Original Article

Positive association between the metabolic syndrome and white blood cell counts in Chinese

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Background and Objectives: The aim was to investigate the association between peripheral circulating white blood cell count (WBC) and the metabolic syndrome among populations in central China. **Methods and Study Design**: In the present study, 5,278 subjects (2,412 women, 2,866 men) aged 18-75 years were recruited through a health check program in Wuhan, China. Biochemical and haematological parameters were measured by standard methods and the metabolic syndrome diagnosed as defined by the Chinese Diabetes Society criteria for Chinese. **Results**: Both WBC counts and prevalence of metabolic syndrome were significantly higher in men than in women ($p<0.01$). Participants in the highest quartile of white blood cell count had significantly higher odds ratio of metabolic syndrome (3.79, 95% CI: 2.64, 5.44), compared with subjects in the lowest quartile. The trend remained significant after adjustment for confounding factors and in further subgroup-analyses. **Conclusions**: Metabolic syndrome prevalence was significantly and positively correlated with the total white blood cell count in this Chinese population.

Key Words: metabolic syndrome, white blood cell count, cardiovascular risk, gender differences, Wuhan

INTRODUCTION

The metabolic syndrome (MS) is characterized by a clustering of cardiovascular risk factors, including abdominal obesity, high blood pressure, increased glucose concentration, and dyslipidemia.[1] In recent years, the prevalence of MS has increased dramatically in both developing and developed countries, and the prevalence of MS in China has been estimated to be 9.8% for men and 17.8% for women, based on a cross-sectional survey conducted in 2000-2001.[2] However, the prevalence is much higher in United States (25.2% in men and 29% in women).[3] Epidemiological evidence and systematic reviews have suggested that MS is strongly associated with increased risk of cardiovascular diseases,[4,5] diabetes,[6] common cancers,[7] and even osteoporosis,[8] and as a result MS has become a significant public health issue worldwide.

Because of the association between inflammation and MS, several studies have examined the relationship between the peripheral circulating white blood cell (WBC) count, an important marker of acute infection, tissue damage and inflammation,[9] and components of MS; the data reveals correlations between WBC and MS in some cross-sectional studies.[10-12] Additionally, there are also prospective studies which have suggested that total WBC counts were positively associated with coronary heart disease and MS.[13,14] However, there are few reports on the association between WBC count and MS among populations in central China. Therefore, the aim of the present study with a representative sample of adults from central China was to investigate the association between WBC counts and MS.

METHODS

Design and study population

A cross-sectional study was conducted among 5,278 subjects (2,412 women, 2,866 men) aged 18-75 years, and the associations between total WBC count and MS were investigated. All subjects were recruited through a general health screening program between September 2011 and December 2013 in Wuhan, China. They visited the Health Examination Centre, Wuhan Puai Hospital in the morning following an overnight fast. None of the included participants had thyroid, renal, hepatic, gastrointestinal,

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or oncology disease or were receiving drugs for hypoglycemia, were taking antioxidant vitamin sup-plementation, or drugs known to affect lipoprotein metabolism. Then ten milliliter of fasting blood was drawn, from which WBC counts and other parameters of biochemistry, necessary to assess the presence or absence of MS, were measured. Haematological indexes deviating from normal reference ranges were considered as abnormal. Gender-specific quartiles of total WBC count were used in the present study. The study was approved by the Research Ethical Committee, School of Biosystem Engineering and Food Science, Zhejiang University (ZJU-BEFS-2014008B), and all subjects gave written informed consent for the use of personal information for analysis.

Criteria for the metabolic syndrome

Diagnosis of MS was made according to the criteria of Chinese Diabetes Society (CDS) for Chinese,[15] when three or four of the following criteria are met: 1) high BMI, as body mass index (BMI) ≥25; 2) high blood pressure, as systolic blood pressure ≥140 mmHg or diastolic blood pressure ≥90 mmHg; or known treatment for hypertension; 3) dyslipidemia, as fasting triacyglycerol ≥1.7 mmol/L (150 mg/dL), or high density lipoprotein cholesterol (HDL-c) <0.9 mmol/L (35 mg/dL) in men and <1.0 mmol/L (39 mg/dL) in women; 4) hyperglycemia, as fasting glucose ≥6.1 mmol/L (109 mg/dL); or known treatment for diabetes.

Parameters measurement

Weight and height were measured on an autoanthropometer (super-view, HW-666) with subjects wearing light clothing and body mass index (BMI) was calculated by the formula of weight (kg)/(height)^2(m^2). Blood pressure was measured by an electronic device (COLIN, VP-100, Japan) after the subjects sat relaxed for 10 mins. The routine examination of blood, including total WBC and differential WBC count, was measured using an autoanalyzer (Sysmex, Kobe, Japan). Biochemical markers such as triacylglycerol (TG) and total cholesterol (TC) concentrations were determined by standard enzymatic dipyridamole methods. High density lipoprotein cholesterol (HDL-c) and low density lipoprotein cholesterol (LDL-c) were measured by differential antibody methods, and blood glucose was measured by hexokinase methods on an auto-biochemical analyzer (Olympus AV400, Japan). Lipoprotein and blood glucose concentrations were reported as mmol/L.

Statistical analyses

Continuous variables were reported as mean±SD and categorical variables were expressed in percentages. All the data were checked for normal distribution and values with skewed distribution (glucose and triacyglycero) were transformed to their ln forms for analyses. Strata-specific differences were assessed using one-way Analysis of Variance (ANOVA) and comparisons of WBC counts according to two groups were performed by independent sample *t*-test. The chi-square test was used for categorical variables. Crude and multivariable adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the MS and its components were computed using the logistic regression and age (continuous), gender (men/women), concentration of hemoglobin (continuous), red blood cells (continuous) and platelet count (continuous) were adjusted in the multivariable model. All analysis was performed using the SPSS software package version 16.0 for windows (SPSS Inc., Chicago, IL, USA). Two-tailed *p* value <0.05 was considered significant.

RESULTS

Characteristics of the study subjects

A total of 5,278 individuals (2,412 women, 2,866 men) were included in this study and the clinical characteristics of study subjects according to quartiles of total WBC count are summarized in Table 1, while values of BMI, blood pressure, TG, LDL/HDL and blood glucose are also shown in Figure 1 by age category and gender. Sub-

Table 1. Characteristics of the study subjects according to quartiles of total WBC count

Characteristics	Quartiles of total WBC count (×10^9/L)				*p* value
	Q1	Q2	Q3	Q4	
No. of MS cases/non-cases	40/1269	79/1284	114/1208	137/1147	0.82
Gender (men/women)	703/606	724/639	729/593	710/574	0.61
Age (years)	42.9 (12.7)	41.7 (12.1)	42.0 (13.0)	41.8 (12.5)	0.06
Blood pressure (mm Hg)					
Systolic	118 (17.3)	120 (17.9)	120 (17.8)	122 (18.0)	<0.01
Diastolic	71.4 (10.1)	73.2 (11.1)	73.5 (10.9)	75.5 (11.8)	<0.01
Body mass index (kg/m^2)	22.5 (2.9)	23.1 (3.2)	23.7 (3.3)	24.3 (3.5)	<0.01
ln fasting blood glucose (mmol/L)	1.58 (0.12)	1.58 (0.13)	1.58 (0.13)	1.58 (0.14)	0.09
ln triglyceride/acyl (mmol/L)	0.01 (0.52)	0.16 (0.56)	0.28 (0.54)	0.37 (0.55)	<0.01
Total cholesterol (mmol/L)	4.49 (0.81)	4.60 (0.85)	4.68 (0.85)	4.70 (0.86)	<0.01
HDL-c (mmol/L)	1.23 (0.27)	1.18 (0.26)	1.15 (0.25)	1.10 (0.24)	<0.01
LDL-c (mmol/L)	2.69 (0.75)	2.82 (0.80)	2.96 (0.79)	2.96 (0.85)	<0.01
Creatinine (μmol /L)	74.8 (16.9)	74.9 (16.6)	75.1 (16.5)	75.6 (18.1)	0.63
Urea nitrogen (mmol/L)	4.93 (1.29)	4.98 (1.24)	4.97 (1.25)	4.90 (1.24)	0.30
Hemoglobin (g/L)	137 (15.4)	139 (15.1)	142 (14.5)	143 (14.6)	<0.01
Platelet count (10^9/L)	206 (53.3)	219 (48.9)	228 (49.7)	249 (58.6)	<0.01
RBC count (10^{12}/L)	4.58 (0.47)	4.66 (0.47)	4.72 (0.46)	4.77 (0.49)	<0.01
WBC count (10^9/L)	4.34 (0.52)	5.43 (0.33)	6.33 (0.35)	7.93 (1.02)	<0.01

MS: metabolic syndrome; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; RBC: red blood cell; WBC: white blood cell.

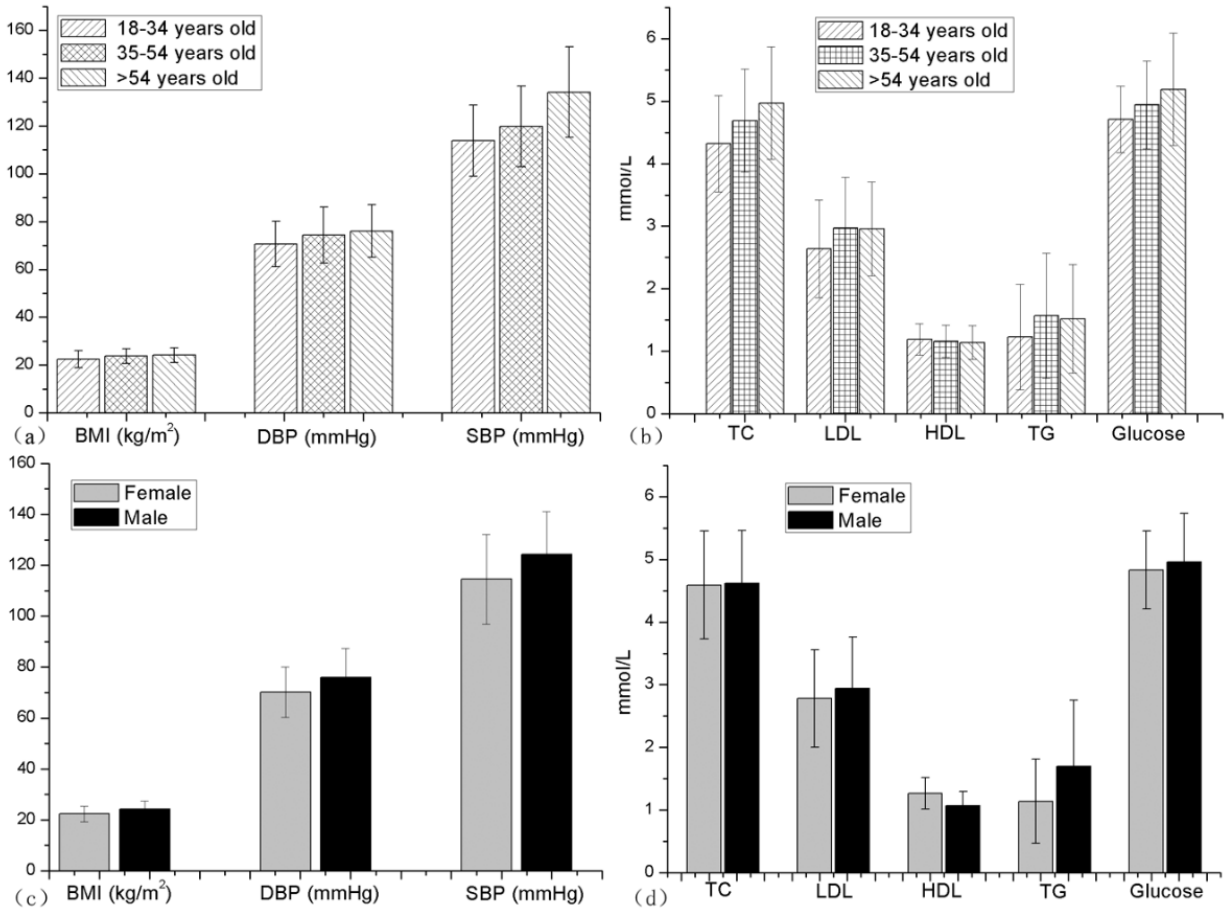

Figure 1. Values of BMI, SBP, DBP, TG, LDL, HDL and blood glucose in age subgroups (a, b) and gender subgroups (c, d). BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; TG: triacylglycerol; LDL: low density lipoprotein cholesterol; HDL: high density lipoprotein cholesterol.

jects allocated in the highest quartile of total WBC count were older and had higher level of BMI, blood pressure, total cholesterol, LDL cholesterol, hemoglobin, red blood cell and platelet count (p<0.01 for all), but lower level of HDL cholesterol (p<0.01). The overall prevalence was 7.8% for MS, 30.6% for high BMI, 17.1% for hypertension, 32.2% for dyslipidemia and 5.4% for hyperglycemia. All these prevalence were found to be significantly higher in men than in women (p<0.01) (Figure 2). Furthermore, the count of total WBC and its subtypes were all significantly higher in men than in women (p<0.0001), as shown in Table 2. Therefore, gender-specific quartiles of WBC count were used in the present study.

Association between potential confounding factors of WBC count and the metabolic syndrome

As shown in Table 3, individuals with older age (≥50 years) or abnormal blood hemoglobin concentration, WBC count and red blood cells (RBC) count, were more likely have high BMI, high blood pressure, high fasting plasma glucose levels, and dyslipidemia than those younger than 50 or with normal levels of hemoglobin, WBC count and RBC count. All these trends were verified by the logistic regression analysis, which showed that crude odds ratios (ORs) of MS for subjects older than 50 was 2.53 (95% CI: 2.04-3.13) compared with their counterparts (age <50 years), for subjects with abnormal blood hemoglobin concentration the OR was 3.26 (95% CI: 1.72-6.17), for subjects with abnormal RBC count the OR was 2.22 (95% CI: 1.50-3.27), and for subjects with abnormal WBC count the OR was 2.81 (95% CI: 1.41-5.61). For each component of MS, the crude ORs are also listed in Table 3. However, subjects with abnormal levels of blood BUN or creatinine, showed no significantly higher

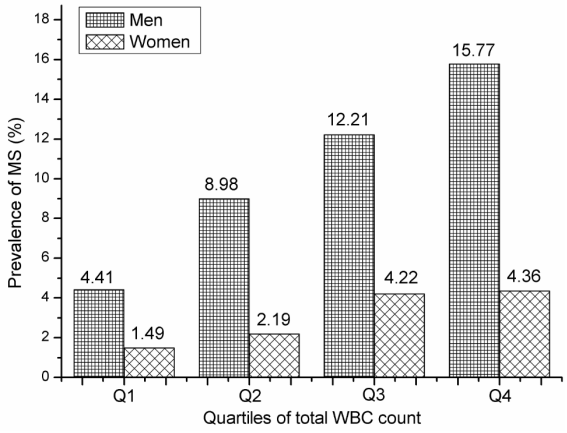

Figure 2. Prevalence of the metabolic syndrome by quartiles of total WBC count among 5,278 subjects. The quartiles of total WBC count were calculated sex-specifically. In men, the cutoff values of WBC count are ≤5.1, 5.2-6.0, 6.1-7.0 and ≥7.1 ($\times 10^9$/L) respectively; in women, the cutoff values are ≤4.7, 4.8-5.6, 5.7-6.5 and ≥6.6 ($\times 10^9$/L) respectively.

Table 2. Gender-specific prevalence of the metabolic syndrome† (%) and WBC counts (10^9/L; mean±SD)

	Men	Women	*p* values
MS	10.4 (N=297)	3.0 (N=73)	<0.01
High BMI	41.0 (N=1174)	17.1 (N=412)	<0.01
Hypertension	20.6 (N=591)	10.8 (N=261)	<0.01
Hyperglycemia	5.7 (N=165)	3.2 (N=77)	<0.01
Dyslipidemia	41.9 (N=1200)	18.7 (N=452)	<0.01
Total WBC	6.25±1.48	5.74±1.39	<0.01
Eosinophil	0.16±0.13	0.12±0.12	<0.01
Basophil	0.037±0.024	0.030±0.021	<0.01
Neutrophil	3.48±1.09	3.26±1.07	<0.01
Monocyte	0.46±0.15	0.38±0.13	<0.01
Lymphocyte	2.11±0.59	1.96±0.53	<0.01

†Metabolic syndrome, high BMI, hypertension, hyperglycemia and dyslipidemia were diagnosed based on Chinese Diabetes Society (CDS) criteria for Chinese people. WBC: white blood cell; MS: metabolic syndrome; BMI: body mass index.

Table 3. Crude odds ratios for the metabolic syndrome by status of confounding factors

	MS	High BMI	Hypertension	Dyslipidemia	Hyperglycemia
Hemoglobin					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	3.26 (1.72, 6.17)	1.38 (0.82, 2.32)	3.84 (2.30, 6.39)	3.79 (2.26, 6.36)	1.44 (0.52, 4.01)
Urea nitrogen					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	0.79 (0.25, 2.56)	1.10 (0.62, 1.96)	1.37 (0.70, 2.66)	0.79 (0.43, 1.45)	3.23 (1.44, 7.23)
Creatinine					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.78 (0.68, 11.37)	1.89 (1.05, 3.38)	1.26 (0.64, 2.45)	1.03 (0.63, 1.69)	1.16 (0.36, 3.70)
White blood cells count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.81 (1.41, 5.61)	2.05 (1.22, 3.44)	1.66 (0.91, 3.05)	2.07 (1.23, 3.47)	1.98 (0.79, 5.01)
Red blood cells count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	2.22 (1.50, 3.27)	2.20 (1.69, 2.89)	1.86 (1.38, 2.52)	1.86 (1.42, 2.42)	0.73 (0.36，1.50)
Platelet count					
Normal (referent)	1.00	1.00	1.00	1.00	1.00
Abnormal	1.15 (0.53, 2.51)	1.71 (1.11, 2.62)	0.82 (0.44, 1.51)	1.46 (0.95, 2.25)	0.99 (0.36, 2.72)
Age					
<50 (referent)	1.00	1.00	1.00	1.00	1.00
≥50	2.53 (2.04, 3.13)	1.62 (1.42, 1.85)	4.52 (3.87, 5.26)	1.40 (1.23, 1.60)	3.56 (2.75, 4.62)
Gender					
Women (referent)	1.00	1.00	1.00	1.00	1.00
Men	3.70 (2.85, 4.81)	3.37 (2.96, 3.83)	2.14 (1.83, 2.51)	3.12 (2.75, 3.54)	1.85 (1.41, 2.44)

MS: metabolic syndrome; BMI: body mass index.

risk of MS or its components (Table 3). Therefore, age, gender, blood level of hemoglobin, platelet and RBC count were ad- justed in the following analysis.

Association between WBC count and the metabolic syndrome

Table 4 presents logistic analysis results for the association of MS (including its components) with WBC count, by quartile of its distribution. After adjustment for age, gender, blood levels of hemoglobin, platelet and RBC, MS prevalence retained a significant association with WBC counts when comparing the highest and lowest quartiles of WBC (OR: 3.16, 95% CI: 2.15-4.65; p<0.01). A significant positive association was still found between WBC counts and each MS component, when comparing the highest quartile of WBC with the lowest. The multiple adjusted OR was 2.78 (95% CI: 2.28-3.38) for high BMI, 1.66 (95% CI: 1.30-2.13) for hypertension, 2.87 (95% CI: 2.36-3.49) for dyslipidemia and 1.98 (95% CI: 1.31-2.99) for hyperglycemia. As high BMI, hypertension, dyslipidemia and hyperglycemia often overlap, in the present study the associations between WBC count and high BMI plus one to three of any other component were also examined. Interestingly, significant positive associations were observed for BMI+1 and BMI+2 components, but not for BMI+0 and BMI+3 components. The multiple adjusted OR was 2.56 (95% CI: 1.99-3.30) for high BMI+1 component, and 3.27 (95% CI: 2.13-5.01) for high BMI+2 component. However, the multiple adjusted OR for high BMI+0 component and BMI+3 components were 1.32 (0.98, 1.76) and 1.46 ((95% CI: 0.55-3.9), respectively.

Subgroup analysis of the association between WBC count and the metabolic syndrome

Table 5 shows the association between blood WBC counts and MS by age (<50 or ≥50) and gender. The positive association between blood WBC count and MS was

consistent for both subgroups, and a significant interaction was observed between age and WBC counts (p<0.01). When investigating the association between WBC counts and components of MS in subgroups, the significant interaction was still observed between age and WBC count for high BMI, hypertension and dyslipidemia, but not for hyperglycemia. No significant interaction between gender and WBC counts was observed in the subgroup-analysis and subjects in the highest quartile of total WBC count had significantly higher odd ratios of all MS components compared with those in the lowest quartile regardless of gender (Table 5).

Table 4. Multivariable adjusted† odds ratios for the metabolic syndrome by total WBC quartiles

	Quartiles of total WBC counts				p for trend
	Q1	Q2	Q3	Q4	
Hypertension					
Multivariable OR	1.00	1.37 (1.08, 1.74)	1.25 (0.98, 1.59)	1.66 (1.30, 2.12)	<0.01
Dyslipdemia					
Multivariable OR	1.00	1.62 (1.34, 1.95)	2.06 (1.71, 2.50)	2.87 (2.36, 3.49)	<0.01
Hyperglycemia					
Multivariable OR	1.00	1.34 (0.89, 2.03)	1.41 (0.93, 2.13)	1.98 (1.31, 2.99)	0.01
High BMI+1 symptom					
Multivariable OR	1.00	1.52 (1.18, 1.97)	1.65 (1.28-2.13)	2.56 (1.99-3.30)	<0.01
High BMI+2 symptom					
Multivariable OR	1.00	2.06 (1.33-3.20)	2.92 (1.92, 4.46)	3.27 (2.13, 5.01)	<0.01
High BMI+3 symptom					
Multivariable OR	1.00	0.37 (0.10, 1.42)	1.46 (0.58, 3.68)	1.46 (0.55, 3.90)	0.41
Metabolicsyndrome					
Multivariable OR	1.00	1.90 (1.27, 2.82)	2.63 (1.80, 3.86)	3.16 (2.15, 4.65)	<0.01

†Multivariable model adjusted for age (continuous), gender (men/women), concentration of hemoglobin (continuous), red blood cells count (continuous) and platelet count (continuous). WBC: white blood cell.

Table 5. Odds ratios for the metabolic syndrome and its components by quartiles of WBC distribution in subgroup analysis

Population subgroup	Q1	Q2	Q3	Q4	p for interaction
Metabolic syndrome					
Gender					0.87
Men	1.00	2.06 (1.31, 3.22)	2.75 (1.78, 4.24)	3.51 (2.26, 5.43)	
Women	1.00	1.38 (0.57, 3.27)	2.16 (0.97, 4.81)	2.24 (1.00, 5.06)	
Age					0.01
<50	1.00	2.61 (1.40, 4.87)	4.29 (2.36, 7.79)	6.26 (3.46, 11.3)	
≥50	1.00	1.47 (0.86, 2.50)	1.85 (1.10, 3.10)	1.75 (1.02, 3.00)	
High BMI					
Gender					0.25
Men	1.00	1.70 (1.35, 2.14)	1.94 (1.54, 2.44)	2.80 (2.20, 3.55)	
Women	1.00	1.38 (0.96, 2.00)	2.08 (1.45，2.97)	2.97 (2.08, 4.26)	
Age					0.04
<50	1.00	1.73 (1.37, 2.20)	2.29 (1.81, 2.91)	3.45 (2.71, 4.40)	
≥50	1.00	1.33 (0.95, 1.85)	1.57 (1.13, 2.19)	2.03 (1.43, 2.88)	
Hypertension					
Gender					0.57
Men	1.00	1.29 (0.97, 1.73)	1.32 (0.99, 1.77)	1.63 (1.21, 2.19)	
Women	1.00	1.53 (1.00, 2.33)	1.08 (0.69, 1.68)	1.81 (1.17,2.81)	
Age					0.03
<50	1.00	1.40 (0.99, 1.99)	1.57 (1.11, 2.22)	2.20 (1.56, 3.09)	
≥50	1.00	1.33 (0.96, 1.84)	1.14 (0.82, 1.60)	1.46 (1.03, 2.07)	
Dyslipidemia					
Gender					0.35
Men	1.00	1.59 (1.26, 1.99)	2.07 (1.65, 2.59)	2.68 (2.12, 3.40)	
Women	1.00	1.72 (1.21, 2.44)	2.11 (1.49, 3.00)	3.45 (2.43, 4.89)	
Age					0.06
<50	1.00	1.60 (1.27, 2.00)	2.14 (1.70, 2.68)	3.42 (2.71, 4.32)	
≥50	1.00	1.64 (1.16, 2.31)	2.03 (1.44, 2.86)	2.07 (1.44, 2.96)	
Hyperglycemia					
Gender					0.45
Men	1.00	1.38 (0.84, 2.24)	1.33 (0.81, 2.17)	1.79 (1.09, 2.94)	
Women	1.00	1.26 (0.58, 2.77)	1.62 (0.76, 3.44)	2.61 (1.25, 5.46)	
Age					0.46
<50	1.00	0.91 (0.50, 1.67)	1.29 (0.73, 2.28)	1.57 (0.89, 2.78)	
≥50	1.00	1.88 (1.06, 3.33)	1.77 (0.98, 3.19)	3.00 (1.68, 5.38)	

WBC: white blood cell.

DISCUSSION

Consistent with studies conducted in South Korea and Thailand,[16,17] the present study found that the prevalence of MS or its components (high BMI, hypertension, dyslipidemia and hyperglycemia) were significantly higher in Chinese men than in women. Besides, total WBC count and all individual differential white blood cells (eosinophil, basophil, neutrophil, monocyte and lymphocyte) were also consistently observed to be significantly higher in men than in women. However, Bain's study[18] investigating gender differences in the total and differential WBC count among Caucasian, Afrocaribbean and African populations obtained opposite results, which indicated women had significantly higher total WBC and neutrophil counts than men in all ethnic groups. It is possible that the small sample size of their study and different ethnicities between Asian and western people may help explain these inconsistencies. Even though gender-differences in prevalence of MS and WBC count are universal and reported in many studies,[16,17] the present study found MS positively correlated with WBC counts regardless of gender. Additionally, although confounding variables were screened and adjusted for, and subgroup analyses were performed, the positive association between MS and WBC count was not materially changed. Moreover, some prospective studies also confirmed the positive association between baseline WBC count and later developing MS incidence,[19,20] which indicates that WBC count might be a useful biomarker for predicting MS and even cardiovascular diseases.

The mechanisms behind the associations reported here are still unclear. It is of interest that an association between WBC count and insulin resistance/secretion has been found in severalstudies.[21-24] Jung et al and Targher et al reported that insulin resistance and fasting insulin increased corresponding to an increase of WBC count.[9,25] The increased risk of diabetes among individuals with elevated WBC, neutrophil and lymphocyte counts, was also attributed partially to insulin resistance/sensitivity by Lorenzo.[26] Moreover, insulin resistance was reported to play an important role in metabolic disturbances leading to recruitment of a series of inflammatory markers.[27,28] Therefore, one of the speculations is that insulin resistance links the association between WBC count and MS prevalence. In addition, adipose tissue is considered to promote local and systemic inflammation and even induce the MS,[29] therefore we examined the association between WBC counts and high BMI plus one to three component aiming to show the progression of MS. Increasing significantly positive association was found for high BMI+0, high BMI+1 and high BMI+2 components, indicating the association between WBC counts and high BMI become stronger with more components being involved. The exception for high BMI+3 components may due to the very limited subjects with all the four components, which also led to a broad confidence interval. On the other hand, besides high BMI, dyslipidemia and hypertension have also been reported to promote the release of IL-8 and TNF-a or damage the vascular endothelium.[30-32] These pro-inflammatory factors and vascular damage could directly or indirectly lead to elevated white blood cell levels, which may account for the association between WBC count and MS based on the present population. Further research is required to identify the importance of WBC counts in MS or other cardiovascular diseases.

Limitations of this study must be considered. First of all, the results from cross-sectional data were used and causal relationship between WBC count and development of MS could not be determined. Secondly, all subjects were restricted to only one province in central China and selection bias has been inevitably introduced, even though the age ranges of the included subjects were wide. Thirdly, lifestyle factors including alcohol drinking and smoking status were not recorded and analyzed. Lastly, we did not measure the insulin resistance which is now regarded as playing an important role in explaining the association between WBC count and MS.

Conclusion

Both white blood cell counts and prevalence of MS were significantly higher in men than in women. Total white blood cell counts were positively associated with MS prevalence, regardless of gender differences. Therefore, the white blood cell count may serve as a useful biomarker for predicting MS, but more prospective studies are needed to verify the association.

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AUTHOR DISCLOSURES

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REFERENCES

1. He Y, Jiang B, Wang J, Feng K, Chang Q, Fan L, Li X, Hu FB. Prevalence of the metabolic syndrome and its relation to cardiovascular disease in elderly Chinese population. J Am Coll Cardiol. 2006;47:1588-94. doi: 10.1016/j.jacc.2005.11.074.
2. Gu D, Reynolds K, Wu X, Chen J, Duan X, Reynolds RF, Whelton PK, He J. Prevalence of the metabolic syndrome and overweight among adults in china. Lancet. 2005;365:1398-405. doi: 10.1016/S0140-6736(05)66375-1.
3. Ford ES, Giles WH, Mokdad AH. Increasing prevalence of the metabolic syndrome among U.S. adults. Diabetes Care. 2004;27:2444-9. doi: 10.2337/diacare.27.10.2444.
4. Isomaa B, Almgren P, Tuomi T, Forsén B, Lahti K, Nissén M, Taskinen MR, Groop L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. Diabetes Care. 2001;24:683-9. doi: 10.2337/diacare.24.4.683.
5. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. Am J Med. 2006;119:812-9. doi: 10.1016/j.amjmed.2006.02.031.
6. Ford ES, Schulze MB, Pischon T, Bergmann, M, Joost HG, Boeing H. Metabolic syndrome and risk of incident diabetes: findings from the European prospective investigation into cancer and nutrition-potsdam study. Cardiovasc Diabetol.

2008;7:35. doi: 10.1186/1475-2840-7-35.
7. Esposito K, Chiodini P, Colao A, Lenzi A, Giugliano D. Metabolic syndrome and risk of cancer: a systematic review and meta-analysis. Diabetes Care. 2012;35:2402-11. doi: 10.2337/dc12-0336.
8. Zhou J, Zhang Q, Yuan X, Wang J, Li C, Sheng H, Qu S, Li H. Association between metabolic syndrome and osteoporosis: a meta-analysis. Bone. 2013;57:30-5. doi: 10.1016/j.bone.2013.07.013.
9. Jung CH, Lee WY, Kim BY, Park SE, Rhee EJ, Park CY et al. The risk of metabolic syndrome according to the white blood cell count in apparently healthy Korean adults. Yonsei Med J. 2013;54:615-20. doi: 10.3349/ymj.2013.54.3.615.
10. 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;68:892-7. doi: 10.1253/circj.68.892.
11. Ohshita K, Yamane K, Hanafusa M, Mori H, Mito K, Okubo M, Hara H, Kohno N. Elevated white blood cell count in subjects with impaired glucose tolerance. Diabetes Care. 2004;27:491-6. doi: 10.2337/diacare.27.2.491.
12. Orakzai RH, Orakzai SH, Nasir K, Santos RD, Rana JS, Pimentel I, Carvalho JA, Meneghello R, Blumenthal RS. Association of white blood cell count with systolic blood pressure within the normotensive range. J Hum Hypertens. 2006;20:341-7. doi: 10.1038/sj.jhh.1001992.
13. Li C, Engström G, Hedblad B. Leukocyte count is associated with incidence of coronary events, but not with stroke: a prospective cohort study. Atherosclerosis. 2010;209:545-50. doi: 10.1016/j.atherosclerosis.2009.09.029.
14. Babio N, Ibarrola-Jurado N, Bulló M, Martínez-González MÁ, Wärnberg J, Salaverría I et al. White blood cell count as risk markers of developing metabolic syndrome and its components in the PREDIMED study. PLoS One. 2013;8:e58354. doi: 10.1371/journal.pone.0058354.
15. Expert panel on metabolic syndrome of Chinese diabetes society. Recommendations on metabolic syndrome of Chinese diabetes society. Chin J Diabetes. 2004;12:156-61. (In Chinese)
16. Kim DJ, Noh JH, Lee BW, Choi YH, Chung JH, Min YK, Lee MS, Lee MK, Kim KW. The associations of total and differential white blood cell counts with obesity, hypertension, dyslipidemia and glucose intolerance in a Korean population. J Korean Med Sci. 2008;23:193-8. doi: 10.3346/jkms.2008.23.2.193.
17. Lohsoonthorn V, Jiamjarasrungsi W, Williams MA. Association of hematological parameters with clustered components of metabolic syndrome among professional and office workers in bangkok, Thailand. Diabetes Metab Syndr. 2007;1:143-9. doi: 10.1016/j.dsx.2007.05.002.
18. Bain BJ. Ethnic and sex differences in the total and differential white cell count and platelet count. J Clin Pathol. 1996;49:664-6. doi: 10.1136/jcp.49.8.664.
19. Meng W, Zhang C, Zhang Q, Song X, Lin H, Zhang D et al. Association between leukocyte and metabolic syndrome in urban Han Chinese a longitudinal cohort study. PLoS One. 2012;7:e49875. doi: 10.1371/journal.pone.0049875.
20. Odagiri K, Uehara A, Mizuta I, Yamamoto M, Kurata C. Longitudinal study on white blood cell count and the incidence of metabolic syndrome. Intern Med. 2011;50:2491-8. doi: 10.2169/internalmedicine.50.5877.
21. Vozarova B, Weyer C, Lindsay RS, Pratley RE, Bogardus C, Tataranni PA. High white blood cell count is associated with a worsening of insulin sensitivity and predicts the development of type 2 diabetes. Diabetes. 2002;51:455-61. doi: 10.2337/diabetes.51.2.455.
22. Hanley AJ, Retnakaran R, Qi Y, Gerstein HC, Perkins B, Raboud j, Harris SB, Zinman B. Association of hematological parameters with insulin resistance and beta-cell dysfunction in nondiabetic subjects. J Clin Endocrinol Metab. 2009;94:3824-32. doi: 10.1210/jc.2009-0719.
23. Festa A, D'Agostino R Jr, Howard G, Mykkanen L, Tracy RP, Haffner SM. Chronic subclinical inflammation as part of the insulin resistance syndrome: the Insulin Rsistance Atherosclerosis Study (IRAS). Circlulation. 2000;102:42-7. doi: 10.1161/01.CIR.102.1.42.
24. De Rooij SR, Nijpel G, Nilsson PM, Nolan JJ, Gabriel R, Mingrone G, Dekker JM. Low-grade chronic inflammation in the relationship between insulin sensitivity and cardiovascular disease (RISC) population: association with insulin resistance and cardiometabolic risk profile. Diabetes Care. 2009;32:1295-301. doi: 10.2337/dc08-1795.
25. Targher G, Seidell JC, Tonoli M, Muggeo M, De Sandre G, Cigolini M. The white blood cell count: its relationship to plasma insulin and other cardiovascular risk factors in healthy men individuals. J Intern Med. 1996;239:435-41. doi: 10.1046/j.1365-2796.1996.815000.x.
26. Lorenzo C, Hanley AJ, Haffner SM. Differential white cell count and incident type 2 diabetes: the Insulin Resistance Atherosclerosis Study. Diabetologia. 2014;57:83-92. doi: 10.1007/s00125-013-3080-0.
27. Kitabchi AE, Temprosa M, Knowler WC, Kahn SE, Fowler SE, Haffner SM et al. Role of insulin secretion and sensitivity in the evolution of type 2 diabetes in the diabetes prevention program: effect of lifestyle intervention and metformin. Diabetes. 2005;54:2404-14. doi: 10.2337/diabetes.54.8.2404.
28. Razani B, Chakravarthy MV, Semenkovich CF. Insulin resistance and atherosclerosis. Endocrinol Metab Clin North Am. 2008;37:603-21. doi: 10.1016/j.ecl.2008.05.001.
29. Ghazarian M, Luck H, Revelo XS, Winer S, Winer DA. Immunopathology of adipose tissue during metabolic syndrome. Turk Patoloji Derg. 2015;31:172-180.
30. Hagita S, Osaka M, Shimokado K, Yoshida M. Adipose inflammation initiates recruitment of leukocytes to mouse femoral artery: role of adipo-vascular axis in chronic inflammation. PLoS One. 2011;6:e19871. doi: 10.1371/journal.pone.0019871.
31. Kawanishi N, Yano H, Yokogawa Y, Suzuki K. Exercise training inhibits inflammation in adipose tissue via both suppression of macrophage infiltration and acceleration of phenotypic switching from M1 to M2 macrophages in high-fat-diet-induced obese mice. Exerc Immunol Rev. 2010;16:105-18.
32. Ohashi K, Parker JL, Ouchi N, Higuchi A, Vita JA, Gokce N et al. Adiponectin promote macrophage polarization toward an anti-inflammatory phenotype. J Biol Chem. 2010;285:6153-60. doi: 10.1074/jbc.M109.088708.