Black-White Divergence in the Relation of White Blood Cell Count to Metabolic Syndrome in Preadolescents, Adolescents, and Young Adults: The Bogalusa Heart Study

WEI CHEN, MD, PHD
SATHANUR R. SRINIVASAN, PHD
JIHUA XU, MD
GERALD S. BERENSON, MD

OBJECTIVE — To examine the association between white blood cell (WBC) count and metabolic syndrome (MetS) by growth periods in black versus white individuals in the general population.

RESEARCH DESIGN AND METHODS — The study cohort consisted of 4,184 black and white preadolescents, adolescents, and adults. In this cohort, 743 adults were followed for 8.1–20.8 years longitudinally.

RESULTS — White versus black subjects had a significantly higher WBC count in all age-groups. WBC count was associated with more MetS components in whites than in blacks. Mean values of WBC increased significantly with increasing number of MetS components with adverse levels in adolescents and adults, with a stronger trend in whites. WBC count was longitudinally associated with MetS in whites only ($P < 0.001$).

CONCLUSIONS — The findings on the association between higher WBC count and MetS beginning in childhood, particularly in whites, underscore a potentially mechanistic link between systemic inflammation, MetS, and cardiovascular risk.

Diabetes Care 33:2474–2476, 2010

Epidemiological and clinical studies have shown that white blood cell (WBC) count, an important cellular marker of systemic inflammation, is associated with coronary heart disease, type 2 diabetes, and multiple components of metabolic syndrome (MetS), including obesity, insulin resistance, hypertension, and dyslipidemia (1–4). The objective of the present study is to examine the association between WBC count and MetS by age-group, cross-sectionally and longitudinally, in black versus white asymptomatic individuals enrolled in the Bogalusa Heart Study.

RESEARCH DESIGN AND METHODS

— Two cross-sectional surveys of children aged 4–17 years in 1988–1993 and two surveys of young adults aged 18–38 years in 1988–1996 were conducted for cardiovascular risk factors, including WBC count. Individuals who had a WBC count outside the clinically normal range (below 2,000 cells/μl or above 12,000 cells/μl) were excluded from analyses to remove influence of acute bacterial infection and other medical disorders. Subjects who were taking medications for hypertension, diabetes, and/or dyslipidemia or had missing values for any of the MetS risk variables were also excluded. The final sample size for the current cross-sectional analysis was 1,137 preadolescents (aged 4–11 years), 1,542 adolescents (aged 12–17 years), and 1,503 adults (aged 18–38 years). In this cohort, a subset of 743 adults was followed for 8.1–20.8 years with a mean follow-up period of 12.7 years.

Statistical methods

BMI (in children), waist circumference (in adults), HDL cholesterol, fasting triglycerides, and fasting glucose were selected as MetS components. In cross-sectional analysis of preadolescents, adolescents, and adults, the sex- and age-specific top quartiles (bottom quartile for HDL cholesterol) were used to define the adverse levels of the MetS components by race group because widely accepted cutoff values are not available for preadolescents and adolescents. In the longitudinal adult cohort, the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATPIII) cutoffs were used to define the adverse levels. Pearson correlation was used to assess the association of WBC count with the MetS components, adjusting for age, sex, and smoking (for adults). The difference in the correlation coefficients between race groups was tested by Fisher z test.

RESULTS

— White versus black subjects had a significantly higher WBC count among preadolescents (6,472 vs. 5,927 cells/μl, $P < 0.001$), adolescents (6,270 vs. 5,697 cells/μl, $P < 0.001$), and adults (6,496 vs. 6,037 cells/μl, $P < 0.001$). The racial differences in prevalence of MetS were significant in preadolescents (whites versus blacks: 18.5 vs. 12.9%, $P < 0.05$) and in adults (14.5 vs. 19.2%, $P < 0.05$), but not in adolescents (15.2 vs. 14.3%, $P > 0.05$). Mean values of WBC increased significantly with the increasing number of MetS components with adverse levels in adolescents ($P < 0.001$ in whites, $P = 0.040$ in blacks) and adults ($P < 0.001$ in whites, $P = 0.015$ in

From the Department of Epidemiology, Tulane Center for Cardiovascular Health, Tulane University, New Orleans, Louisiana.
Corresponding author: Gerald S. Berenson, berenson@tulane.edu.
Received 30 March 2010 and accepted 19 August 2010. Published ahead of print at http://care.diabetesjournals.org on 26 August 2010. DOI: 10.2337/dc10-0619.

Table 1—*Pearson correlation coefficients of white blood cell count with MetS variables by age groups and race, adjusting for age, sex, and smoking (for adults)*

	Cross-sectional analysis					
	Preadolescents		Adolescents		Adults	
	Whites	Blacks	Whites	Blacks	Whites	Blacks
n	712	425	902	642	1,082	421
Age (years)	4–11	4–11	12–17	12–17	18–38	18–38
BMI	0.104**	0.017	0.159***	0.115**	0.219***	0.133**
Waist circumference					0.214***	0.112*
Systolic BP	0.095*	0.107*	0.082*	0.018	0.144***	0.032†
Diastolic BP	0.022	0.048	0.065	−0.017	0.136***	−0.028‡
Glucose	−0.081*	−0.085	−0.051	−0.139***	−0.012	0.002
Log-insulin	0.072	0.042	0.105**	−0.030‡	0.237***	0.097†
Log-HOMA-IR	0.051	−0.018	0.052	−0.041	0.192***	0.083
HDL cholesterol	−0.088*	−0.084	−0.109**	−0.032	−0.076*	−0.032
Log-triglycerides	0.115**	0.149**	0.179***	0.140***	0.305***	0.122*†
Heart rate	0.156***	0.082	0.141***	0.152***	0.104**	0.127**
Uric acid	0.046	0.033	0.096**	0.071	0.148***	0.062

	Longitudinal analysis			
	Baseline		Follow-up	
	Whites	Blacks	Whites	Blacks
n	538	205	538	205
BMI	0.180***	0.039	0.221***	0.086
Waist circumference	0.197***	0.005†	0.224***	0.028†
Systolic BP	0.139**	0.055	0.134**	0.190**
Diastolic BP	0.134**	−0.016	0.121**	0.241***
HDL cholesterol	−0.075	0.050	−0.129**	0.009
Log-triglycerides	0.163***	0.092	0.171***	0.071
Heart rate	0.111**	0.061	0.097*	0.090
Uric acid	0.134**	0.034	0.119**	0.007

Different from zero: *$P < 0.05$; **$P < 0.01$; ***$P < 0.001$. Racial difference: †$P < 0.05$; ‡$P < 0.01$. BP, blood pressure; HOMA-IR, homeostasis model assessment of insulin resistance.

blacks). Table 1 shows Pearson correlation coefficients of WBC count with MetS risk variables by race and age-groups, adjusting for age sex and smoking (for adults), in cross-sectional and longitudinal analyses. In general, WBC was associated with more MetS variables in whites than in blacks, especially among adults, in both cross-sectional and longitudinal analyses. Furthermore, in the longitudinal analyses, the mean values of baseline WBC count increased significantly with the increasing number of MetS components with adverse levels at follow-up in whites ($P < 0.001$), but not in blacks ($P = 0.137$).

CONCLUSIONS — The present study demonstrated a pronounced black-white difference in the relationship between WBC count and MetS risk variables in children and young adults in both cross-sectional and longitudinal analyses. The Coronary Artery Risk Development in Young Adults (CARDIA) study investigated correlates of leukocyte count in 4,981 black and white young adults aged 18–30 years similar to the age range of the present study cohort; however, the data were not analyzed separately by race group (5). In the Atherosclerosis Risk in Communities (ARIC) study, the associations of WBC count with sociodemographic and cardiovascular risk factors were examined in 4,832 white and 1,830 black nonsmokers aged 45–64 years; this cross-sectional analysis did not show black-white difference in the associations for most of the risk factors (6). Therefore, the findings of the black-white contrasts in the present study need confirmation, particularly in populations of similar ages.

In the present study, WBC count was significantly lower in blacks than in whites; this racial difference persisted from childhood into adulthood. This observation is consistent with reports from other studies (5–7). However, levels of C-reactive protein, another biomarker of inflammation, were found to be significantly higher in blacks than in whites in our previous report in a cohort from the same community (8). Although blacks have higher prevalence rates of type 2 diabetes and cardiovascular disease (9), studies, including ours, in both children and adults showed lower prevalence of MetS in blacks (10–12). It is proposed that the ethnic differences in triglycerides and HDL cholesterol levels lead to underdiagnosis of MetS in blacks (12). In the cross-sectional analysis of the present study, the prevalence of MetS was found to be lower in black preadolescents but higher in black adults than their white counterparts. Taken together, the pathophysiological mechanisms underlying the association between WBC count and

MetS in racial groups may be divergent and need to be elucidated.

Acknowledgments— This study was supported by grants HD-061437 and HD-062783 from the National Institute of Child Health and Human Development, grant 0855082E from American Heart Association, grant 546145G1 from Tulane University, and grant AG-16592 from the National Institute on Aging.

No potential conflicts of interest relevant to this article were reported.

C.W. generated the concept and design, reviewed the literature, analyzed the data, and wrote the manuscript. S.R.S. interpreted data, contributed to the discussion, and reviewed/edited the manuscript. J.X. determined biochemical data. G.S.B. generated the concept and design and reviewed/edited the manuscript.

References

1. Madjid M, Awan I, Willerson JT, Casscells SW. Leukocyte count and coronary heart disease: implications for risk assessment. J Am Coll Cardiol 2004;44:1945–1956
2. Pickup JC. Inflammation and activated innate immunity in the pathogenesis of type 2 diabetes. Diabetes Care 2004;27:813–823
3. 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 [retracted in: Endocr J 2006;53:871]. Endocr J 2006;53:133–139
4. Bardini G, Dicembrini I, Cresci B, Rotella CM. Inflammation markers and metabolic characteristics of subjects with 1-h plasma glucose levels. Diabetes Care 2010; 33:411–413
5. Friedman GD, Tekawa I, Grimm RH, Manolio T, Shannon SG, Sidney S. The leucocyte count: correlates and relationship to coronary risk factors: the CARDIA study. Int J Epidemiol 1990;19:889–893
6. Nieto FJ, Szklo M, Folsom AR, Rock R, Mercuri M. Leukocyte count correlates in middle-aged adults: the Atherosclerosis Risk in Communities (ARIC) Study. Am J Epidemiol 1992;136:525–537
7. Shaper AG, Lewis P. Genetic neutropenia in people of African origin. Lancet 1971; 2:1021–1023
8. Patel DA, Srinivasan SR, Xu JH, Li S, Chen W, Berenson GS. Distribution and metabolic syndrome correlates of plasma C-reactive protein in biracial (black-white) younger adults: the Bogalusa Heart Study. Metabolism 2006;55:699–705
9. Grundy SM. Metabolic syndrome pandemic. Atheroscler Thromb Vasc Biol 2008;28:629–636
10. Chen W, Bao W, Begum S, Elkasabany A, Srinivasan SR, Berenson GS. Age-related patterns of the clustering of cardiovascular risk variables of syndrome X from childhood to young adulthood in a population made up of black and white subjects: the Bogalusa Heart Study. Diabetes 2000;49:1042–1048
11. Park YW, Zhu S, Palaniappan L, Heshka S, Carnethon MR, Heymsfield SB. The metabolic syndrome: prevalence and associated risk factor findings in the US population from the Third National Health and Nutrition Examination Survey, 1988–1994. Arch Intern Med 2003; 163:427–436
12. Sumner AE. Ethnic differences in triglyceride levels and high-density lipoprotein lead to underdiagnosis of the metabolic syndrome in black children and adults. J Pediatr 2009;155(Suppl. 7):e7–e11