Association of cell blood counts and cardiometabolic risk factors among young obese children

Roya Kelishadi, MD, Mahin Hashemipour, MD, Parastou Ashtijou, MD, Parisa Mirmoghtadaee, MD, Parinaz Poursafa, MSc, Noushin Khavarian, MD, Shohreh Ghatrehsamani, MD.

ABSTRACT

الأهداف: تحديد العلاقة بين تعداد كريات الدم الحمراء، و السمنة، وعوامل خطر الإصابة بالقلب ذات الصلة بالأيض في الأطفال.

الطريقة: أجريت دراسة مقطعية خلال الفترة من 1 نوفمبر 2007 حتى 1 اكتوبر 2008م في عيادة أبحاث متلازمة الأيض و السمنة – قسم الوقائي لأمراض القلب للأطفال – مركز أبحاث أصفهان لأمراض القلب الوعائية – أصفهان – إيران. ضمت الدراسة 326 طفل (172 أنثى، 154 ذكر) مصابين بالسمنة تتراوح أعمارهم من 12-6 عام.

النتائج: بلغ متوسط عمر المشتركين 2.7 ± 8.8 عام. تم تسجيل ارتفاع إحصائي مهم في معدل كثافة الجسم (BMI)، و محيط الخصر (WC)، و ثلاثي الجليسريد (TG)، و البروتين الشحمي خفيف الكثافة (LDL)، من خلال ربع خلايا الدم البيضاء (WBC)، و نسبة الخصر للأرداف، و الكلويسترول الكلي من خلال ربع الصفيحات. تم تسجيل ارتفاع مماثل لمعدل كثافة الجسم BMI، و محيط الخصر للأرداف، و ضغط الدم الإنقباضي، و LDL-C، و TG من الربع الثاني، و الرابع لخلايا الدم الحمراء. نظراً لارتفاع مكملات متلازمة الأيض، ارتفعت معدل كثافة الجسم BMI، و خلايا الدم البيضاء WBC، و ثلاثي الجليسريد TG بشكل مهم إحصائي. سجلت العلاقة المرتفعة بين تعداد خلايا الدم البيضاء WBC و ثلاثي الجليسريد TG. رفع تعداد WBC خطورة ارتفاع BMI معدل كثافة الجسم (OR=1.45, [CI] 95%; 1.11-1.65, p=0.001)، وارتفاع محيط الخصر (OR; 1.47, CI 95%; 1.15-1.74, p=0.001)، و ارتفاع ثلاثي الجليسريد (CI 95%; 1.241.06-1.44, p=0.005).

خاتمة: وجدنا علاقات مهمة إحصائية بين مكملات خلايا الدم البيضاء و عوامل خطر الإصابة بالقلب ذات الصلة بالأيض في الأطفال الصغار المصابين بالسمنة. تعتبر هذه النتائج دليل مثبت لحالة الالتهابات للأفراد المصابين بالسمنة و الأطفال الصغار.

Objectives: To determine the association of cell blood count with obesity and cardiometabolic risk factors in children.

Methods: This cross-sectional study was conducted from 1st November 2007 to 1st October 2008 in the Obesity and Metabolic Syndrome Research Clinic of the Preventive Pediatric Cardiology Department, Isfahan Cardiovascular Research Center, Isfahan, Iran. It comprised 326 (172 girls and 154 boys) obese children aged 6-12 years.

Results: The mean age of participants was 8.8 ± 2.7 years. A significant increasing trend in the mean body mass index (BMI), waist circumference (WC), triglycerides (TG), total- and low density lipoprotein (LDL)- cholesterol were documented across the quartiles of the white blood cell (WBC) count, and for waist-to-hip ratio and total cholesterol across platelet quartiles. A similar increasing trend was documented for BMI, waist and hip circumference, diastolic blood pressure, LDL-C, and for TG from the second to the fourth quartile of the red blood cells. By the increase in the number of components of metabolic syndrome, the mean BMI, WBC, and TG increased significantly. The highest correlation was documented between WBC count and TG. The WBC count increased the risk of increased BMI (odds ratio [OR]=1.45, confidence interval [CI] 95%; 1.11-1.65, p=0.001), increased WC (OR; 1.47, CI 95%; 1.15-1.74, p=0.001), and high TG (CI 95%; 1.241.06-1.44, p=0.005).

Conclusion: We found significant associations between CBC components and cardiometabolic risk factors in young obese children. These findings are confirmatory evidence of the pro-inflammatory state of obese individuals, even in young children.

Saudi Med J 2010; Vol. 31 (4): 406-412

From the Pediatric Preventive Cardiology Department (Kelishadi, Poursafa, Khavarian, Ghatrehsamani), Isfahan Cardiovascular Research Center, the Pediatric Endocrinology Department (Hashemipour), Endocrine Research Center, the Pediatrics Department (Ashtijou), Community Medicine Department (Mirmoghtadaee), Isfahan University of Medical Sciences, Isfahan, Iran.

Received 21st December 2009. Accepted 1st March 2010.

Address correspondence and reprint request to: Associate Professor Roya Kelishadi, Head, Pediatric Preventive Cardiology Department, Isfahan Cardiovascular Research Center, Isfahan University of Medical Sciences, PO Box 81465-1148, Isfahan, Iran. Tel. +98 (311) 3377881-8. Fax. +98 (311) 3373435. E-mail: kroya@aap.net / Kelishadi@med.mui.ac.ir

Metabolic syndrome (MetS) is an emerging health problem worldwide, and considered as a risk prediction tool that could provide a useful metric for the scale and progress of the global epidemic of chronic diseases, notably diabetes, and cardiovascular diseases.[1] Whatever the definition and cutoff values considered for this clustering of risk factors, its components include abdominal obesity, high blood pressure, glucose intolerance, as well as, dyslipidemia in terms of elevated serum triglycerides (TG), and low levels of high density lipoprotein-cholesterol (HDL-C).[1,2] The MetS originates from early life,[2] therefore, early prevention and control of its components might be beneficial for late complications in adulthood.[3] Different pathophysiologic mechanisms have been proposed for the MetS, it is suggested to be associated with a pro-inflammatory state that contributes to insulin resistance.[4-7] Some studies have suggested an association between hematological parameters and the MetS components. Some studies have found that a higher number of white blood cells (WBC), and red blood cells (RBC) increased the odds ratio (OR) of MetS in both genders,[8] or only in males.[9] There are controversial results on the association of the components of the cell blood count (CBC) with obesity and cardiometabolic risk factors.[10-12] Previous studies have shown that markers of inflammation are high in adolescents with MetS.[13-16] Although the determination of CBC is simply available and an inexpensive procedure, and might provide important information for the pro-inflammatory state in individuals with the MetS, limited experience exists on the association of hematologic factors and the components of MetS in children. Two studies among Taiwanese adolescents found significant associations between WBC count and components of the MetS, notably with BMI.[5,17] The objective of this study was to determine the association of the WBC, RBC, and platelet counts with measures of generalized and abdominal obesity, as well as, cardiometabolic risk factors, including the components of MetS in a sample of obese children aged 6-12 years.

Methods. This cross-sectional study was conducted from 1st November 2007 to 1st October 2008 among 326 obese children. They were randomly selected from obese children who were referred from schools, health care centers, and public or private clinics to the Obesity and Metabolic Syndrome Research Clinic of the Preventive Pediatric Cardiology Department, Isfahan Cardiovascular Research Center (ICRC), a collaborating center of the World Health Organization, and affiliated to Isfahan University of Medical Sciences, Isfahan, Iran. Children with simple obesity, and aged 6-12 years were eligible for this study. Those children with mental retardation, chronic medical problems, chronic drug use, abnormal face, or other signs compatible with genetic syndromes, and history of any infectious disease in the previous 2 weeks were not included in this study. In order to rule out any infectious or underlying hematologic disorder, exclusion criteria were considered as hematologic indexes higher than the 95th percentile, namely, WBC more than 15000 cells/mm^3, platelets more than 500,000 cells/mm^3 or hemoglobin more than 16 mg/dL.[18] This study was approved by the Ethics Committee of ICRC. Informed written consent was obtained from the parents and an oral consent from children.

Physical examination. All measurements were made by the same trained team of general physicians and nurses under the supervision of the same pediatrician, by using calibrated instruments and following standard protocols. Height and weight were measured, and body mass index (BMI) was calculated as weight (kg) divided by height squared (m^2). The waist circumference (WC) was measured with a non-elastic tape at a point midway, between the lower border of the rib cage and the iliac crest at the end of normal expiration. Hip circumference (HiC) was measured at the widest part of the hip at level of the greater trochanter to the nearest half centimeters, and waist-to-hip ratio (WHR) was calculated. Blood pressure (BP) was measured according to a standard protocol.[19]

Laboratory examination. While one of the parents accompanied his or her child, fasting blood samples were taken from the ante-cubital vein between 8:00 and 9:30 A.M. Laboratory measurements were performed in the ICRC central laboratory with adherence to the external national and international quality control. Serum fasting blood glucose (FBG), TG, total cholesterol (TC), low density lipoprotein-cholesterol (LDL-C) and HDL-C were measured by standard kits (Pars Azmoun, Tehran, Iran) using an auto-analyzer (Hitachi, Tokyo, Japan). A complete blood profile including WBC, RBC, and platelet counts were measured using an automated cell counter (SYSMEX K-1000, Kobe, Japan). The MetS was defined based on the criteria analogous to Adult Treatment Panel (ATP) III modified for children and adolescents[20] as 3 or more of the following: fasting TG (>100 mg/dL), HDL-C (<50 mg/dL), WC (>75th percentile for age and gender in the population studied),[21] systolic blood pressure (SBP), or diastolic blood pressure (DBP [>90th percentile for gender, age, and height from the National Heart, Lung, and Blood

Disclosure. This study was funded by the Vice Chancellery for Research, Isfahan University of Medical Sciences, Isfahan, Iran.

Institute's recommended cutoff point,[19] and FBG (≥100 mg/dL). It should be noted that the modified ATP III definition[20] used a cutoff of >110 mg/dl for FBG, but similar to our national study,[22] however, we used the last recommendation of the American Diabetes Association.[23] The WBC, RBC, and platelet counts were categorized to quartiles.

Data were analyzed by the Statistical Package for Social Sciences version 15.0 (SPSS Inc., Chicago, IL, USA). Descriptive data were expressed as mean ± standard deviation (SD) for continuous variables. Analyses were initially stratified by gender, but as the differences were not significant, results are presented for girls and boys combined. The analysis of variance (ANOVA) was used to compare the mean value of anthropometric measures and cardiometabolic risk factors across the quartiles of WBC count and its subtypes (lymphocyte and neutrophil counts), as well as quartiles of RBC and platelet counts. A Kruskal-Wallis test was applied when applicable because of non-homogeneity of variance, or non-normality of the data. Partial correlation analysis was conducted for the association of CBC with anthropometric measures, and cardiometabolic risk factors. Similar analyzes were conducted for the assessment of mean CBC, anthropometric measures and cardiometabolic risk factors according to the number of the components of the MetS. Standardized coefficients (ß) from regression analysis adjusted by age and gender were obtained for the association of CBC with anthropometric measures, and cardiometabolic risk factors. After the adjustment for age and gender, a logistic regression model was employed to evaluate the associations of CBC with anthropometric measures and cardiometabolic risk factors. The significance level was set at $p<0.05$.

Results. The study comprised 326 children (172 girls and 154 boys) with a mean age of 8.8 ± 2.7 years. Their characteristics are presented in **Table 1**. The characteristics of children according to the quartiles of WBC count and its subtypes (neutrophils and lymphocytes) are presented in **Table 2**. It shows a significant increasing trend in mean BMI, WC, TG, TC, and LDL-C from the lowest to highest quartile. When studying the quartiles of neutrophils and lymphocytes separately, such a significant trend was documented for BMI, WC, HiC, LDL-C, and TG. Similar analysis according to the quartiles of RBC showed significant increase in mean BMI, WC, HiC, DBP, LDL-C, from the lowest to highest quartile, and increase in TG from the second to the fourth quartile. The corresponding figure for platelet counts was significant for WHR and TC (**Table 2**). The differences were not significant in terms of gender. All the children studied had at least one component of the MetS. As presented in **Table 3**, by the increase in the number of the MetS components from 1 to >3, the mean BMI, WBC, and TG increased significantly. The mean FBG was not significantly different between groups with one and 2 MetS components, but it was significantly higher in those with >3 components than in 2 other groups. The mean HDL-C decreased significantly by the increase in the number of the MetS components. Partial correlation analysis revealed weak, but significant correlations of WBC with BMI, WC, HiC, TC, LDL-C, TG, and DBP. Such correlations were documented for RBC count with BMI and DBP, as well as, for platelet counts with WHR and TC. The highest correlation was documented between WBC count and TG (r=0.3, p=0.01). The WBC count was related with BMI (ß=0.34, $p<0.0001$), WC (ß=0.37, $p<0.0001$) and TG (ß=0.31, $p<0.0001$). The WBC count increased the risk of increased BMI (odds ratio [OR]: 1.45, CI 95%: 1.11-1.65, p=0.001), increased WC (OR: 1.47, CI 95%: 1.15-1.74, p=0.001), and high TG (OR: 1.24 CI 95%: 1.06-1.44, p=0.005). The multiple linear regression analysis adjusted for age and gender showed that WBC count was positively related with BMI (ß=0.34, $p<0.0001$), WC (ß=0.37, $p<0.0001$) and TG (ß=0.31, $p<0.0001$). The logistic regression analysis showed that WBC count increased the risk of increased BMI (OR: 1.45, CI 95%: 1.11-1.65, p=0.001), increased WC (OR: 1.47, CI 95%:1.15-1.74, p=0.001), and high TG (OR: 1.24, CI 95%: 1.06-1.44, p=0.005).

Table 1 - Characteristics of the study population (n=326).

Variables	Mean ± standard deviation
Age (years)	8.8 ± 2.7
Body mass index (kg/m^2)	23.5 ± 4.0
Waist circumference(cm)	83.2 ± 10.9
Hip circumference (cm)	91.7 ± 11.0
Waist-to-hip ratio	0.9 ± 0.06
Systolic blood pressure (mm Hg)	94.2 ± 11.09
Diastolic blood pressure (mm Hg)	58.2 ± 9.4
Fasting blood glucose (mg/dL)	87.4 ± 8.9
Total cholesterol (mg/dL)	177.8 ± 30.9
LDL-cholesterol (mg/dL)	106.3 ± 31.3
HDL-cholesterol (mg/dL)	45.9 ± 10.5
Triglycerides (mg/dL)	132.5 ± 80.3
White blood cells (/mL [%])	7260 ± 1910
Neutrophil	52.6 ± 10.2
Lymphocyte	39.5 ± 9.9
Monocyte	4.9 ± 2.8
Eosinophil	2.4 ± 2.1
Basophil	0.2 ± 0.2
Red blood cells (/ml)	(4.9 ± 0.4) ×10^6
Platelets (/ml)	(294.9 ± 65.6) ×10^3
Hemoglobin (gr/dL)	13.3 ± 0.9

LDL - low density lipoprotein, HDL - high density lipoprotein

Table 2 - Characteristics of children according to the quartiles of cell blood count.

Characteristics	Quartile 1	Quartile 2	Quartile 3	Quartile 4	*P*-value
WBC count (×10³)	3.4 - 6.0	6.01 - 7.04	7.05 - 8.2	8.2 - 13.7	
BMI (kg/m²)	22.3 ± 3.4	23.4 ± 3.8	24.1 ± 3.9	24.2 ± 4.6	0.01
WC (cm)	80.3 ± 10.6	83.8 ± 11.2	84.6 ± 10.6	85.3 ± 11.0	0.04
HiC (cm)	89.7 ± 10.2	91.7 ± 10.8	93.3 ± 11.3	92.10 ± 11.57	0.21
WHR	0.8 ± 0.06	0.9 ± 0.04	0.9 ± 0.07	0.9 ± 0.05	0.11
SBP (mm Hg)	94.6 ± 11.2	94.5 ± 9.5	94.4 ± 12.1	93.4 ± 11.2	0.92
DBP (mm Hg)	58.7 ± 8.5	57.6 ± 9.3	58.2 ± 10.05	58.2 ± 9.6	0.45
FBG (mg/dL)	87.04 ± 8.5	86.5 ± 7.2	87.3 ± 8.9	88.8 ± 10.8	0.52
TC (mg/dL)	167.2 ± 31.5	181.7 ± 30.0	177.3 ± 29.4	185.4 ± 30.5	0.003
LDL C (mg/dL)	97.4 ± 28.5	109.8 ± 30.4	108.05 ± 36.3	110.8 ± 27.9	0.04
HDL-C (mg/dL)	47.4 ± 11.6	45.7 ± 10.2	43.9 ± 9.6	46.4 ± 10.3	0.20
TG (mg/dL)	108.9 ± 38.5	122.5 ± 31.0	141.4 ± 35.8	157.8 ± 35.2	0.002
Neutrophils (%)	26.90 - 45.80	45.81 - 52.0	52.01 - 58.75	58.76 - 81.60	
BMI (kg/m²)	22.2 ± 3.0	23.2 ± 4.0	23.5 ± 4.9	25.9 ± 3.8	0.004
WC (cm)	80.7 ± 9.0	82.1 ± 10.7	84.0 ± 12.9	86.0 ± 10.6	0.02
HiC (cm)	89.4 ± 10.5	90.6 ± 10.9	92.4 ± 12.6	95.6 ± 10.4	0.02
WHR	0.91 ± 0.05	0.90 ± 0.07	0.91 ± 0.06	0.92 ± 0.05	0.51
SBP (mm Hg)	94.1 ± 10.7	96.1 ± 11.2	93.6 ± 11.1	94.4 ± 10.1	0.52
DBP (mm Hg)	58.5 ± 8.7	58.3 ± 10.5	57.0 ± 10.7	58.2 ± 8.3	0.51
FBG (mg/dL)	87.3 ± 10.6	87.5 ± 7.8	85.2 ± 7.3	89.1 ± 9.1	0.15
TC (mg/dL)	174.2 ± 30.7	178.9 ± 30.1	180.3 ± 25.7	173.2 ± 31.3	0.35
LDL-C (mg/dL)	99.2 ± 31.6	102.7 ± 28.7	107.4 ± 29.9	110.5 ± 27.5	0.02
HDL-C (mg/dL)	46.1 ± 9.2	46.3 ± 9.8	46.5 ± 11.1	45.1 ± 11.2	0.52
TG (mg/dL)	118.4 ± 36.1	127.9 ± 37.1	138.5 ± 36.3	152.1 ± 36.3	0.08
Lymphocytes (%)	14.20 - 33.60	33.61 - 39.75	39.76 - 45.30	45.31 - 98.30	
BMI (kg/m²)	22.5 ± 3.4	23.0 ± 4.7	23.8 ± 4.0	24.5 ± 3.8	0.02
WC (cm)	81.1 ± 9.9	81.8 ± 11.2	83.9 ± 12.1	86.6 ± 10.9	0.03
HiC (cm)	89.8 ± 10.6	89.9 ± 11.6	93.3 ± 10.9	94.4 ± 10.7	0.02
WHR	0.9 ± 0.05	0.9 ± 0.06	0.9 ± 0.07	0.9 ± 0.05	0.41
SBP (mm Hg)	94.1 ± 10.9	96.1 ± 12.3	92.6 ± 11.1	94.5 ± 10.1	0.51
DBP (mm Hg)	58.5 ± 8.7	58.3 ± 10.5	57.0 ± 10.7	58.2 ± 8.3	0.51
FBG (mg/dL)	87.3 ± 10.6	87.5 ± 7.9	85.3 ± 7.3	89.2 ± 9.0	0.11
TC (mg/dL)	174.7 ± 32.7	180.9 ± 30.1	181.4 ± 28.7	173.2 ± 32.3	0.33
LDL-C (mg/dL)	99.1 ± 30.6	105.5 ± 27.8	107.8 ± 38.8	110.8 ± 26.6	0.02
HDL-C (mg/dL)	46.3 ± 9.2	45.3 ± 9.8	45.5 ± 11.1	46.1 ± 11.0	0.94
TG (mg/dL)	126.7 ± 34.4	132.4 ± 34.1	136.5 ± 36.2	138.3 ± 32.9	0.04
RBC count (×10⁶)	1.66 - 4.71	4.72 - 4.91	4.92 - 5.21	5.22 - 6.43	
BMI (kg/m²)	22.6 ± 4.3	23.1 ± 4.3	23.8 ± 3.5	24.8 ± 4.7	0.006
WC (cm)	81.7 ± 10.6	82.5 ± 12.2	82.2 ± 9.5	86.6 ± 10.9	0.025
HiC (cm)	89.6 ± 10.2	90.7 ± 9.6	91.8 ± 11.7	94.8 ± 11.8	0.026
WHR	0.9 ± 0.06	0.9 ± 0.07	0.9 ± 0.06	0.9 ± 0.04	0.38
SBP (mm Hg)	92.8 ± 10.0	95.6 ± 12.2	94.1 ± 10.7	94.8 ± 11.8	0.75
DBP (mm Hg)	58.3 ± 9.2	60.6 ± 10.7	61.8 ± 7.0	64.1 ± 10.1	0.008
FBG (mg/dL)	86.9 ± 7.8	86.4 ± 7.9	89.1 ± 9.9	87.0 ± 9.9	0.31
TC (mg/dL)	174.8 ± 30.4	177.8 ± 31.0	178.6 ± 30.7	181.1 ± 32.4	0.68
LDL-C (mg/dL)	102.5 ± 29.0	104.8 ± 25.3	108.3 ± 32.4	110.9 ± 38.3	0.04
HDL-C (mg/dL)	44.6 ± 9.4	47.0 ± 11.9	46.4 ± 10.1	45.3 ± 10.7	0.57
TG (mg/dL)	129.5 ± 36.5	128.8 ± 35.5	130.1 ± 35.9	144.2 ± 73.0	0.008
Platelet count (×10³)	86.0 - 251.0	251.01 - 288.50	288.51 - 337.0	337.01 - 488.0	
BMI (kg/m²)	23.3 ± 4.5	23.4 ± 3.3	23.5 ± 4.1	23.8 ± 3.9	0.91
WC (cm)	82.6 ± 11.6	82.5 ± 11.2	83.3 ± 10.5	84.3 ± 10.5	0.76
HiC (cm)	92.8 ± 11.3	91.0 ± 10.7	91.4 ± 11.1	91.6 ± 11.1	0.79
WHR	0.8 ± 0.05	0.9 ± 0.08	0.9 ± 0.05	0.9 ± 0.04	0.002
SBP (mmHg)	94.4 ± 11.4	93.9 ± 11.4	92.2 ± 8.8	96.5 ± 13.0	0.45
DBP (mmHg)	58.1 ± 11.1	58.4 ± 7.7	57.9 ± 9.7	58.1 ± 9.3	0.30
FBG (mg/dL)	85.6 ± 8.4	88.6 ± 7.6	86.8 ± 7.7	88.17 ± 11.39	0.20
TC (mg/dL)	171.6 ± 31.8	173.7 ± 29.7	182.7 ± 30.6	183.9 ± 31.2	0.04
LDL-C (mg/dL)	100.7 ± 35.3	102.9 ± 30.7	110.2 ± 29.8	112.0 ± 28.6	0.12
HDL-C (mg/dL)	46.0 ± 9.6	44.0 ± 10.3	46.8 ± 11.5	45.9 ± 10.3	0.48
TG (mg/dL)	124.6 ± 36.4	148.6 ± 39.7	131.1 ± 36.7	128.51 ± 38.5	0.08

Data are expressed as mean ± standard deviation. *p*-value was obtained by analysis of variance. WBC - white blood cell, BMI - body mass index, WC - waist circumference, HiC - hip circumference, WHR - waist-to-hip ratio, SBP - systolic blood pressure, DBP - diastolic blood pressure, FBG - fasting blood glucose, TC - total cholesterol, LDL-C - low-density lipoprotein-cholesterol, HDL-C - high density lipoprotein-cholesterol, TG - triglycerides, RBC - red blood cell

Table 3 - Characteristics of children according to the number of the metabolic syndrome components.

Variables	Number of the metabolic syndrome components			*P*-value
	1	2	≥3	
Number of children (%)	88 (27.0)	112 (34.3)	126 (38.7)	
Body mass index (kg/m^2)	22.2 ± 3.7	23.3 ± 3.3	24.6 ± 4.6	<0.001
Waist circumference (cm)	79.6 ± 11.2	81.8 ± 8.9	86.7 ± 11.4	<0.001
Hip circumference* (cm)	88.7 ± 10.1	90.2 ± 9.4	94.8 ± 12.0	<0.001
Waist-to-hip ratio	0.9 ± 0.07	0.9 ± 0.05	0.9 ± 0.05	0.11
Systolic blood pressure* (mm Hg)	92.1 ± 9.6	93.3 ± 9.8	96.7 ± 12.2	0.05
Diastolic blood pressure* (mm Hg)	58.2 ± 8.4	58.0 ± 8.8	62.6 ± 10.3	0.32
Fasting blood glucose (mg/dL)	86.5 ± 7.1	86.1 ± 9.2	89.1 ± 9.3	0.03
Total cholesterol (mg/dL)	172.4 ± 32.2	179.0 ± 32.3	179.9 ± 28.8	0.28
LDL-cholesterol (mg/dL)	100.5 ± 31.0	110.9 ± 34.4	105.4 ± 28.2	0.14
HDL-cholesterol* (mg/dL)	56.9 ± 8.8	47.1 ± 9.6	40.04 ± 7.2	<0.001
Triglycerides* (mg/dL)	80.9 ± 37.6	112.2± 37.0	176.2 ± 37.5	<0.001
White blood cells (×10^3)	6.7 ± 1.7	7.4 ± 2.0	7.5 ± 1.9	0.03
Neutrophil* (%)	52.3 ± 9.1	51.8 ± 11.7	54.4 ± 9.6	0.26
Lymphocyte (%)	38.4 ± 9.4	38.6 ± 11.7	40.4 ± 8.8	0.29
Red blood cells (×10^6)	4.9 ± 0.3	4.9 ± 0.5	4.9 ± 0.3	0.93
Platelets (×10^3)	288.2 ± 65.0	293.3 ± 68.1	301.2 ± 65.2	0.42

Data are expressed as mean ± standard deviation. *values obtained from Kruskal-Wallis test, LDL - low-density lipoprotein, HDL - high density lipoprotein

Discussion. This study in young children, documented significant associations between WBC count and cardiometabolic risk factors, and indexes of generalized and abdominal obesity. We found a significant increasing trend in the mean BMI and serum lipids by the increase in the WBC count, and increase in WBC count by the increase in the number of the components of the MetS, without significant difference in terms of gender. The most consistent association found by different types of analysis was documented between WBC counts and measures of generalized and abdominal obesity, namely, BMI and WC, as well as, with serum TG level. The MetS is also associated with a hypercoagulate state, but investigations on its association with platelets count revealed different results.[10-11] Findings of a study among Japanese females suggested that platelet count may be a potential marker associated with the clustering of MetS components.[11] A study showed individuals with the MetS had higher platelet and WBC counts than those with zero to 2 of its components.[12] All these studies, conducted among adult populations, suggested that hematologic factors may serve as markers of a prothrombotic and proinflammatory state of the MetS, and contributors to atherosclerotic risk.

Previous studies have also documented an association of higher WBC count with obesity in adults,[9,24-27] and adolescents.[5,17] Such associations might be confirmatory evidence of the pro-inflammatory state of obese individuals of different age groups, even in young children, as documented in the current study. Some of our findings are consistent with 2 previous studies conducted among adolescents. In a study among 1657 Taiwanese adolescents aged 14-19 years, those in the highest quartile of WBC had higher BMI than those in the first and second quartiles of WBC. In addition, boys in the highest WBC quartile had lower HDL-C levels than those in the third WBC quartile. In addition, among boys, WBC count was positively related with BMI and TG, and negatively related to HDL-C. In girls, only BMI was positively correlated with WBC count. The WBC count was not significantly different between those adolescents with MetS, or those without.[17] In a recent study among 596 Taiwanese children and adolescents, aged 10-13 years, the BMI of boys in the highest quartile of WBC was higher than in those in the first 2 WBC quartiles. In girls, the BMI was higher in the third WBC quartile than in those in the first 2 quartiles. The lipid profile did not follow any regular trend across the WBC quartiles, TC, and LDL-C of boys in the second quartile were significantly higher than in the first and fourth quartiles, and the TG levels of those in the first quartile were significantly lower than that in the third and fourth quartiles. Among girls, TG and FBG levels were significantly lower in the first, than the 2 highest WBC quartiles. In addition, WBC count was positively correlated to BMI and TG, but negatively correlated to FBG among boys, and positively correlated to BMI and FBG among girls.[5]

We found regular increasing trends of BMI and WC, namely, measures of generalized and abdominal obesity, as well as, serum lipids other than HDL-C across the WBC quartiles. We did not find any difference in terms of gender, which can be because of the young age group included in our study, before the establishment of pubertal changes. Although the mechanisms by which the WBC count is associated with cardiometabolic risk factors remains to be determined, it is suggested that it can be related to the activation of vascular endothelial cells by the presence of atherosclerotic risk factors, and in turn production of new cytokines that along with cytokines released from the adipose tissue will activate the WBCs.[27]

In our study, higher measures of generalized and abdominal obesity, namely, BMI, WC, and HiC, as well as DBP were associated with higher RBC count, and positive correlation was documented between BMI and RBC count. The associations between RBC count and the MetS components might be mediated by insulin resistance, however, as some studies among adults have considered mechanisms not related to insulin resistance,[28] underlying pathophysiology needs to be determined in future studies. Given that high WBC counts are predictors of acute cardiovascular events, the increasing number of WBCs by increasing the number of the MetS components might be confirmatory evidence on the higher risk of future cardiovascular diseases of obese children than in their normal weight counterparts. The findings of this study on the significant correlation of the total WBC count, as well as its subtypes, namely, the lymphocyte and neutrophil counts among obese children are in agreement with previous studies among adults.[29] Although higher cholesterol level and WHR were observed in highest platelet quartile, but no significant correlation was documented between platelet counts and cardiometabolic risk factors. It is suggested that platelet function, rather than the number, might be associated with these risk factors.[30]

The main limitation of this study is that the findings from different analyses of hematological factors associated with cardiometabolic risk factors should be interpreted with caution given the cross-sectional nature of the associations. As we did not measure the insulin level, the role of insulin resistance in the correlations documented cannot be assessed. In addition, as we did not assess the pubertal stage of the children studied, the influences of puberty on cardiometabolic risk factors cannot be determined. However, because of the young age of the children studied, we suggest that most of them have been in the pre-pubertal stage; the lack of gender difference in the associations documented that is contrary to the aforementioned studies among adolescents and adults might support this suggestion. The novelty of this study is the low-age group enrolled in this study. In addition, contrary to previous studies in the pediatric age group that has included WBC count as the only hematologic factor, we also studied the RBC and platelet counts, as well as the number of WBC subtypes. Moreover, in this study, children with WBC counts more than 15,000 cell/ml were not included in the study, whereas most previous studies enrolled subjects with high WBC, which imply possible infection, or acute stress.

In conclusion, we found significant associations between CBC components and cardiometabolic risk factors in young obese children. These findings might be a confirmatory evidence of the pro-inflammatory state of obese individuals even in young children, and the possible higher risk of cardiovascular diseases later in life among young obese children.

Acknowledgment. *The authors gratefully acknowledge all members of the large team working on this project, as well as the children who participated in this study.*

References

1. Cameron AJ, Zimmet PZ, Shaw JE, Alberti KG. The metabolic syndrome: in need of a global mission statement. ***Diabet Med*** 2009; 26: 306-309.
2. Silveira VM, Horta BL. [Birth weight and metabolic syndrome in adults: meta analysis] ***Rev Saude Publica*** 2008; 42: 10-18. Portuguese.
3. Steinberger J, Daniels SR, Eckel RH, Hayman L, Lustig RH, McCrindle B, et al. Progress and challenges in metabolic syndrome in children and adolescents: a scientific statement from the American Heart Association Atherosclerosis, Hypertension, and Obesity in the Young Committee of the Council on Cardiovascular Disease in the Young; Council on Cardiovascular Nursing; and Council on Nutrition, Physical Activity, and Metabolism. ***Circulation*** 2009; 119: 628-647.
4. Cornier MA, Dabelea D, Hernandez TL, Lindstrom RC, Steig AJ, Stob NR, et al. The metabolic syndrome. ***Endocr Rev*** 2008; 29: 777-822.
5. Wu CZ, Hsiao FC, Lin JD, Su CC, Wang KS, Chu YM, et al. Relationship between white blood cell count and components of metabolic syndrome among young adolescents. ***Acta Diabetol*** 2010; 47: 65-71.
6. Chen J, Wildman RP, Hamm LL, Chen J, Wildman RP, Hamm LL, et al. Association between inflammation and insulin resistance in U.S. nondiabetic adults: results from the Third National Health and Nutrition Examination Survey. ***Diabetes Care*** 2004; 27: 2960-2965.
7. Ford ES. The metabolic syndrome and C-reactive protein, fibrinogen, and leukocyte count: findings from the Third National Health and Nutrition Examination Survey. ***Atherosclerosis*** 2003; 168: 351-358.
8. Wang YY, Lin SY, Liu PH, Cheung BM, Lai WA. Association between hematological parameters and metabolic syndrome components in a Chinese population. ***J Diabetes Complications*** 2004;18: 322-327.

9. Kim JA, Choi YS, Hong JI, Kim SH, Jung HH, Kim SM. Association of metabolic syndrome with white blood cell subtype and red blood cells. ***Endocr J*** 2006; 53: 133-139.
10. Tavil Y, Sen N, Yazici HU, Hizal F, Abaci A, Cengel A. Mean platelet volume in patients with metabolic syndrome and its relationship with coronary artery disease. ***Thromb Res*** 2007; 120: 245-250.
11. Kotani K, Sakane N, Saiga K, Mu H, Kurozawa Y. Clustered components of the metabolic syndrome and platelet counts in Japanese females. ***Clin Chem Lab Med*** 2007; 45: 376-379.
12. 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: 705-711.
13. Roberts CK, Chen AK, Barnard RJ. Effect of a short-term diet and exercise intervention in youth on atherosclerotic risk factors. ***Atherosclerosis*** 2007; 191: 98-106.
14. Kelishadi R, Hashemi M, Mohammadifard N, Asgary S, Khavarian N. Association of changes in oxidative and proinflammatory states with changes in vascular function after a lifestyle modification trial among obese children. ***Clin Chem*** 2008; 54: 147-153.
15. de Ferranti SD, Gauvreau K, Ludwig DS, Newburger JW, Rifai N. Inflammation and changes in metabolic syndrome abnormalities in US adolescents: findings from the 1988-1994 and 1999-2000 National Health and Nutrition Examination Surveys. ***Clin Chem*** 2006; 52: 1325-1330.
16. Ford ES, Ajani UA, Mokdad AH, National Health and Nutrition Examination. The metabolic syndrome and concentrations of C-reactive protein among U.S. youth. ***Diabetes Care*** 2005; 28: 878-881.
17. Hsieh CH, Pei D, Kuo SW, Chen CY, Tsai SL, Lai CL, et al. Correlation between white blood cell count and metabolic syndrome in adolescence. ***Pediatr Int*** 2007; 49: 827-832.
18. McClatchey KD, Alkan S, editors. Clinical Laboratory Medicine. 2nd ed. Philadelphia (PA): Lippincott, Williams and Wilkins; 2001. p. 557-560.
19. National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents. The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents. ***Pediatrics*** 2004; 114: 555-576.
20. de Ferranti SD, Gauvreau K, Ludwig DS, Neufeld EJ, Newburger JW, Rifai N. Prevalence of the metabolic syndrome in American adolescents: findings from the Third National Health and Nutrition Examination Survey. ***Circulation*** 2004; 110: 2494-2497.
21. Kelishadi R, Gouya MM, Ardalan G, Hosseini M, Motaghian M, Delavari A, et al. First reference curves of waist and hip circumferences in an Asian population of youths: CASPIAN study. ***J Trop Pediatr*** 2007; 53: 158-164.
22. Kelishadi R, Ardalan G, Gheiratmand R, Adeli K, Delavari A, Majdzadeh R, et al. Paediatric metabolic syndrome and associated anthropometric indices: the CASPIAN Study. ***Acta Paediatr*** 2006; 95: 1625-1634.
23. Genuth S, Alberti KG, Bennett P, Buse J, Defronzo R, Kahn R, et al. Follow-up report on the diagnosis of diabetes mellitus. ***Diabetes Care*** 2003; 26: 3160-3163.
24. Ryu SY, Kim KS, Park J, Kang MG, Han MA. The association between circulating inflammatory markers and metabolic syndrome in Korean rural adults. ***J Prev Med Public Health*** 2008; 41: 413-418.
25. Shim WS, Kim HJ, Kang ES, Ahn CW, Lim SK, Lee HC, et al. The association of total and differential white blood cell count with metabolic syndrome in type 2 diabetic patients. ***Diabetes Res Clin Pract*** 2006; 73: 284-291.
26. Nagasawa N, Tamakoshi K, Yatsuya H, Hori Y, Ishikawa M, Murata C, et al. Association of white blood cell count and clustered components of metabolic syndrome in Japanese men. ***Circ J*** 2004; 68: 892-897.
27. Tong PC, Lee KF, So WY, Ng MH, Chan WB, Lo MK, et al. White blood cell count is associated with macro- and microvascular complications in Chinese patients with type 2 diabetes. ***Diabetes Care*** 2004; 27: 216-222.
28. 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: 273-277.
29. Brun JF, Aloulou I, Varlet-Marie E. Hemorheological aspects of the metabolic syndrome: markers of insulin resistance, obesity or hyperinsulinemia? ***Clin Hemorheol Microcirc*** 2004; 30: 203-209.
30. Wang YY, Lin SY, Liu PH, Cheung BM, Lai WA. Association between hematological parameters and metabolic syndrome components in a Chinese population. ***J Diabetes Complications*** 2004; 18: 322-327.