, the analysis was performed after adjusting for sex differences. The obese group has significantly higher WBC, red blood cell, and platelet counts, as well as high serum leptin levels and Homeostasis Model Assessment of insulin resistance (HOMA-IR) scores compared with those of the control group. In all participants, BMI-SDS significantly correlated with WBC and platelet counts. Platelet count correlated with serum leptin and glucose levels, whereas WBC count correlated with serum leptin, insulin, HOMA-IR, and glucose levels. Statistical analysis showed that serum leptin level significantly influenced the platelet count and HOMA-IR score affected WBC count. Increased platelet and WBC counts in adolescents with obesity may increase the risk of thrombosis.

Key words: adipocytokine, body mass index, obesity, platelet, white blood cell

Received: June 17, 2024 Accepted: August 1, 2024 Advanced Epub: August 26, 2024

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Introduction

Obesity is often correlated with chronic inflammation, which is characterized by low-grade systemic inflammation and the secretion of inflammatory adipokines from adipose tissue, such as interleukin-6, tumor necrosis factor-α, monocyte chemoattractant protein-1, and resistin (1). Chronic inflammation contributes to the pathogenesis of various conditions, including insulin resistance, metabolic syndrome, type 2 diabetes, hypertension, cardiovascular disease, dyslipidemia, and thrombosis (1, 2). Furthermore, obesity-induced inflammation influences metabolic functions in insulin-responsive tissues, including bone. In the bone marrow, hyperplasia can lead to increased migration of immune cells into the circulation, potentially exacerbating chronic inflammatory responses in peripheral tissues (3).

Complete blood count is a relatively cost-effective procedure for monitoring peripheral immune cell levels. Several studies have reported a positive association between obesity and elevated platelet and white blood cell (WBC) counts (4–6), suggesting that obesity-induced inflammation may result in increased peripheral blood cell counts and a higher risk of thrombosis (7). Most research on the relationship between hematological parameters and anthropometric indices has focused on adults (4, 6), indicating a research gap in studies involving adolescents with obesity. Given the global rise in childhood obesity (8, 9), including in Japan (10), understanding the relationship between peripheral blood cell counts, body mass index standard deviation score (BMI-SDS), and adipocytokines in adolescents is crucial for identifying and mitigating thrombosis risk in this population.

In this context, this study aimed to further explore the implications of obesity on blood cell counts and overall health in adolescents with obesity in Japan.

Subjects and Methods

Study participants

Adolescents with simple obesity were recruited from the pediatric clinic of Kawachi General Hospital. This study was conducted according to the principles of the Declaration of Helsinki. The study protocol was approved by the Kawachi General Hospital Review Board for Human Studies (study approval number: 2019-003), and written informed consent was obtained from the parents of the adolescent participants. The adolescents were also asked to provide consent before entering the study. The study group comprised 31 adolescents with simple obesity (obesity group; 23 boys and 8 girls; mean age: 13.1 ± 3.1 yr). The control group consisted of 28 participants (15 boys and 13 girls; mean age: 13.3 ± 1.9 yr) with normal blood pressure and no family history of diabetes mellitus. No significant differences in age or sex were observed between the obese and control groups.

Blood samples were collected in the morning after an overnight fast and were separated by centrifugation; the resulting serum was stored at −80°C until analysis. All samples used in this study were stored under the same conditions. Serum glucose levels were determined using a glucose oxidase assay. Enzyme-linked immunosorbent assay kits were used to measure the serum levels of plasminogen activator inhibitor-1 (PAI-1), P-selectin, and thrombopoietin (all Abcam. Ltd., Cambridge, UK), leptin (Proteintech, Rosemont, IL, USA), insulin (Mercodia AB, Uppsala, Sweden), and adiponectin (R&D Systems Inc., Minneapolis, ML, USA). The mean intra-assay coefficients of variation (CV) for leptin and insulin were 3.7% and 9.5%, respectively, with lower detection limits of 2.0 pg/mL and 7.8 pmol/L, respectively. For PAI-1, P-selectin, and thrombopoietin, the lower detection limits were 16 pg/mL, 3.6 ng/mL, and 11 pg/mL with mean intra-assay CVs values of 3.3%, 5.6%, and 5.1%, respectively. The mean intra-assay CV for adiponectin was 3.5%, with a lower detection limit of 0.246 ng/mL.

A standardized biochemistry analyzer (Canon Medical TBA-120FR; Tochigi, Japan) was used to determine the glucose, aspartate aminotransferase, alanine transaminase, and uric acid levels. A complete blood profile, including WBC count, RBC count, and platelet count, was measured using an automated cell counter (Sysmex series analyzer, Sysmex XN-1000). Before blood collection, we confirmed that the participants had no history of infectious disease within the previous 2 weeks. To rule out any infection or underlying hematologic disorder, participants with a WBC count < 3,200 or > 12,500 cells/mm^3 and a platelet count > 440,000 cells/mm^3 were excluded. Because peripheral blood parameters such as WBC, RBC, platelet, hemoglobin, and hematocrit values were all higher in boys than in girls, each blood parameter was adjusted for sex based on the average value. WBC, RBC, platelet, hemoglobin, and hematocrit values were corrected by multiplying the female values by 1.18-, 1.09, 1.21,1.07, and 1.05 times, respectively, to make them equivalent to male values.

Definitions of overweight or obesity

Children's physiques were assessed based on the percentage of overweight (POW) calculated using the following formula:

POW (%) = 100 × (measured weight − standard weight)/standard weight.

Standard weight was determined from the 2000 Annual Report of School Health Statistics of the Japanese Ministry of Education, Culture, Sports, Science, and Technology based on age- and sex-specific weight for height. The Japanese standard weight was calculated using an approximate equation derived from the height and weight distributions of each age group (11).

The criterion for overweight/obesity was a POW ≥ 20% (≥ 120% of the standard weight). The normal range for school-aged children is between −20% and 20%. In

doi: 10.1297/cpe.33.2024-0045

Japan, POW, which is calculated using the modified weight-for-height method, is used not only in medical institutions but also in schools as a parameter to assess childhood obesity. As tall students are easily defined as overweight, whereas short students tend to be evaluated as underweight, the POW method appears to be more appropriate than BMI% for school-age children (12).

Obesity, defined by POW in this study, approximates the BMI standard established by the Japanese Association for Human Auxology (13), defined as a BMI equal to or greater than the 90th percentile. Simple obesity is defined as a weight greater than the normal weight if energy intake exceeds energy expenditure. It excludes patients with type 2 diabetes and symptomatic obesity, such as endocrine diseases. Participants in the obese group were not treated with medications and did not show any evidence of endocrine malfunction or recent medication use.

Statistical analysis

All statistical analyses were performed using JMP 6 software (SAS Institute Inc., Cary, NC, USA). Data are expressed as mean ± standard deviation. Comparisons between the two groups were performed using Dunnett's test. Univariate linear correlations were checked using Pearson's r coefficient, and univariate regression was used to analyze the associations between WBC and platelet counts and several other variables. Stepwise multiple regression analysis was performed to assess the independent predictive effects of variables (e.g., age, sex, BMI-SDS, Homeostasis Model Assessment of insulin resistance [HOMA-IR] score, and serum insulin, leptin, glucose, adiponectin, PAI-1, and P-selectin levels) on WBC and platelet counts. Multivariate modeling was performed using forward stepwise regression. Stepwise regression included $p = 0.25$ as the criterion for entry into the model, and $p = 0.10$ as the criterion to remain in the model.

Results

The anthropometric and biochemical characteristics of the participants are summarized in **Table 1**. The mean serum insulin level, HOMA-IR score, aspartate aminotransferase, alanine transaminase, and uric acid levels were significantly higher in the obese group than in the control group. Additionally, mean serum leptin and PAI-1 levels were higher in the obesity group than in the control group (**Table 1**).

The WBC ($p < 0.0001$), RBC ($p = 0.047$), platelet ($p = 0.0032$), neutrophil ($p = 0.0002$), lymphocyte ($p = 0.0003$), and monocyte ($p = 0.0025$) counts were all significantly higher in the obese group than in the control group (**Table 2**). In all participants, BMI-SDS showed significant correlations with WBC count ($r = 0.448$, $p = 0.0005$) and platelet count ($r = 0.392$, $p = 0.0026$) (**Fig. 1**. A and B). Additionally, neutrophils ($r = 0.377$, $p = 0.0046$), monocytes ($r = 0.344$, $p = 0.0100$), and lymphocytes ($r = 0.375$, $p = 0.0048$) count significantly correlated with BMI-SDS (**Fig. 1**. C and D). The WBC count was significantly correlated with serum leptin levels ($r = 0.525$, $p < 0.0001$) (**Fig. 2**. A), HOMA-IR ($r = 0.407$, $p = 0.0015$), and serum glucose levels ($r = 0.318$, $p = 0.0150$) (**Fig. 2**. B). Platelet count was significantly correlated with serum leptin levels ($r = 0.465$, $p = 0.0002$) (**Fig. 2**. C), serum PAI-1 levels ($r = 0.403$, $p = 0.0020$), and serum glucose levels ($r = 0.277$, $p = 0.0355$) (**Fig.**

Table 1. Anthropometric and biochemical characteristics of the participants

	Control	Obesity	*P*
N	28	31	
Male/Female	15/13	23/8	.0985
Age (yr)	13.3 ± 1.9	13.1 ± 3.1	.7748
BMI-SDS	–0.16 ± 0.97	2.12 ± 0.59	< .0001
Glucose (mg/dL)	96 ± 18	103 ± 14	.0944
Insulin (pmol/L)	565 ± 421	813 ± 461	.0355
HOMA-IR	1.74 ± 1.74	2.83 ± 1.98	.0216
HOMA-β	71.0 ± 74.3	90.7 ± 53.0	.2500
HbA1c (%)	5.35 ± 0.10	5.52 ± 0.33	.2268
AST (U/L)	20.3 ± 4.8	26.7 ± 9.9	.0027
ALT (U/L)	16.6 ± 9.3	38.5 ± 37.1	.0037
Uric Acid (mg/dL)	5.00 ± 1.06	5.97 ± 1.46	.0091
Leptin (ng/mL)	4.63 ± 5.33	15.5 ± 5.1	< .0001
Adiponectin (mg/mL)	3.58 ± 2.12	2.71 ± 2.01	.1121
PAI-1 (pg/mL)	55.1 ± 12.7	64.8 ± 8.8	.0009
P-selectin (ng/mL)	92 ± 23	107 ± 23	.016
Thrombopoietin (ng/mL)	65.4 ± 23.1	63.0 ± 25.3	.7140

Mean values ± SD. BMI-SDS, body mass index standard deviation score; HOMA-IR, Homeostasis Model Assessment of insulin resistance; HOMA-β, Homeostasis Model Assessment of beta cell function; HbA1c, hemoglobin A1c; AST, aspartate aminotransferase; ALT, alanine aminotransferase; PAI-1, plasminogen activator inhibitor-1.

doi: 10.1297/cpe.33.2024-0045

Table 2. Mean levels of platelets, white blood cells, white blood cell subtypes, red blood cells, hemoglobin, and hematocrit adjusted for sex

	Control	Obesity	*P*
Platelet (× 10^4/mm^3)	28.6 ± 4.6	32.9 ± 5.7	.0032
WBC (/mm^3)	6,180 ± 1,260	8,360 ± 1,920	< .0001
Neutrophil (/mm^3)	3,440 ± 970	4,860 ± 1,630	.0002
Lymphocyte (/mm^3)	2,160 ± 540	2,770 ± 650	.0003
Basophil (/mm^3)	31.1 ± 21.7	36.2 ± 18.3	.3353
Eosinophil (/mm^3)	211 ± 246	276 ± 210	.2908
Monocyte (/mm^3)	348 ± 107	440 ± 113	.0025
RBC (× 10^4/mm^3)	488 ± 32	508 ± 43	.047
Hemoglobin (g/dL)	14.2 ± 0.8	14.4 ± 1.3	.4868
Hematocrit (%)	42.2 ± 2.3	42.9 ± 3.9	.3988

Mean values ± SD. WBC, white blood cell; RBC, red blood cell.

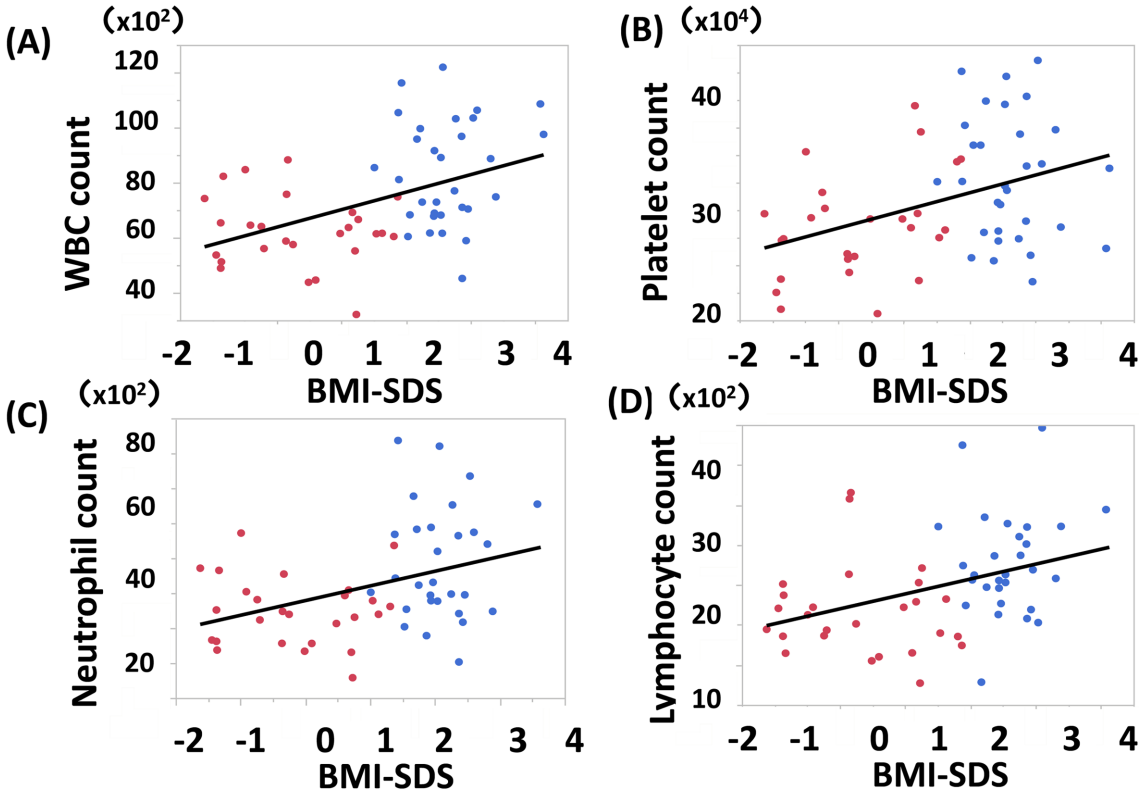

Fig. 1. (A) Relationship between body mass index standard deviation score (BMI-SDS) and white blood cell (WBC) count in all study participants (r = 0.448, p = 0.0005). (B) Relationship between BMI-SDS and platelet count in all participants (r = 0.392, p = 0.0026). (C) Relationship between BMI-SDS and neutrophil count in all participants (r = 0.377, p = 0.0046). (D) Relationship between BMI-SDS and lymphocyte count in all participants (r = 0.375, p = 0.0048). Red circles, healthy controls; blue circles, adolescents with simple obesity.

2. D). Serum insulin levels were strongly correlated with WBC count (r = 0.362, p = 0.0049); however, no significant correlation was found with platelet count. In stepwise multiple regression analysis, serum leptin (p = 0.0121) was a significant predictor for platelet count and HOMA-IR (p = 0.0308) for WBC count.

Discussion

This study revealed elevated levels of WBCs, RBCs, and platelets compared with those of controls. Obesity impacts blood cell production by altering bone marrow homeostasis and hematopoietic stem cell differentiation, leading to elevated WBC and RBC counts (3, 14–16). Additionally, obesity may lead to low-grade inflammation, affecting immune cell responses and secretion of inflammatory cytokines from the bone marrow, potentially contributing to higher blood cell counts (6). Adipokines, bioactive substances secreted by adipose tissue, significantly impact platelet and WBC function, affecting various physiological and pathological processes (17–21). Adipokines such as leptin

doi: 10.1297/cpe.33.2024-0045

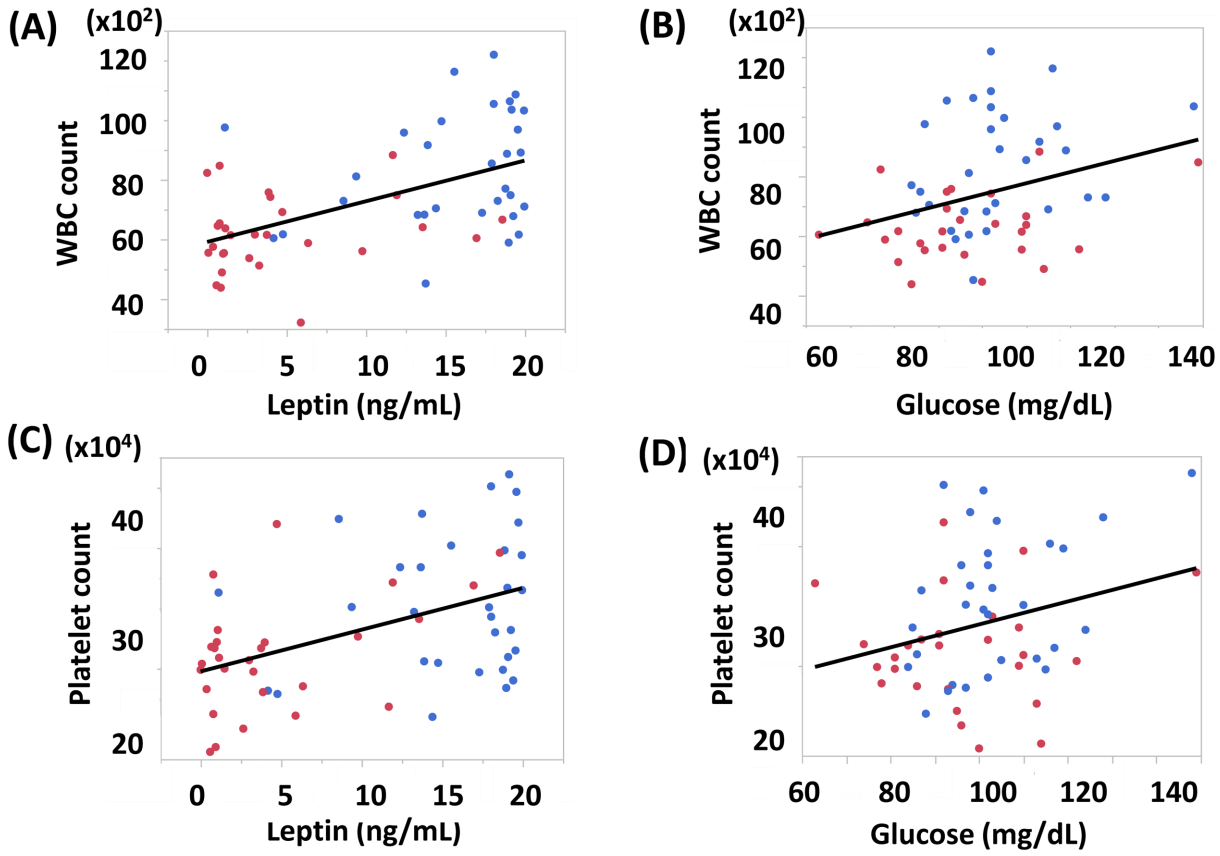

Fig. 2. (A) Relationship between serum leptin level and white blood cell (WBC) count in all study participants ($r = 0.525$, $p < 0.0001$). (B) Relationship between serum glucose level and WBC count in all participants ($r = 0.318$, $p = 0.0150$). (C) Relationship between serum leptin level and platelet count in all participants ($r = 0.465$, $p = 0.0002$). (D) Relationship between serum glucose level and platelet count in all participants ($r = 0.277$, $p = 0.0355$). Red circles, healthy controls; blue circles, adolescents with simple obesity.

and adiponectin are associated with markers of platelet hyperactivity, hypercoagulability, hypofibrinolysis, and increased leukocyte counts (22, 23). Statistical analysis using stepwise multiple regression identified leptin as the most significant factor affecting platelet count. Leptin increases platelet count by various mechanisms such as promoting platelet aggregation (17, 18, 21) and increasing platelet-reactive T cell levels, which enhance platelet activation (24).

Our study revealed higher levels of serum P-selectin in the obese group than in the control group. P-selectin, a marker of platelet activation, mediates the rolling of platelets on activated endothelial cells and promotes thrombogenesis by stabilizing GP IIb/IIIa-fibrinogen connections, facilitating the production of large, stable platelet aggregates in venous thrombi. Epidemiological evidence has shown that P-selectin expression increases in obesity and may reflect persistent *in vivo* platelet and endothelial activation (25). Moreover, in hypocalorically fed humans, physiological leptin administration increases P-selectin levels, indicating the role of leptin in obesity-associated platelet activation and aggregation (26). Furthermore, we found that the serum PAI-1 levels were higher in the obese group than in the control group. Leptin likely contributes to an increase in PAI-1 levels (27). At high concentrations, PAI-1 inhibits fibrinolysis and consequently promotes a thrombotic state.

Our study revealed significant correlations between WBC and platelet counts and BMI and serum glucose levels. These findings are consistent with previous studies indicating that obesity is associated with increased WBC counts, serves as a risk factor for atherosclerosis (28), and correlates with BMI in boys (29). Additionally, another study reported a positive correlation between WBC count and fasting plasma glucose in adults (30). These associations may have plausible underlying mechanisms. Hyperglycemia stimulates myelopoiesis and activates neutrophils in the bone marrow of obese mice (15, 16), whereas both obesity and high glucose levels promote thrombopoiesis through the interaction of neutrophil-derived S100A8/A9 with thrombopoietin, which activates megakaryocytes and increases platelet production in the bone marrow (7, 14). Furthermore, the WBC count was strongly correlated with serum insulin levels, suggesting that insulin may increase WBC counts. This aligns with a previous study demonstrating that insulin increases peripheral blood neutrophil counts and phagocytic capacity in non-diabetic cardiac surgical patients (31), as well as studies indicating a positive relationship between insulin secretion and resistance

doi: 10.1297/cpe.33.2024-0045

and increased WBC count (32, 33). Horne *et al.* reported that the neutrophil (N)/lymphocyte (L) ratio correlates with the risk of cardiovascular disease in adults (34). However, in the present study, the N/L ratio did not show significant correlations with any of the examined parameters.

This study has three limitations. First, the relatively small sample size of 59 participants may limit the power and generalizability of our analysis. Second, the cross-sectional design of the study prevents us from establishing causality regarding the observed relationships. Third, the exact mechanisms by which obesity affects blood cell production remain under investigation, necessitating further research to elucidate these interactions fully.

In conclusion, our study found that adolescents with obesity exhibited elevated peripheral blood cell counts compared with those in the control group. The significant correlations of BMI-SDS and serum leptin levels with WBC and platelet counts highlight the impact of obesity and adipokines on bone marrow and blood cell function. These findings suggest that the risk of obesity-associated thrombosis may emerge during adolescence, highlighting the importance of early detection of blood count abnormalities to identify and mitigate thrombosis risk in this population.

Conflict of interests: None of the authors has any potential conflicts of interest associated with this research.

Acknowledgements

This work was supported by a Grant-in-Aid for Scientific Research (C) from the Japanese Society for the Promotion of Science (Grant no. 21K11662).

References

1. Khanna D, Khanna S, Khanna P, Kahar P, Patel BM. Obesity: A chronic low-grade inflammation and its markers. Cureus 2022;14: e22711. [Medline]
2. Ellulu MS, Patimah I, Khaza'ai H, Rahmat A, Abed Y. Obesity and inflammation: the linking mechanism and the complications. Arch Med Sci 2017;13: 851–63. [Medline] [CrossRef]
3. Benova A, Tencerova M. Obesity-induced changes in bone marrow homeostasis. Front Endocrinol (Lausanne) 2020;11: 294. [Medline] [CrossRef]
4. Jesri A, Okonofua EC, Egan BM. Platelet and white blood cell counts are elevated in patients with the metabolic syndrome. J Clin Hypertens (Greenwich) 2005;7: 705–11, quiz 712–3. [Medline] [CrossRef]
5. Jeong HR, Lee HS, Shim YS, Hwang JS. Positive associations between body mass index and hematological parameters, including RBCs, WBCs, and platelet counts, in Korean children and adolescents. Children (Basel) 2022;9: 109. [Medline]
6. Jamshidi L, Seif A. Association between obesity, white blood cell and platelet count. Zahedan J Res Med Sci 2017;19: e4955.
7. Purdy JC, Shatzel JJ. The hematologic consequences of obesity. Eur J Haematol 2021;106: 306–19. [Medline] [CrossRef]
8. Sanyaolu A, Okorie C, Qi X, Locke J, Rehman S. Childhood and adolescent obesity in the United States: a public health concern. Glob Pediatr Health 2019;6: 2333794X1989130. [Medline] [CrossRef]
9. Di Cesare M, Sorić M, Bovet P, Miranda JJ, Bhutta Z, Stevens GA, *et al*. The epidemiological burden of obesity in childhood: a worldwide epidemic requiring urgent action. BMC Med 2019;17: 212. [Medline] [CrossRef]
10. Takaya J, Higashino H, Takaya R, Sakaguchi H, Tanoue J, Higashide T, *et al*. Effect of the COVID-19 pandemic lockdown on the physique of school-age children in Japan. Ann Pediatr Endocrinol Metab 2023;28: 124–30. [Medline] [CrossRef]
11. Murata M, Ito K. On the optimal weight in school age children. In: Murata M (ed) Report of research on nutrition, exercise and recreation from the viewpoint of health and QOL in children, supported by Health, Labour and Welfare for research on Health Services in 2002.2003; 10–13 (in Japanese).
12. Dobashi K. Evaluation of obesity in school-age children. J Atheroscler Thromb 2016;23: 32–8. [Medline] [CrossRef]
13. Kato N. Construction of BMI for age references for Japanese children from the 2000 national growth survey. J Japan Assoc Hum Auxol 2009;15: 37–44.
14. Kraakman MJ, Lee MK, Al-Sharea A, Dragoljevic D, Barrett TJ, Montenont E, *et al*. Neutrophil-derived S100 calcium-binding proteins A8/A9 promote reticulated thrombocytosis and atherogenesis in diabetes. J Clin Invest 2017;127: 2133–47. [Medline] [CrossRef]
15. Nagareddy PR, Murphy AJ, Stirzaker RA, Hu Y, Yu S, Miller RG, *et al*. Hyperglycemia promotes myelopoiesis and impairs the resolution of atherosclerosis. Cell Metab 2013;17: 695–708. [Medline] [CrossRef]
16. Nagareddy PR, Kraakman M, Masters SL, Stirzaker RA, Gorman DJ, Grant RW, *et al*. Adipose tissue macrophages promote myelopoiesis and monocytosis in obesity. Cell Metab 2014;19: 821–35. [Medline] [CrossRef]
17. Konstantinides S, Schäfer K, Koschnick S, Loskutoff DJ. Leptin-dependent platelet aggregation and arterial thrombosis suggests a mechanism for atherothrombotic disease in obesity. J Clin Invest 2001;108: 1533–40. [Medline] [CrossRef]
18. Konstantinides S, Schäfer K, Loskutoff DJ. The prothrombotic effects of leptin possible implications for the risk of cardiovascular disease in obesity. Ann N Y Acad Sci 2001;947: 134–41, discussion 141–2. [Medline] [CrossRef]
19. Samocha-Bonet D, Justo D, Rogowski O, Saar N, Abu-Abeid S, Shenkerman G, *et al*. Platelet counts and platelet activation markers in obese subjects. Mediators Inflamm 2008;2008: 834153. [Medline] [CrossRef]
20. Yudkin JS, Kumari M, Humphries SE, Mohamed-Ali V. Inflammation, obesity, stress and coronary heart disease: is

interleukin-6 the link? Atherosclerosis 2000;148: 209–14. [Medline] [CrossRef]
21. Nakata M, Yada T, Soejima N, Maruyama I. Leptin promotes aggregation of human platelets via the long form of its receptor. Diabetes 1999;48: 426–9. [Medline] [CrossRef]
22. Umano GR, Pistone C, Tondina E, Moiraghi A, Lauretta D, Miraglia Del Giudice E, *et al*. Pediatric obesity and immune system. Front Pediatr 2019;7: 487. [Medline] [CrossRef]
23. Buis DTP, Christen T, Smit RAJ, de Mutsert R, Jukema JW, Cannegieter SC, *et al*. The association between leptin concentration and blood coagulation: Results from the NEO study. Thromb Res 2020;188: 44–8. [Medline] [CrossRef]
24. Ren H, Zhao H, Wang T, Yang Y, Han Z, Liu B, *et al*. Leptin enhances in vitro secretion of IgG antiplatelet antibodies by splenocytes and peripheral blood mononuclear cells from patients with chronic idiopathic thrombocytopenic purpura. Clin Immunol 2006;120: 205–11. [Medline] [CrossRef]
25. De Pergola G, Pannacciulli N, Coviello M, Scarangella A, Di Roma P, Caringella M, *et al*. sP-selectin plasma levels in obesity: association with insulin resistance and related metabolic and prothrombotic factors. Nutr Metab Cardiovasc Dis 2008;18: 227–32. [Medline] [CrossRef]
26. Canavan B, Salem RO, Schurgin S, Koutkia P, Lipinska I, Laposata M, *et al*. Effects of physiological leptin administration on markers of inflammation, platelet activation, and platelet aggregation during caloric deprivation. J Clin Endocrinol Metab 2005;90: 5779–85. [Medline] [CrossRef]
27. Singh P, Peterson TE, Barber KR, Kuniyoshi FS, Jensen A, Hoffmann M, *et al*. Leptin upregulates the expression of plasminogen activator inhibitor-1 in human vascular endothelial cells. Biochem Biophys Res Commun 2010;392: 47–52. [Medline] [CrossRef]
28. Veronelli A, Laneri M, Ranieri R, Koprivec D, Vardaro D, Paganelli M, *et al*. White blood cells in obesity and diabetes: effects of weight loss and normalization of glucose metabolism. Diabetes Care 2004;27: 2501–2. [Medline] [CrossRef]
29. Wu CZ, Lin JD, Li JC, Kuo SW, Hsieh CH, Lian WC, *et al*. Association between white blood cell count and components of metabolic syndrome. Pediatr Int 2009;51: 14–8. [Medline] [CrossRef]
30. Nakanishi N, Sato M, Shirai K, Nakajima K, Murakami S, Takatorige T, *et al*. Associations between white blood cell count and features of the metabolic syndrome in Japanese male office workers. Ind Health 2002;40: 273–7. [Medline] [CrossRef]
31. Rassias AJ, Givan AL, Marrin CAS, Whalen K, Pahl J, Yeager MP. Insulin increases neutrophil count and phagocytic capacity after cardiac surgery. Anesth Analg 2002;94: 1113–9. [Medline] [CrossRef]
32. Kuo TY, Wu CZ, Lu CH, Lin JD, Liang YJ, Hsieh CH, *et al*. Relationships between white blood cell count and insulin resistance, glucose effectiveness, and first- and second-phase insulin secretion in young adults. Medicine (Baltimore) 2020;99: e22215. [Medline] [CrossRef]
33. Ren Z, Luo S, Liu L. The positive association between white blood cell count and metabolic syndrome is independent of insulin resistance among a Chinese population: a cross-sectional study. Front Immunol 2023;14: 1104180. [Medline] [CrossRef]
34. Horne BD, Anderson JL, John JM, Weaver A, Bair TL, Jensen KR, *et al*. Intermountain Heart Collaborative Study Group. Which white blood cell subtypes predict increased cardiovascular risk? J Am Coll Cardiol 2005;45: 1638–43. [Medline] [CrossRef]

doi: 10.1297/cpe.33.2024-0045