Manuscript #294

1. Title:
Characterize the "dose-response" curve of the association between diabetic status, as described by fasting insulin and fasting glucose, and lipidemias.

Short title:
Insulin and dyslipidemias

2. Writing group:
(lead) H. Michael Arrighi, Rongling Li, Louis Smith, Fred Brancati, Gerardo Heiss

3. Timeline:
The target date for manuscript completion is 1 year from receipt of the data.

4. Rationale:
NIDDM (non-insulin dependent diabetes mellitus) patients are at an increased risk of CHD (coronary heart disease) and its associated mortality at rates 3-fold greater than that among non-diabetics. CVD (cardiovascular disease) risk factors, including, dyslipidemias are more common among diabetics than nondiabetes.

Haffner et al (1990) examined the relationship between cardiovascular disease (CVD) and hyperinsulinenima in the San Antonio Heart study. In the Mexican-American subjects who developed NIDDM in the 8-year follow-up and relative to those who did not develop NIDDM, a more atherogenic pattern of CVD risk factors was present including: lower levels of HDL cholesterol and increased LDL cholesterol. This study demonstrated that subjects who develop NIDDM are at increased risk for CVD and CAD (coronary artery disease).

A strong, nearly linear relationship of an OGTT (oral glucose tolerance test) and fasting triglycerides and fasting and 2-hour serum insulin concentrations was seen in Mauritians (Zimmet 1991). No relationships were seen between the 2-hour plasma glucose and HDL cholesterol. Only among men, was a relationship observed between total cholesterol and OGTT. Both men and women were observed to have increasing blood pressure with increasing 2-hour plasma glucose levels from an OGTT. However, among men the shape of the trend line appear supra-linear and among women the relationship was suggestive of a linear relationship.

A discussion was held with Dr. Aaron Folsom regarding ARIC Manuscript #179a, entitled "Fatty acids and insulin" to clarify if this proposal overlapped. The conclusion reached was that this proposal and Dr. Folsom's work do not overlap.

5. Main Study Question:
1) Using cross-sectional data, describe the shape of the curve ("dose-response") of the association between diabetic status (fasting insulin and fasting glucose) and lipids, and lipoprotein fractions.
2) Do these associations vary with fasting time, date of examination, and study site?
3) Do these associations vary with demographic factors: age, gender, and race?

6. Plan of Analysis:
The analyses will be race and gender-specific. The analysis will model and characterize the shape (dose-response curve) of the association between fasting insulin and fasting glucose with each of the serum
cholesterol measurements including subfractions (total, HDL, LDL, VLDL, triglycerides, and subfractions). The following lipid measure are of particular interest: HDDL, HDL2, Lp(a), and triglycerides. These lipid measures have strong associations with NIDDM. Fasting glucose is needed to help establish diabetic status. Variables for their potential confounding and effect-modifying role will be age, medication for diabetes, medications affecting cholesterol level, field center, examination dates, and anthropometric measurements, date diagnosed as diabetic. Date of onset of diabetes is preferable than date of diagnosis but this date is rarely available. Fasting time will also be assessed as a potential confounder.

Subjects will be excluded from the analysis if they are using insulin or did not fast.

7. Data requested:
Visit 1 data: fasting plasma insulin, fasting blood glucose, fasting time, diagnosis of diabetes, date of diagnosis of diabetes, diabetes medication, demographic variables (age, gender, and race), medications affecting cholesterol levels, serum cholesterol levels, (total, HDL, LDL, VLDL, triglycerides, and subfractions), field center, dates of examination, anthropometric measurements.

REFERENCES:


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