Serum Lipoproteins in African Americans and Whites With Non–Insulin-Dependent Diabetes in the US Population

Catherine C. Cowie, PhD, MPH; Barbara V. Howard, PhD; Maureen I. Harris, PhD, MPH

Background Despite the significant role that dyslipidemia is believed to play in the development of cardiovascular disease in diabetes, most studies examining diabetic dyslipidemia in the United States have not been population based, and very little data are available for African Americans with diabetes. We used data from a national survey to compare the effect of diabetes on lipid concentrations in African-American and white men and women. In addition, we examined other factors related to lipid concentrations and controlled for these factors in our analyses.

Methods and Results The Second National Health and Nutrition Examination Survey included a representative sample of 4177 African Americans and whites in the US civilian noninstitutionalized population 20 to 74 years old. These persons were classified as having non–insulin-dependent diabetes mellitus (NIDDM) (n=720) or as being nondiabetic (n=3457) based on an oral glucose tolerance test and a medical history of diabetes. Subjects were given an interview and physical examination that included measurement of serum lipoproteins, body mass index, body fat distribution, dietary fat intake, alcohol consumption, frequency of smoking, and use of medications. By univariate analysis, a worse profile of mean cholesterol, triglycerides, and high-density lipoprotein cholesterol levels was generally apparent in NIDDM than in nondiabetic subjects, regardless of race or sex; a similar pattern was found for the prevalence of abnormal concentrations of these lipids. Lipid profiles appeared to be worse in whites with NIDDM than in African Americans. For mean total and low-density lipoprotein cholesterol, concentrations tended to be worse in women with NIDDM than in men. When other factors significantly affecting lipid levels were adjusted by multivariate analysis, we found that in all race/sex groups, total cholesterol was higher in NIDDM than in nondiabetic subjects but differences were not significant (P=.54), triglyceride concentrations were significantly higher in NIDDM subjects (P<.0001), and high-density lipoprotein cholesterol concentrations were lower in NIDDM subjects (P=.003). An interaction of diabetes with race was found for low-density lipoprotein cholesterol (P=.0001), where concentrations were substantially lower in NIDDM than in nondiabetic subjects among African Americans (P<.01) but slightly higher in NIDDM subjects among whites (P=.33). For other lipids, no differential effect of NIDDM was found by race or sex.

Conclusions In African-American and white men and women in the United States, NIDDM is associated with a pattern of dyslipidemia that may potentiate the atherosclerotic process. Diabetic treatment should include aggressive treatment of dyslipidemia to reduce this increased risk.


Key Words • diabetes • lipoproteins • cholesterol • race

Cardiovascular disease is the major cause of morbidity and mortality in individuals with non–insulin-dependent diabetes mellitus (NIDDM). In the United States, more than 27% of adults who have been diagnosed with NIDDM have angina or a history of previous myocardial infarction, a rate that is two to three times that of persons without a medical history of diabetes.1 Cardiovascular disease accounts for 75% of deaths among individuals with diabetes, with ischemic heart disease alone the cause of 50% of deaths.2 The age-standardized death rate from all cardiovascular disease and specifically from ischemic heart disease for diabetic men and women in the United States is approximately 2.5 times that of their nondiabetic counterparts.3 Risk factors for cardiovascular disease cluster in persons with NIDDM compared with persons without the disease.1,2,4-8 In particular, dyslipidemia, hypertension, and obesity.

Despite the significant role that dyslipidemia is believed to play in the development of cardiovascular disease in diabetes, most studies examining dyslipidemia in subjects with diabetes in the United States have not been population based, and very little data are available on African Americans with diabetes. The Second National Health and Nutrition Examination Survey (NHANES II) measured serum lipoprotein levels in subjects with and without NIDDM in the US population. We used these data to compare the effect of NIDDM on lipid concentrations in African Americans and whites and in men and women. In addition, we examined other factors related to lipid concentrations and controlled for these factors in our analyses.

Methods

Population

Data are drawn from the NHANES II conducted in 1976 through 1980.9-10 This survey included a sample of the general US population 20 to 74 years old (n=15 357), which was representative by age, sex, race (African American and white), geographic region, and level of income. The NHANES II data
have provided national estimates of the prevalence of diabetes and impaired glucose tolerance. Household interviews were conducted to obtain demographic and medical history information, including whether subjects had a medical history of physician-diagnosed diabetes. Seventy-seven percent of the interviewed sample participated in a physical examination. Data on examined participants have been found to be similar to those from the 1976 NHIS (for which the 96% response rate approximates true population values) on more than 70 health-related variables; examined persons are also similar in distribution to the total US population according to age, sex, race, income, and region. A representative half-sample of examined participants (excluding subjects with previously diagnosed diabetes) were eligible for an oral glucose tolerance test (OGTT). This test was administered according to recommendations of the National Diabetes Data Group. Subjects fasted overnight for 10 to 16 hours; a fasting venous blood sample was taken; 75 g of glucose (Glucola, Miles/Ames) was ingested; and venous blood samples were taken 2 hours later. Plasma glucose was measured using a microadaptation of the national glucose oxidase reference method. The OGTT was completed by 66% of eligible subjects. Previous studies have shown that persons who received the OGTT differed little or not at all from the total NHANES II interviewed sample without a medical history of diabetes with respect to age, sex, race, income, family history of diabetes, and a number of other demographic, clinical, and medical history factors.

By World Health Organization criteria, individuals who received the OGTT were classified by their plasma glucose values as having diabetes (fasting plasma glucose >7.8 mmol/L and/or 2-hour glucose ≥11.1 mmol/L; n=192) or as being nondiabetic (fasting plasma glucose <7.8 mmol/L and 2-hour plasma glucose <11.1 mmol/L; n=3522). Of the 558 examined participants who reported a medical history of diabetes, 14 appeared to have insulin-dependent diabetes based on age at diagnosis of <30 years, continuous use of insulin since diagnosis, and body mass index (weight [kg] divided by height [m] squared) <27 for men and <25 for women. These subjects were excluded from analysis. The remaining 544 subjects and all persons with diabetes detected by OGTT during the survey were considered to have NIDDM.

This report concerns the examined subsample of 439 African Americans (195 men and 244 women) and 3738 whites (1751 men and 1987 women) 20 to 74 years old. Of these, 720 had NIDDM and 3457 were nondiabetic. Persons of other races (n=81, 1.8%) were excluded because inferences from this small heterogeneous group would be limited. In linear regression analyses for prediction of factors related to mean lipid concentration, 26 persons (0.6%) using lipid-lowering drugs were also excluded.

The validity of self-reported data on a medical history of diabetes in the NHANES II has been analyzed in detail, with the potential for bias considered to be low or nonexistent. The rate of agreement between diabetes based on self-report from interview and medical records is >95%, with no difference by sex. Medical records are relatively accurate for the diagnosis of diabetes. Evidence against a reporting bias by race in the NHANES II is given by the similar proportions of African Americans and whites with a medical history of NIDDM who reported current use of insulin or oral hypoglycemic agents (65% of blacks and 60% of whites) and use of a written diet alone (14% of blacks and 15% of whites). In addition, blacks and whites are similar with regard to the proportion of NIDDM determined by OGTT (45% of blacks and 50% of whites).

**Measures of Lipoproteins and Other Variables**

Serum total cholesterol, fasting (≥10 hours) triglyceride, and high-density lipoprotein (HDL) cholesterol levels were measured according to the Lipid Research Clinics protocol. Lipid analyses were performed on zeolite-treated isopropanol extracts using a Technicon Auto-Analyzer II (AALII), which uses a Lieberman-Burchard reagent for cholesterol and a fluorimetric measurement of triglycerides. Assays were standardized using controls provided by the Clinical Chemistry Standardization Section, Centers for Disease Control and Prevention. HDL cholesterol was determined on a supernatant fraction obtained after treatment of the sera with heparin and manganese chloride. Low-density lipoprotein (LDL) cholesterol was estimated by the Friedewald formula (LDL cholesterol = total cholesterol – HDL cholesterol – triglycerides/5) for subjects whose triglyceride concentration was <400 mg/dL. Individuals with a medical history of diabetes were not asked to fast, and thus their fasting triglyceride and LDL cholesterol values could not be determined. For total cholesterol, 1.0% of values were imputed (based on sex, age, and, in women, hormone/birth control pill use) because they were unavailable for study subjects; results from our study were nearly identical whether imputed values were included or excluded. For triglycerides and HDL cholesterol, values were obtained for 99.3% and 83.7% of subjects, respectively. Analyses by Sempos et al did not show any detectable bias in national prevalence estimates due to loss of NHANES II sample data. Abnormal lipid concentrations were defined on the basis of guidelines of the National Cholesterol Education Program (NCEP).

In addition to the presence of NIDDM, variables considered potentially to affect lipid concentrations included age, sex, race, body mass index, body fat distribution assessed by skinfold-thickness ratio, total daily fat intake (as percent of calories) based on 24-hour recall, average alcohol intake in the previous 3 months (in number of drinks per week, with beer, wine, and liquor in equivalents of 1.5 oz of 86 proof liquor per drink), current smoking (in number of cigarettes smoked daily), current use of birth control pills, and use in the last week of hormones, diuretics, or steroids.

**Statistical Analyses**

To provide estimates that were representative of the US population, data were weighted by the inverse of the participation rate of study subjects according to age, sex, race, income, and geographic location. Standard errors of mean values and proportions were obtained by the Taylor Series linearization method using the computer program SUDAAN, which was developed for complex survey designs; these were used to construct 95% confidence intervals.

Linear regression analysis was used to assess the effects of the variables described above on mean total cholesterol, LDL cholesterol, HDL cholesterol, and fasting triglyceride levels. To examine whether the variables were associated with a more unfavorable lipidoprotein concentration in diabetic relative to nondiabetic subjects or whether diabetes had a worse effect on lipoprotein concentration in certain subgroups, we included all interactions of diabetes with these variables. Because lipid concentrations are affected by whether women are premenopausal or postmenopausal, we controlled for this effect by including the interaction of sex × age. Because hormones may affect lipids differently in women than in men, we included the interaction of sex × hormone use; hormones, however, were used almost exclusively in women (98.0%).

In preparation for linear regression analyses, correlation matrices of the predictive factors were examined for collinearity. We performed multiple linear regression analysis using the SURVEYREG program for complex surveys. Continuous variables were standardized to control rounding errors that may introduce imprecision in parameter and variance estimation. Squared terms of continuous variables were included in all models to examine whether relations were nonlinear. All other variables were coded categorically. Because the distribution of fasting triglycerides was not normally distributed, values for this lipid were log-transformed for regression analyses and then back-transformed for presentation of results.
To arrive at a final regression model, we eliminated variables by a backward stepwise procedure examining sequentially the statistical significance of coefficients and effects on outcome based on mean estimates. Models were hierarchical, in that whenever a squared or interaction term was included, related lower-order terms were retained.

Results

Lipids by Diabetes Status, Race, and Sex

Mean unadjusted lipid and lipoprotein concentrations are shown for men and women by race, age, and diabetes status (Figs 1 through 4). Mean total cholesterol concentrations (Fig 1) appeared to be higher in NIDDM than in nondiabetic subjects among whites at all ages (in whom differences were more pronounced in younger than in older subjects) and among younger African Americans. Total cholesterol levels tended to be higher in diabetic whites than in diabetic African Americans and in diabetic women than in diabetic men of either race. Mean LDL cholesterol levels (Fig 2) appeared to be lower in African Americans with NIDDM than in nondiabetic subjects. In white women and in older white men, LDL cholesterol levels appeared to be higher in those with NIDDM. Mean LDL cholesterol levels tended to be higher in diabetic whites than in diabetic African Americans and in diabetic women than in diabetic men. Mean HDL cholesterol levels (Fig 3) appeared to be lower in NIDDM than in nondiabetic subjects, except in the youngest men. Mean HDL cholesterol levels tended to be lower in diabetic whites than in diabetic African Americans and appeared to be higher in diabetic women than in diabetic men, except in the youngest age group. Mean fasting triglyceride concentrations (Fig 4) appeared to be higher in diabetic than in nondiabetic subjects, especially in whites.

The prevalence of abnormal lipid concentrations by race, sex, and diabetes status in persons 40 to 69 years old is shown in Fig 5. The prevalence of total cholesterol of >240 mg/dL tended to be higher in diabetic than in nondiabetic subjects, except in African-American men; prevalence was particularly high (46% to 49%) in white
diabetic subjects. Prevalence of LDL cholesterol of >160 mg/dL appeared to be higher in NIDDM than in nondiabetic subjects among white women but lower in NIDDM subjects among African Americans; prevalence was highest in white diabetic subjects of either sex. The prevalence of HDL cholesterol of <35 mg/dL tended to be higher in diabetic than in nondiabetic subjects in all race/sex groups. The prevalence of fasting triglycerides of >250 mg/dL appeared to be higher in NIDDM than in nondiabetic subjects, and rates were highest in white diabetic subjects of either sex.

Characteristics That Influence Serum Lipids, by Diabetes Status

The Table shows the prevalence of characteristics that may affect lipid concentrations. Compared with nondiabetic subjects, NIDDM subjects were older and a higher proportion were women. A higher proportion of diabetic subjects were African American. NIDDM subjects had higher body mass index (particularly in women) and a more central body fat distribution than nondiabetic subjects. Alcohol use and smoking were less frequent in NIDDM than in nondiabetic subjects. Birth control pills were used less frequently in diabetic than in nondiabetic women, whereas hormones (98.0% of which were used by women) tended to be used more frequently (consistent with their older age). A higher proportion of diabetic subjects used diuretics. The prevalence of steroid use was low for both diabetic and nondiabetic subjects.

Lipids by Diabetes Status, Race, and Sex, Adjusted for Covariates

Because of limitations of small sample size in some cells of the stratified univariate analyses above, linear regression analysis was used to obtain more powerful information concerning lipid levels according to diabetes status, race, and sex. Mean total cholesterol level adjusted for the covariates in the Table was higher in NIDDM than in nondiabetic subjects (Fig 6), but differences were not statistically significant (P=.54; differences by diabetes status were similar for all race and sex groups. Concentrations were highest for white women and lowest for African-American men. Results were similar when only diabetic subjects detected by OGTT were analyzed. The effect of diabetes status on LDL cholesterol was different in African Americans.
than in whites ($P=.0001$) (Fig 7): mean adjusted LDL cholesterol was substantially lower in NIDDM than in nondiabetic subjects among African Americans ($P<.01$) but slightly higher in NIDDM than in nondiabetic subjects among whites ($P=.33$). Mean LDL cholesterol was highest in white men and lowest in African-American women. Mean adjusted HDL cholesterol was lower in NIDDM than in nondiabetic subjects (Fig 8) ($P=.003$), with similar differences for all four race/sex groups. Mean HDL cholesterol was lowest in white men and highest in African-American women. Mean HDL cholesterol was significantly lower in whites than in African Americans ($P<.0001$) and in men than in women ($P<.0001$). Similar patterns were evident when only diabetic subjects as determined by OGTT were included, although HDL cholesterol levels in nondiabetic subjects were not significantly different ($P=.17$). Mean fasting triglyceride concentrations (Fig 9) were markedly higher in diabetic than in nondiabetic subjects ($P<.0001$), with similar differences in all four race/sex groups, and concentrations were highest in white men and lowest in African-American women. Mean triglycerides was significantly higher in whites than in African Americans ($P<.0001$) and in men than in women ($P<.0001$).

Discussion

The administration of the glucose tolerance test to a large group of individuals in the NHANES II has afforded the opportunity for examining, on a population basis, the associations of diabetes with lipoproteins in the United States. It offers the further advantage of having a cohort that systematically included a sample of African Americans. Because the majority of individuals with diabetes mellitus in the United States have NIDDM, we confined our analysis to these subjects by eliminating individuals who were thin, were diagnosed at an early age, and were receiving insulin therapy continuously since diagnosis, and thus were presumed to have IDDM. The results indicate that the pattern of dyslipidemia that has been repeatedly described in smaller samples of individuals with diabetes in the United States is generally observed in the population as a whole and in African Americans, although there may be quantitative differences in its extent.

Cholesterol

There was a substantially lower HDL cholesterol concentration in individuals with NIDDM in all age groups and in both races and sexes. This was significant even after adjustment for obesity, alcohol consumption, and other covariates known to influence HDL cholesterol. A lower HDL cholesterol level has been one of the most consistent observations in other studies of lipoproteins among individuals with NIDDM, both in the United States and in other countries5,29-32 and may be extremely important in understanding the increased risk of atherosclerosis among individuals with NIDDM.

Although lower HDL cholesterol is almost universally observed in individuals with NIDDM, surprisingly little is known about the mechanism for this decline. One possibility is that the lower HDL is a reflection of
<table>
<thead>
<tr>
<th>Characteristics of US African Americans and Whites 20 to 74 Years Old by Diabetes Status</th>
<th>NIDDM (n=720) (95% CI)</th>
<th>Nondiabetic (n=3457) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, y</td>
<td>56.8 (55.8-57.8)</td>
<td>41.8 (41.0-42.5)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men, %</td>
<td>40.3 (36.3-44.3)</td>
<td>48.0 (45.9-50.2)</td>
</tr>
<tr>
<td>Women, %</td>
<td>59.7 (55.7-63.7)</td>
<td>52.0 (49.8-54.1)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
</tr>
<tr>
<td>African American, %</td>
<td>14.7 (9.5-20.0)</td>
<td>10.2 (7.7-12.7)</td>
</tr>
<tr>
<td>White, %</td>
<td>85.3 (80.1-90.5)</td>
<td>89.8 (87.3-92.3)</td>
</tr>
<tr>
<td>Mean BMI, weight in kg/height in m²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>28.8 (27.9-29.8)</td>
<td>25.1 (25.0-25.3)</td>
</tr>
<tr>
<td>Men</td>
<td>27.1 (26.3-28.0)</td>
<td>25.5 (25.3-25.7)</td>
</tr>
<tr>
<td>Women</td>
<td>30.0 (28.6-31.3)</td>
<td>24.8 (24.4-25.2)</td>
</tr>
<tr>
<td>Mean subcapular-to-triceps skinfold ratio</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.27 (1.22-1.32)</td>
<td>1.14 (1.12-1.17)</td>
</tr>
<tr>
<td>Men</td>
<td>1.69 (1.60-1.78)</td>
<td>1.48 (1.44-1.51)</td>
</tr>
<tr>
<td>Women</td>
<td>0.99 (0.95-1.03)</td>
<td>0.83 (0.81-0.85)</td>
</tr>
<tr>
<td>Mean fat intake, % of calories</td>
<td>37.6 (36.5-38.7)</td>
<td>36.4 (36.0-36.8)</td>
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<tr>
<td>Alcohol intake, drinks per week*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>55.5 (50.1-61.0)</td>
<td>32.1 (29.0-34.8)</td>
</tr>
<tr>
<td>&lt;2</td>
<td>26.3 (21.1-31.6)</td>
<td>34.6 (32.8-36.3)</td>
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<tr>
<td>2 to &lt;5</td>
<td>6.3 (3.3-9.4)</td>
<td>17.6 (15.8-19.3)</td>
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<tr>
<td>≥5</td>
<td>11.8 (7.8-15.8)</td>
<td>15.8 (14.6-17.1)</td>
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<tr>
<td>No. of cigarettes per day (current)</td>
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<td></td>
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<tr>
<td>None</td>
<td>73.5 (68.2-78.7)</td>
<td>63.9 (61.8-65.9)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>8.7 (5.1-12.4)</td>
<td>13.2 (11.8-14.5)</td>
</tr>
<tr>
<td>≥20</td>
<td>17.8 (13.5-22.1)</td>
<td>23.0 (21.2-24.8)</td>
</tr>
<tr>
<td>Current birth control pill use (women), %</td>
<td>3.6 (0.0-7.2)</td>
<td>10.7 (8.9-12.4)</td>
</tr>
<tr>
<td>Hormone use in past week, %</td>
<td>6.9 (3.9-10.0)</td>
<td>4.8 (4.0-5.6)</td>
</tr>
<tr>
<td>Current birth control pills or hormone use in past week, %</td>
<td>9.0 (5.3-12.7)</td>
<td>9.9 (8.6-11.3)</td>
</tr>
<tr>
<td>Diuretic use in past week, %</td>
<td>26.7 (22.1-31.4)</td>
<td>8.1 (7.2-9.0)</td>
</tr>
<tr>
<td>Steroid use in past week, %</td>
<td>0.1 (0.0-0.3)</td>
<td>0.3 (0.1-0.5)</td>
</tr>
<tr>
<td>Duration of diabetes, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5</td>
<td>20.9 (17.4-24.5)</td>
<td></td>
</tr>
<tr>
<td>5 to 14</td>
<td>22.6 (19.2-26.0)</td>
<td></td>
</tr>
<tr>
<td>≥15</td>
<td>6.8 (5.3-8.3)</td>
<td></td>
</tr>
<tr>
<td>Undiagnosed</td>
<td>49.7 (44.0-55.4)</td>
<td></td>
</tr>
<tr>
<td>Diabetes therapy in previously diagnosed subjects, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td>22.4 (17.9-26.9)</td>
<td></td>
</tr>
<tr>
<td>Orals</td>
<td>34.8 (29.0-40.5)</td>
<td></td>
</tr>
<tr>
<td>Neither</td>
<td>42.9 (38.2-47.6)</td>
<td></td>
</tr>
</tbody>
</table>

NIDDM indicates non–insulin-dependent diabetes mellitus; CI, confidence interval; and BMI, body mass index.

*Beer, wine, and liquor in equivalents of 1.5 oz of 86 proof liquor per drink.

impaired triglyceride metabolism, since the HDL compartment is augmented during lipolysis of triglyceriderich lipoproteins.\(^{33}\) When HDL cholesterol concentrations were compared in the diabetic and nondiabetic groups after adjustment for triglyceride concentrations, the HDL cholesterol remained lower but the difference was substantially diminished (data not shown), suggesting the lower HDL level is induced in part by altered triglyceride metabolism. However, at least a part of the HDL decline may be a result of fundamental alterations...
in the processes that regulate HDL metabolism. Some studies have shown that individuals with NIDDM have higher levels of hepatic lipase and lower activities of lipoprotein lipase. Both of these changes would effectively lower HDL concentrations. More recent studies have suggested that there may be abnormalities in activities of cholesterol ester transfer protein and LCAT in individuals with diabetes, which could also explain the lowered HDL cholesterol level.

There was no difference in the mean concentrations of LDL cholesterol in white men or women with NIDDM compared with nondiabetic subjects, whereas in African-American men and women, there were lower levels of LDL among those with NIDDM. This was also reflected by the percent of individuals with abnormal LDL as defined by NCEP criteria. Compared with nondiabetic subjects, the proportion with elevated LDL cholesterol levels was similar in white diabetic men and higher in white diabetic women, whereas in African-American men and women the proportion was lower among NIDDM subjects. In previous studies of LDL concentrations in individuals with NIDDM, some have shown that individuals with NIDDM have elevated cholesterol, whereas others have shown no change in total or LDL cholesterol levels. The racial differences observed in the NHANES II data may provide some explanation as to why previous reports, in which racial groups have not been distinguished, have been equivocal.

There have been some studies of possible metabolic alterations in persons with NIDDM that might affect LDL. Overproduction of very-low-density lipoprotein (VLDL) and impaired clearance (see below) may lead to increased LDL concentrations. On the other hand, because insulin has been shown to stimulate LDL clearance and receptor activity, the hyperinsulinemia in those with NIDDM might result in lower LDL concentrations. Thus, the presence of one or the other of these mechanisms would determine whether there would be either mild elevations or decreases in LDL concentration. Other work has focused on abnormali-
ties in composition of LDL in individuals with NIDDM, such as glycation, oxidation, and altered size and density; these have been found to be frequent and can be related to potential atherogenic mechanisms. Thus, it remains important to monitor LDL levels in individuals with diabetes and to reduce levels to or below target values.

Patterns of total cholesterol concentration in NIDDM generally reflected those of LDL. An exception was that African Americans with NIDDM, who had lower concentrations of LDL than did nondiabetic subjects, had higher concentrations of total cholesterol. Total cholesterol reflects a combination of LDL, HDL, and VLDL cholesterol, the latter of which was not directly measured in the present study. The consistent observation of elevated triglycerides in NIDDM (see below) reflects elevated VLDL and thus elevated VLDL cholesterol levels. This could account for the differences in pattern between LDL and total cholesterol in African Americans with NIDDM. It should be emphasized that data for triglycerides, and therefore the calculation of LDL, were possible only in newly diagnosed diabetic subjects. One might postulate that increases in cholesterol become more apparent as hyperglycemia persists. This is an unlikely explanation for the differing patterns of LDL and total cholesterol, because when data for total cholesterol in the newly diagnosed diabetic subjects were analyzed separately (data not shown) in African Americans, total cholesterol levels remained higher in those with NIDDM.

Triglycerides

Consistently higher triglyceride concentrations were observed in individuals with NIDDM than in nondiabetic subjects of either sex and race. This is consistent with observations from previous studies. Of note, however, is that adjusted triglycerides were only approximately 30% higher in NIDDM subjects. Some reports from clinic-based samples of individuals with NIDDM have shown much higher levels of triglycerides. This probably represents individuals with concomitant hyperlipidemia. The observed differences in triglyceride concentrations, especially if they represent greater amounts of cholesterol-rich, potentially atherogenic remnants, may be extremely important in explaining the atherosclerotic process in individuals with diabetes. Some prospective studies have shown that plasma triglyceride concentration is a predictor of coronary heart disease in persons with diabetes. More studies are needed to determine to what extent triglycerides are a risk factor for atherosclerosis in diabetic individuals in the United States.

Race and Sex Differences

These data have afforded the first opportunity to examine the lipoprotein patterns in a representative sample of African Americans with NIDDM. Because the prevalence of NIDDM in the United States is higher in African Americans than in whites, it is especially important to understand its influence on risk factors for arteriosclerosis in this racial group. Compared with nondiabetic African Americans, African Americans with NIDDM have lower concentrations of HDL cholesterol and elevated concentrations of triglycerides, and the order of magnitude of difference appears to be similar to that of whites. Lower HDL cholesterol levels have been consistently associated with increased risk for atherosclerosis in all populations studied. Although elevated triglycerides are not always associated with atherosclerosis, in the case of individuals with diabetes, it has been postulated that the elevated triglycerides may be particularly atherogenic. The association between triglycerides and coronary heart disease should be examined in African Americans. On the other hand, there appears to be racial differences in the influence of diabetes on LDL cholesterol; in whites with diabetes there tended to be higher levels of LDL, whereas in African Americans with diabetes there were lower levels. As discussed above, the metabolic consequences of diabetes on LDL metabolism may depend on the extent to which both the production and catabolic processes are influenced. Race may be one of the determinants that influences this balance. Although there are no specific studies of LDL cholesterol composition in African Americans with diabetes, it is likely that the compositional changes in LDL cholesterol believed to be atherogenic, such as glycation, susceptibility to oxidation, and the presence of small dense particles, are probably present in African Americans as well. Thus, it is still important to treat elevated LDL cholesterol concentrations when they are observed in African-American patients with NIDDM.

Of interest is that the associations of diabetes with elevated LDL and total cholesterol levels in univariate analyses appeared to be greater in women, especially among whites. A number of longitudinal population-based studies have examined the relative magnitude of the increased risk conferred by diabetes on atherosclerosis in men compared with women. In several of the studies, women with diabetes were shown to have a greater increase in cardiovascular disease risk than men. The observation of a potentially greater effect of diabetes on LDL cholesterol is a possible partial explanation for this difference.

In summary, results from the NHANES II have shown that in both whites and African Americans in the United States, NIDDM is associated with a pattern of dyslipidemia, including lower HDL cholesterol, higher triglycerides, and in whites somewhat higher LDL cholesterol, which can potentiate the atherosclerotic process. Atherosclerotic heart disease is the leading cause of death among individuals with diabetes, and a recent clinical trial has suggested that treatment of dyslipidemia may reduce coronary heart disease in individuals with diabetes. It is thus important that, in addition to the control of glucose, dyslipidemia be treated aggressively in an attempt to reduce risk for cardiovascular disease.

Acknowledgments

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