DIFFERENTIAL IMPACT OF CARDIOVASCULAR DISEASE (CVD) RISK FACTOR CLUSTERING ON CVD AND RENAL DISEASE AMONG AFRICAN-AMERICAN AND WHITE PATIENTS WITH TYPE 2 DIABETES MELLITUS

Objectives: To determine if clustering of cardiovascular disease (CVD) risk factors has a differential impact on CVD and renal disease among African Americans compared to Whites with type 2 diabetes.

Design: Cross-sectional.

Methods: Prevalent CVD, macroalbuminuria, and CVD risk factors were measured in 323 African-American and White adult patients with type 2 diabetes. CVD risk factors were dichotomized according to standard guidelines. Data were analyzed by race according to the presence of any 3 or more CVD risk factors.

Results: Despite a similar prevalence of hypertension, the prevalence of macroalbuminuria in the presence of 3 or more CVD risk factors tended to be higher among African Americans compared to Whites (28.9% vs 13.6%, \(P=0.05\)). The presence of 3+ CVD risk factors was associated with an odds ratio (OR) of 2.5 (\(P=0.001\), 95% CI, 1.44–4.27) for macroalbuminuria in African Americans compared to an OR of 1.4 (\(P=0.25\), 95% CI, 0.78–2.53) in Whites. The race/3+ CVD risk factors interaction was statistically significant (\(P=0.007\)). Conversely, the presence of 3+ risk factors was associated with an OR of 1.6 (\(P=0.019\), 95% CI, 1.08–2.28) for CVD in Whites compared to an OR of 0.8 (\(P=0.287\), 95% CI, 0.54–1.20) in African Americans. The prevalence of any CVD in the presence of 3+ risk factors was 61% and 49% in Whites and African Americans respectively (\(P=0.217\)). The race/3+ CVD risk factors interaction was statistically significant (\(P=0.029\)).

Conclusions: These findings suggest that among persons with diabetes, a clustering of 3+ CVD risk factors is more predictive for renal disease among African Americans, and more predictive for CVD in Whites. Further research should clarify the impact of CVD risk factor clustering on the incidence of vascular disease among African Americans and Whites with type 2 diabetes. (Ethn Dis. 2002;12:530–534)

Key Words: Diabetes Mellitus, Cardiovascular Disease, Risk Factors

INTRODUCTION

In addition to being at increased risk for type 2 diabetes mellitus, African Americans suffer disproportionately from the disease, with an increased mortality rate and a greater prevalence of end-stage renal disease (ESRD). However, while overall cardiovascular disease (CVD) mortality appears to be greater among African Americans compared to Whites, among individuals with diabetes, CVD and ischemic heart disease mortality (IHD) rates are lower for African Americans. Both African-American males and females with diabetes have lower death rates from both IHD and CVD, compared to Whites. This phenomenon may be due to higher competing mortality in African Americans from other diabetes-related conditions such as nephropathy.

CVD risk factors tend to cluster together, with CVD morbidity/mortality risk increasing proportionately with the number of risk factors present. Individuals with type 2 diabetes typically have one or more additional CVD risk factors, and the major cause of death in this group is CVD. However, neither the prevalence of CVD risk factor clustering, nor its association with vascular disease, has been adequately described, especially in African Americans with diabetes. We hypothesized that the effect of CVD risk factor clustering on risk of CVD and nephropathy may differ between African Americans and Whites. This study examines CVD risk factor clustering and its association with CVD and nephropathy by race in type 2 diabetes.

METHODS

Three hundred and twenty-three individuals with a diagnosis of type 2 diabetes mellitus were recruited from the Family Medicine ambulatory care unit at Wake Forest University School of Medicine and a community health clinic. Potential participants were identified through a computerized database and invited by mail to receive a free screening to determine the prevalence and number of risk factors for both CVD and renal disease. Those interested in the screening called the clinic and were scheduled for an initial appointment. Thirty-one percent of those contacted agreed to participate, with similar response rates from African Americans and Whites. This study was approved by our institutional review board (IRB), and written informed consent was obtained from each participant.

Height and weight were measured during a physical examination, and a body mass index (BMI = wt in kg/ht in m\(^2\)) was derived for each subject. Obesity was defined as a BMI ≥28. Blood pressure (BP) was measured on the left arm of each subject after a 5-minute...
This study examines CVD risk factor clustering and its association with CVD and nephropathy by race in type 2 diabetes.

Rest, with the subject in a seated position. The presence of hypertension was determined by the subject having a systolic BP \( \geq 140 \) mm Hg, a diastolic BP \( \geq 90 \) mm Hg, or currently receiving anti-hypertensive medications. Smoking status was determined by questionnaire.

After a 12-hour fast, each patient had venous blood drawn for determination of lipid levels and glycosylated hemoglobin (HbA\(_1c\)). Total cholesterol was determined by enzymatic assay. High-density lipoprotein (HDL) cholesterol was measured using a precipitation technique.\(^9\) Low-density lipoprotein cholesterol (LDL) was estimated using the Friedewald formula.\(^10\) Hyperlipidemia was defined as either a total cholesterol \( \geq 240 \) mg/dL, LDL \( \geq 160 \) mg/dL, or HDL \( < 35 \) mg/dL. HbA\(_1c\) was determined using the BioRad column procedure (Richmond, Calif). Urinary albumin excretion was assessed from an overnight urine collection and analyzed by radioimmunoassay to determine urinary albumin excretion ratios (UAER).\(^11\) An overnight urine collection involves collecting all urine voided after going to bed, as well as the first morning void. Macroalbuminuria was used as a marker for nephropathy and was defined as a UAER \( > 0.2 \) g albumin/g creatinine. Cardiovascular disease was determined from patient interview, medical history, and chart review, and was defined as either a previous abnormal electrocardiogram, significant findings on coronary angiography, history of bypass surgery, angioplasty, classic angina, stroke, signs of asymmetric carotid pulses or bruits, the presence of a neurologic abnormality on memory, verbal, motor, or sensory examination, asymmetric or diminished dorsalis pedis or posterior tibial pulses, or a history of claudication. Medical histories were verified by examination of medical records.

Means and standard deviations were calculated for each study variable. Chi-square and analysis of variance procedures were used to evaluate differences in demographic and clinical measures between groups. Logistic regression analysis was used to identify independent predictors of macroalbuminuria and CVD. Three models were used to adjust for the following: 1) unadjusted; 2) sex and duration of diabetes; 3) sex, diabetes duration, insulin treatment, and HbA\(_1c\), with separate analyses performed by race. Significance was established as \( P<.05 \). All statistical procedures were carried out using the Statistical Package for the Social Sciences for Personal Computers (SPSS, Inc, Chicago, Ill).

RESULTS

Table 1 presents demographic and clinical variables by race for the study sample. Compared to Whites, African Americans were more likely to be female, to be treated with insulin, to be obese and to have higher HbA\(_1c\) levels, and were less likely to have low HDL levels. No racial differences were found for age, diabetes duration, smoking, or elevated total or LDL cholesterol, or BP. Risk factor sums ranged from 0 to 5, and were equally common among African Americans and Whites (Figure 1). The prevalence of macroalbuminuria in the presence of any 3 or more CVD risk factors tended to be higher among African Americans compared to Whites (28.9% vs 13.6%, respectively; \( P=0.05 \)) (Table 2). Conversely, the prevalence of CVD in the presence of 3+ risk factors was 61% and 49% in Whites and African Americans respectively, although this difference was not statistically significant (\( P=.217 \)).

Table 3 gives odds ratios (OR) for macroalbuminuria and CVD in the presence of 3+ CVD risk factors. After adjustment for all covariates, regression analyses indicated that the presence of 3+ risk factors was associated with an OR of 2.5 (\( P=.001 \), 95% CI, 1.44–4.27) for macroalbuminuria in African Americans compared to an OR of 1.4 (\( P=.25 \), 95% CI, 0.78–2.53) in Whites. The race/3+ CVD risk factors

| Table 1. Demographic and clinical characteristics of 323 White and African-American patients with type 2 diabetes mellitus |
|-----------------|-----------------|-----------------|-----------------|
| Variables       | White (N=170)   | African American (N=153) | \( P \) Value |
| Age (mean ± SD) | 58.9 ± 12.1     | 57.2 ± 12.1     | .211           |
| Female (%)      | 48.2            | 69.9            | \(<.001\)      |
| Diabetes duration (years) | 8.4 ± 7.7     | 8.7 ± 8.0       | .702           |
| Glycosylated hemoglobin (% ± SD) | 6.9 ± 1.8     | 7.7 ± 2.4       | .001           |
| Current cigarette smoker (%) | 18.2         | 22.0            | .372           |

<table>
<thead>
<tr>
<th>Diabetes treatment</th>
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<tbody>
<tr>
<td>Insulin (%)</td>
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<tr>
<td>Oral agents (%)</td>
</tr>
<tr>
<td>Hypertensive (%)</td>
</tr>
<tr>
<td>Body mass index (% ≥28.0)</td>
</tr>
<tr>
<td>Total cholesterol (% ≥240 mg/dl)</td>
</tr>
<tr>
<td>HDL-cholesterol (% &lt;35 mg/dl)</td>
</tr>
<tr>
<td>LDL-cholesterol (% ≥160 mg/dl)</td>
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<tr>
<td>Macroalbuminuria (%)</td>
</tr>
<tr>
<td>CVD* (%)</td>
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</tbody>
</table>

\* CVD = cardiovascular disease.
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Fig 1. Prevalence of CVD risk factors among patients with type 2 diabetes mellitus, by race (all comparisons non-significant)

The interaction was significant (P=.007) for macroalbuminuria. The presence of 3+ risk factors was associated with an OR of 1.6 (P=.019, 95% CI, 1.08–2.28) for CVD in Whites compared to an OR of 0.8 (P=0.287, 95% CI, 0.54–1.20) in African Americans. The race/3+ CVD risk factors interaction was also significant (P=.029) for CVD.

DISCUSSION

Individuals with CVD typically exhibit more than one risk factor for the disease, and risk factor clustering has been observed frequently in the general population. Seventeen percent of participants in the Framingham Offspring Study,5 and 14.4% of the participants in the First National Health and Nutrition Examination (NHANES I) Epidemiologic Follow-up Study6 were found to have at least 3 known CVD risk factors. Others have found that factors proposed to make up the insulin resistance syndrome (abdominal obesity, hyperlipidemia, hyperglycemia, and hypertension) are found together in 25% to 80% of the general population, depending on the age and ethnicity of the sample.12–15

Due to an increased risk of CVD, one might expect that persons with diabetes would also be likely to have multiple risk factors for the disease. The present study found that the clustering of 3 or more CVD risk factors is common in this population. These risk factors occurred in isolation only 7.7% of the time. Approximately 33% of subjects had any 2 risk factors while 32.2% had any 3 or more. The risk factor prevalence rates were similar for African-American and White participants.

The tendency of these CVD risk factors to cluster suggests a common pathogenesis, although other environmental and/or genetic factors are involved, as each risk factor can occur in isolation. Insulin resistance and abnormal sympathoadrenal activity have been suggested as causal factors for risk factor clustering.16 Insulin resistance is often accompanied by hyperinsulinemia and a down regulation of lipoprotein lipase activity, leading to dyslipidemia.17 Hyperinsulinemia has also been postulated to stimulate the sympathetic nervous system, which may lead to adverse vascular and renal effects, thereby contributing to the pathogenesis of hypertension.18

Coronary heart disease morbidity and mortality, and mortality from CVD, occur less frequently in African Americans with diabetes compared to Whites. The 2nd National Health and Nutrition Examination Study indicated that, compared to African Americans, Whites with newly diagnosed diabetes were 2.3 times as likely to have a history of angina, and 3 times as likely to have suffered a myocardial infarction.8 In addition, African Americans with diabetes are less likely to die from either IHD or CVD, compared to their White counterparts, a pattern that has existed at least since the 1980s.19,20 Among men, the age-adjusted mortality rates with IHD listed as the underlying cause of death (from 1996) are 354.5 vs 642.2/100,000 for African Americans and Whites, respectively.1 Among women, age-adjusted rates are 316.4 vs 495.9/100,000 for African Americans and Whites, respectively. A similar pattern exists for mortality from CVD. It is possible that competing mortality due to other diabetes-related conditions, such as nephropathy, account for these ethnic differences, as African Americans are significantly more likely to develop diabetic ESRD compared to Whites.3,4

Our results support this hypothesis, as clusters of 3 or more CVD risk factors were associated with an increased risk of macroalbuminuria only in African Americans.

The question of why risk factor clustering may be associated with renal

Table 2. Prevalence of renal disease and cardiovascular disease by race and number of cardiovascular disease risk factors among persons with type 2 diabetes

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Macroalbuminuria</th>
<th>Cardiovascular Disease</th>
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<tbody>
<tr>
<td></td>
<td>Whites</td>
<td>African Americans</td>
</tr>
<tr>
<td>Zero or any one</td>
<td>9.1%</td>
<td>1.8%</td>
</tr>
<tr>
<td>Any two</td>
<td>5.4%</td>
<td>17.0%</td>
</tr>
<tr>
<td>Any three or more</td>
<td>13.6%</td>
<td>28.9%</td>
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</table>
function in African Americans is unanswered. Although hypertension increases the risk of developing renal disease in most populations, its effect seems to be enhanced in African Americans.21,22 Perhaps high BP and/or its interaction with other risk factors produces renal impairment prior to CVD in African Americans. It is also possible that genetic or biologic factors are responsible as there is evidence suggesting that African Americans are genetically more susceptible to developing renal disease.23 Other possible explanations could include differences in socioeconomic status; lack of access to, and/or lack of utilization of, healthcare services; diet; stress; or other environmental variables, although these factors would also tend to increase the risk of CVD in this population.

Risk for CVD has been found to increase proportionately with the number of risk factors.5-7 While we found this to be true in Whites with diabetes, clusters of 3 or more risk factors were not associated with CVD in African Americans. It has been suggested that the lower CVD mortality rate in African Americans with diabetes may involve insulin resistance. African Americans may be less likely than Whites to have the insulin resistant variant of type 2 diabetes which may lead to a lower CVD risk factor profile.24,25 In addition, metabolic abnormalities may have a weaker association with insulin resistance in this population.26 These factors may impact CVD risk in African Americans with type 2 diabetes. However, much of the more favorable risk factor profile found between those with the insulin sensitive and insulin resistant variants of type 2 diabetes involve more favorable lipid and lipoprotein levels.24,25 While the observed favorable lipid profile could be cardio-protective, a more favorable lipid profile is a consistent finding in African Americans compared to Whites, both with27-29 and without30-32 diabetes. This more favorable lipid profile would tend to reduce CVD mortality among African Americans compared to Whites in samples without diabetes as well, a finding which has not been documented as African Americans in the general population appear to suffer similar or greater overall mortality from CVD.33 Our results suggest that the lower CVD mortality found in African Americans with diabetes compared to Whites is partially due to a more detrimental, or earlier, effect of CVD risk factor clustering on renal function in this population.

While these data concentrate on differences by race there is not consensus within the scientific community or from federal health statistics regarding the meaning of concepts such as race and ethnicity.34 Given this lack of consensus, the absence of explicit race definitions may be a limitation to our data although self-report agreement appears to be very high among African Americans and Whites.35 Other limitations include possible selection bias, confounding by variables not controlled for or measured, limitations of statistical power and the generalizability of our sample population.

In conclusion, multiple CVD risk factors were equally common in both African Americans and Whites with diabetes. Although the prevalence of certain risk factors, such as hypertension and high cholesterol, has declined in the United States over the past 2 decades, the prevalence of obesity and diabetes has increased,36-38 underscoring the importance of risk factor prevention and control. The differential association of risk factor clustering found in the present study may partially explain the higher ESRD rates and lower IHD and CVD mortality among African Americans compared to Whites with diabetes. Additional research should be directed toward the elucidation of the pathophysiological basis for the ethnic differences in the impact of CVD risk factors on the occurrence of renal disease and CVD in patients with diabetes mellitus.

**REFERENCES**


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Table 3. Odds ratios (95% CI) of cardiovascular disease and renal disease according to presence or absence of three or more cardiovascular disease risk factors

<table>
<thead>
<tr>
<th>Macroalbuminuria</th>
<th>Cardiovascular Disease</th>
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<tbody>
<tr>
<td>Whites</td>
<td>African American</td>
</tr>
<tr>
<td>Model 1†</td>
<td>1.4 (0.86–2.39)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>1.5 (0.87–2.65)</td>
</tr>
<tr>
<td>Model 3†</td>
<td>1.4 (0.78–2.53)</td>
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</table>

<table>
<thead>
<tr>
<th>Whites</th>
<th>African American</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1†</td>
<td>1.5 (1.08–2.05)</td>
</tr>
<tr>
<td>Model 2†</td>
<td>1.6 (1.11–2.29)</td>
</tr>
<tr>
<td>Model 3†</td>
<td>1.6 (1.08–2.28)</td>
</tr>
</tbody>
</table>

* Model 1 plus gender and diabetes duration.
† Model 1 plus gender, diabetes duration, glycosylated hemoglobin, and insulin treatment. Race/3 plus CVD risk factors interaction term for presence of macroalbuminuria, \(P=.007\) (Model 3); Race/3 plus CVD factors interaction term for presence of CVD, \(P=.029\) (Model 3).
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AUTHOR CONTRIBUTIONS

Design and concept of study: Summerson, Konen, Spangler

Acquisition of data: Summerson, Konen

Data analysis and interpretation: Summerson, Bell, Konen, Spangler

Manuscript draft: Summerson, Bell, Spangler

Statistical expertise: Summerson

Acquisition of funding: Konen

Administrative, technical, or material assistance: Konen

Supervision: Konen