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Metabolism Clinical and Experimental 57 (2008) 1375 – 1379
Metabolism
Clinical and Experimental
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White blood cell count and abdominal fat distribution in female obese adolescents

Jeong A. Kim[a], Hye Soon Park[b,*]

[a]Department of Family Medicine, Cheil General Hospital and Women's Health Care Center, Kwandong University, Kangneung, Kangwon 210-701, South Korea
[b]Department of Family Medicine, Ulsan University College of Medicine, Seoul 136-736, South Korea

Received 30 July 2007; accepted 1 May 2008

Abstract

The association between abdominal fat distribution and inflammatory markers is currently a subject of debate. Here, we delineate the relationship between white blood cell (WBC) counts and abdominal fat distribution in female obese adolescents. A total of 102 female obese adolescent subjects were analyzed. Anthropometry, WBC count, blood pressure, fasting plasma glucose, lipid profiles, and fasting insulin concentrations were measured. Subcutaneous adipose tissue (SAT) and visceral adipose tissue areas were calculated using computed tomography. Mean values of waist circumference ($P < .05$), total adipose tissue (TAT) ($P < .01$), and SAT ($P < .01$) were significantly higher in the group with the higher WBC count. The WBC count was positively related to body mass index, waist circumference, and TAT and SAT areas after adjustment for age and metabolic risk factors ($P < .01$). Among the WBC components, neutrophils were positively associated with body mass index ($P < .01$), waist circumference ($P < .01$), and TAT ($P < .05$). The WBC count escalated with a graded increase in TAT or SAT (P for trend $< .01$). Our findings collectively indicate that the WBC count is positively related to abdominal adiposity in female obese adolescents. Moreover, this relationship is more distinguishable with subcutaneous than visceral adiposity.

1. Introduction

In adults, adiposity plays a crucial role in inflammatory responses; and visceral adipose tissue (VAT) is an important factor in this process [1-3]. However, limited research dealing with the effects of fat distribution on metabolic risk factors in adolescents has been reported. Compared with adults, adolescents have a higher proportion of subcutaneous fat, particularly female subjects. Although the influence of subcutaneous fat is more modest than that of visceral fat, subcutaneous adipose tissue (SAT) also affects the inflammatory process [4,5]. Therefore, it would be interesting to establish the component of fat distribution that affects inflammation in obese adolescents, a high-risk group for cardiovascular diseases.

Inflammation can be measured by monitoring the levels of several inflammatory cytokines, such as interleukin-6 and tumor necrosis factor (TNF)–α. White blood cell (WBC) count is a fairly inexpensive and frequently performed procedure that provides important information. Therefore, establishing the association between WBC count and fat distribution may be useful, particularly in clinical applications.

A study performed on healthy adolescents revealed a significant correlation between leukocytes and body mass index (BMI) or percentage of body fat [6]. A national health and nutrition examination survey of the US population additionally showed that obesity is associated with significantly higher WBC count in adolescents [7]. However, to our knowledge, there have been no attempts to determine the relationship between WBC count and abdominal fat distribution in adolescents, particularly from direct measurements of subcutaneous and visceral fat. In addition, subjects are limited to obese female adolescents because fat distribution and inflammatory activity differ according to age and sex [8-12]. Therefore, the objective of this study was to determine whether a relationship exists between WBC count and abdominal fat distribution in female adolescents via direct computed tomographic (CT) measurements of visceral and subcutaneous fat.

* Corresponding author. Tel.: +82 2 3010 3813; fax: +82 2 3010 3815.
E-mail address: hyesoon@amc.seoul.kr (H.S. Park).

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doi:10.1016/j.metabol.2008.05.005

2. Methods

2.1. Study subjects

We enrolled 102 obese female adolescents (aged 10-19 years) who visited the Obesity Clinic of Asan Medical Center for the management of obesity between March 2002 and February 2005 in Seoul, Korea. Subjects were classified as obese adolescents (≥95th BMI percentile) according to the Korean cutoff point for BMI by sex and age [13]. Subjects were requested to inform us of whether there was a possibility of current infectious disease. Adolescents reporting possible infectious diseases were subsequently excluded. Patients with hypothyroidism, Cushing disease, severe debilitating diseases, or intentional weight reduction during the preceding 6 months were additionally excluded, along with those treated with antiobesity agents or insulin. This study was approved by the Institutional Review Board of Asan Medical Center.

2.2. Anthropometric and laboratory measurements

Body weight and height were measured while subjects wore light clothing without shoes. Body mass index was calculated as weight in kilograms divided by height in square meters. Waist circumference measurements were obtained from the narrowest point between the lower extent of the rib cage and iliac crest.

Cross-sectional abdominal VAT and SAT areas were measured by CT with a Siemens Somaton Scanner (Erlangen, Germany). Each subject was placed in the supine position, and a cross-sectional scan 10 mm thick centered at the L4-5 vertebral disc space was obtained using a radiograph of the skeleton as a reference to establish the scan position to the nearest millimeter. The area of total adipose tissue (TAT) was measured by delineation with a graph pen, followed by computation of the adipose tissue area with an attenuation range of −190 to −30 HU. The abdominal VAT area was measured by drawing a line within the muscle wall surrounding the abdominal cavity, and SAT area was calculated by subtracting VAT from TAT areas.

Blood pressure was measured in a sitting position after a 10-minute rest period. Two readings each of systolic and diastolic blood pressure were recorded at 5-minute intervals, and the averages were used for data analysis. Fasting blood samples were obtained in the morning after an 8-hour overnight fasting period. Fasting plasma glucose, total cholesterol, triglyceride, and high-density lipoprotein cholesterol levels were measured with an autoanalyzer (Hitachi 747 autoanalyzer, Tokyo, Japan). A human insulin-specific radioimmunoassay kit (Linco Research, St Charles, MO) was used to assess insulin levels. The index of insulin resistance was measured using the homeostasis model of assessment (HOMA) method [14]. White blood cell counts were determined with an autoanalyzer (Sysmex XE-2100, Kobe, Japan).

2.3. Statistical analysis

All descriptive statistical results are presented as means ± standard deviation and range. All variables were evaluated for normality using the Kolmogorov-Smirnov test. Variables with nonnormal distribution (such as visceral fat, insulin, HOMA, fasting plasma glucose, and triglyceride) were transformed logarithmically before analysis. A univariate general linear model (GLM) test was performed for comparing adiposity after dividing by the median WBC count subsequent to adjusting for age and metabolic risk factors (systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein, triglyceride, and fasting plasma glucose). Pearson correlation coefficients were calculated to determine the association between WBC total or differential counts and adiposity (BMI, waist circumference, TAT, SAT, VAT) after adjustment for age and metabolic risk factors. Values representing abdominal adiposity (TAT, SAT, VAT) were arbitrarily divided into quartiles, and the univariate GLM test was performed to calculate P for linear trend after adjusting for age and metabolic risk factors. All calculations were performed using SPSS version 12.0 (SPSS, Chicago, IL). A 2-tailed $P < .05$ was considered significant.

3. Results

Demographic and clinical characteristics of subjects are shown in Table 1. In total, 102 female adolescents with a mean age of 15.6 ± 3.0 years and BMI of 30.0 ± 4.5 kg/m^2 were examined. Mean WBC was 6964.0 ± 1504.1 cells per microliter, with minimum and maximum counts of 3600 and 11 300 cells per microliter, respectively. Five subjects among 102 participants had abnormally elevated WBC levels (WBC >10 000 cells per microliter).

Table 1
Basic characteristics of study subjects (N = 102)

Variables	Mean ± SD	Range
Age (y)	15.6 ± 3.0	10-19
WBC count (cells/μL)	6964.0 ± 1504.1	3600-11 300
BMI (kg/m^2)	30.0 ± 4.5	22.2-47.5
Waist circumference (cm)	91.4 ± 9.7	73.0-128.0
TAT (cm^2)	362.4 ± 109.0	108.5-707.8
SAT (cm^2)	297.0 ± 95.1	62.3-517.3
VAT (cm^2)	65.4 ± 25.6	24.6-190.5
Systolic blood pressure (mm Hg)	119.0 ± 16.7	83-157
Diastolic blood pressure (mm Hg)	63.5 ± 13.7	56-103
Total cholesterol (mg/dL)	169.8 ± 35.9	110-259
High-density lipoprotein cholesterol (mg/dL)	48.5 ± 9.7	29-83
Triglycerides (mg/dL)	105.5 ± 56.0	34-302
Fasting plasma glucose (mg/dL)	91.3 ± 11.4	73-161
Insulin (μIU/mL)	13.7 ± 7.4	3.5-35.8
HOMA	3.3 ± 2.4	0.7-16.1

Data are means ± SD (range).

Table 2
Differences in abdominal adiposity after categorizing by median WBC counts in female obese adolescents

Variables	WBCs (cells/μL)		
	≤6800 (n = 51)	>6800 (n = 51)	*P*
BMI (kg/m^2)	29.2 ± 4.0 (22.4-40.0)	30.8 ± 4.8 (22.2-47.5)	NS
Waist circumference (cm)	89.2 ± 8.4 (73.0-106.5)	93.7 ± 10.6 (74.5-128.0)	<.05
TAT (cm^2)	332.2 ± 105.0 (108.5-624.5)	393.8 ± 105.1 (188.3-707.8)	<.01
SAT (cm^2)	268.7 ± 90.5 (62.3-515.9)	326.4 ± 91.7 (124.6-517.3)	<.01
VAT (cm^2)	63.5 ± 24.6 (24.6-133.2)	67.5 ± 26.7 (35.4-190.5)	NS
Insulin (μIU/mL)	12.1 ± 5.5 (3.5-32.8)	15.5 ± 8.8 (3.6-35.8)	NS
HOMA	2.7 ± 1.4 (0.7-7.2)	3.6 ± 2.1 (0.7-8.8)	NS

Visceral adipose tissue, insulin, and HOMA were log transformed. Univariate GLM test was performed after adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglycerides, and fasting plasma glucose. NS indicates not significant.

The differences in abdominal adiposity after classification based on the median WBC count are shown in Table 2. The mean values of waist circumference ($P < .05$), TAT ($P < .01$), and SAT ($P < .01$) were markedly elevated in the group with the higher WBC count. However, VAT was not significantly different between the 2 groups. Mean WBC counts from each quartile of abdominal adiposity (TAT, SAT, VAT) are presented in Fig. 1. White blood cell counts escalated linearly with a graded increase in TAT or SAT (P for trend < .01). However, no significant association was observed between VAT and WBC counts.

Correlation analyses of WBC counts and adiposity or metabolic risk factors are presented in Table 3. Upon adjustment solely for age, entire adiposity indicators, such as BMI, waist circumference, TAT, SAT, and VAT, were positively related to WBC counts. However, after adjustment for other metabolic risk factors (systolic and diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglyceride, and fasting plasma glucose), VAT was not correlated with the WBC count. White blood cell counts were positively related to BMI ($P < .01$), waist circumference ($P < .01$), TAT ($P < .01$), and SAT ($P < .01$).

The correlation between WBC differential counts and adiposity is shown in Table 4. After adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglyceride, and fasting plasma glucose, only neutrophil counts were positively related to BMI ($P < .01$), waist circumference ($P < .01$), and TAT ($P < .05$). Lymphocyte and basophil counts were negatively related to BMI and waist circumference. Subcutaneous adipose tissue or VAT was not associated with WBC differential counts.

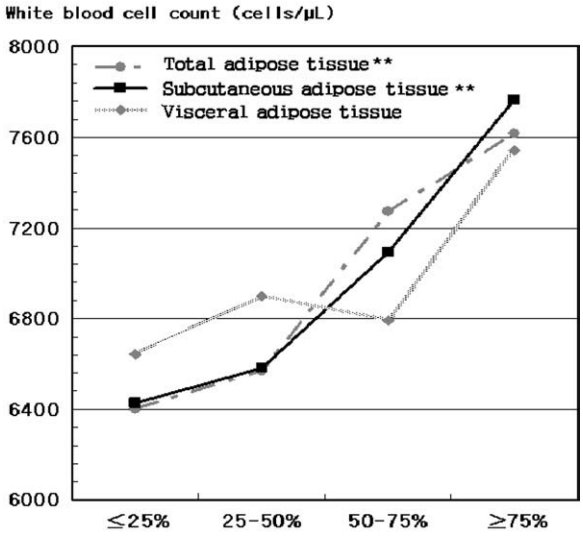

Fig. 1. White blood cell count according to quartiles of abdominal adiposity (TAT, SAT, and VAT) in female obese adolescent subjects. Univariate GLM test was performed after adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglyceride, and fasting plasma glucose. *$P < .05$ for linear trend. **$P < .01$ for linear trend.

4. Discussion

Our findings show that the WBC count in obese female adolescents is strongly related to subcutaneous rather than

Table 3
Correlations between WBC counts and abdominal adiposity or metabolic parameters in female obese adolescents

Variables	r^a	*P*	R^b	*P*
BMI	0.34	<.01	0.31	<.01
Waist circumference	0.32	<.01	0.31	<.01
TAT	0.37	<.001	0.33	<.01
SAT	0.35	<.001	0.31	<.01
VAT	0.24	<.05	0.20	NS
Systolic blood pressure	0.18	NS	0.22	<.05
Diastolic blood pressure	0.04	NS	−0.08	NS
Total cholesterol	0.02	NS	0.06	NS
High-density lipoprotein cholesterol	−0.17	NS	−0.12	NS
Triglycerides	0.15	NS	0.07	NS
Fasting plasma glucose	−0.09	NS	−0.14	NS
Insulin	0.15	NS	0.12	NS
HOMA	0.13	NS	0.12	NS

Visceral adipose tissue, insulin, and HOMA were log transformed. Partial correlation analysis was performed.

[a] Correlation coefficient was obtained after adjustment for age.

[b] Correlation coefficient was obtained after adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglycerides, and fasting plasma glucose.

Table 4
Correlations between WBC components and abdominal adiposity in female obese adolescents

	Neutrophil	Lymphocyte	Monocyte	Eosinophil	Basophil
BMI	0.291**	−0.239*	−0.156	−0.196	−0.301**
Waist circumference	0.335**	−0.296**	−0.148	−0.177	−0.264*
TAT	0.210*	−0.189	−0.046	−0.131	−0.214*
SAT	0.182	−0.161	−0.035	−0.126	−0.189
VAT	0.135	−0.135	−0.024	−0.050	−0.149

Partial correlation analysis was performed after adjustment for age, systolic blood pressure, diastolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, triglyceride, and fasting plasma glucose.

* $P < .05$.

** $P < .01$.

visceral adiposity. Because of growth spurts, adolescents have a characteristic fat distribution with higher amounts of subcutaneous fat, particularly in girls [15-18]. These characteristic changes in fat distribution based on growth may contribute to the more significant relationship observed between WBC and SAT, relative to VAT, in our study.

Adipose tissue is not a simple energy storage organ, but additionally displays endocrine function [19]. As the degree of obesity increases, adipose tissue is infiltrated to a greater extent by macrophages, which may initiate a proinflammatory status [20]. A recent study on subjects referred for further evaluation of leukocytosis demonstrated that, after smoking, obesity is the second most common cause of leukocytosis [21]. Leptin, interleukin-6, and TNF-α have been implicated in this phenomenon [22-24]. It is important to determine the connection between inflammation and adiposity because inflammation is one of the primary metabolic risk factors. Recent studies demonstrate that inflammation is a risk factor for ischemic stroke independent of atherosclerosis severity, and a separate predictor of diabetes [25,26].

The importance of inflammation in metabolic risk in the adolescent group has been reported [20,27,28], although studies on this subject are limited and the effects on later life remain unclear at present. A study by the National Health and Nutrition Examination Survey [29] on American children disclosed that inflammation is strongly related to obesity. Association of inflammatory markers with cardiovascular risk factors, such as heart rate, systolic blood pressure, plasma fibrinogen, and homocysteine, has been demonstrated in a young age group [30-32]. In addition, the WBC count may have potential as a predictor for all-cause mortality, particularly cardiovascular disease mortality [33]. Therefore, identification of at-risk patients in this age group via a simple test would certainly be clinically meaningful and cost-effective. From this perspective, it is appropriate to use the WBC count as an inflammatory marker, rather than other cytokines, if the subject is not infectious.

Subcutaneous fat is a less significant metabolic risk factor than visceral fat. However, abdominal SAT may also contribute to metabolic derangement [4,5]. Leptin, an important adipokine, is released by SAT rather than VAT [34,35]; and TNF-α expression is further increased in the SAT area of obese subjects [36]. With regard to the association between specific WBC types and anthropometric variables, our results are consistent with earlier observations that neutrophils are positively related to adiposity. Neutrophils are strongly related to percentage of body fat [6] and increased BMI in adults [21]. The current study extends previous findings on the positive relationship between neutrophils and central adiposity (waist circumference and TAT) as well as total heaviness (BMI) in adolescents.

The present study has some limitations. The principal limitation is the cross-sectional design of the study, which makes it difficult to determine causality with regard to the observed relationships. In addition, our results may not be generally applicable because the study subjects were limited to female obese adolescents. A similar study with lean age- and puberty-matched girls would aid in further elucidating the relationship between WBC count and fat distribution.

Our experiments provide fundamental data on the relationship between the WBC count and abdominal fat distribution in female obese adolescents, based on direct CT measurements of subcutaneous and visceral fat. In conclusion, our results show that the WBC count is positively related to abdominal adiposity in female obese adolescents. Moreover, this relationship is more pronounced with SAT than VAT.

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