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

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Running Head: White Blood Cells and Metabolic Syndrome

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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 4184 black and white preadolescents, adolescents and adults. In this cohort, 743 adults were followed 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 white, underscore a potentially mechanistic link between systemic inflammation, MetS and cardiovascular risk.

Epidemiologic and clinical studies have shown that white blood cell (WBC) count, an important cellular marker of systemic inflammation, is associated with coronary heart disease, type2 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 groups, cross-sectionally and longitudinally, in black versus white asymptomatic individuals enrolled in the Bogalusa Heart Study.

RESEARCH DESIGN AND METHODS

Study cohort. Two cross-sectional surveys of children aged 4-17 years in 1988-93 and two surveys of young adults aged 18-38 years in 1988-96 were conducted for cardiovascular risk factors, including WBC count. Individuals who had a WBC count outside the clinical 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 1137 preadolescents (ages 4-11 years), 1542 adolescents (ages 12-17 years) and 1503 adults (ages 18-38 years). In this cohort, a subset of 743 adults was followed 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 groups 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’s Z-test.

RESULTS

White versus black subjects had a significantly higher WBC count among preadolescents (6472 vs 5927 cells/µL, \( p<0.001 \)), adolescents (6270 vs 5697 cells/µL, \( p<0.001 \)) and adults (6496 vs 6037 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 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. CARDIA study investigated correlates of leukocyte count in 4981 black and white young adults aged 18-30 years which were similar to the age range of the present study cohort; however, the data were not analyzed separately by race groups (5). In ARIC study, the associations of WBC count with sociodemographic and cardiovascular risk factors were examined in 4832 white and 1830 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 in 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 high-density lipoprotein 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 ethnic groups may be divergent and need to be elucidated.

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

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

| Cross-sectional Analysis | Preadolescents (4-11 years) | Adolescents (12-17 years) | Adults (18-38 years) |
|--------------------------|-----------------------------|---------------------------|---------------------|
|                          | Whites (n=712) | Blacks (n=425) | Whites (n=902) | Blacks (n=642) | Whites (n=1082) | Blacks (n=421) |
| 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 (n=538) | Follow-up (n=538) |
|--------------------------|------------------|------------------|
|                          | Whites (n=205) | Blacks (n=205) | Whites (n=538) | Blacks (n=538) |
| 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***       |
| Glucose                  | -0.059         | 0.006          | 0.079         | 0.021          |
| 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          |

BMI=body mass index; BP=blood pressure; HOMA-IR=homeostasis model assessment of insulin resistance; HDL=high-density lipoprotein
Different from zero: * p<0.05; ** P<0.01; *** P<0.001
Racial difference: † p<0.05; ‡ p<0.01