Study Purpose and Rationale

The purpose of this observational study is to evaluate differences in glucose tolerance and other factors related to the metabolic syndrome among adolescents from four prominent ethnic groups. Various studies have shown that the prevalence of obesity and metabolic syndrome is increasing among adults in the US. This also extends to higher incidence of childhood obesity and metabolic syndrome. Particular ethnic groups, such as South Asians, are at risk for developing early and fatal cardiovascular disease related to microvascular changes from impaired glucose tolerance.

If we are able to identify ethnic sub-groups at risk for developing microvascular disease as a result of impaired glucose tolerance and possible future diabetes, healthcare providers may be able to implement and encourage targeted lifestyle changes to prevent progression of disease.

This study aims to evaluate the existence, if any, of differences in modifiable risk factors – such as impaired glucose tolerance - among adolescents of different ethnic groups. These potentially at-risk groups can then be identified early and interventions can be made to modify their risk for progression to disease.

Hypothesis

Even in early adulthood, during adolescent years (age 18-25), differences in glucose tolerance exist when adolescents of South Asian, Hispanic, African American, and Caucasian descent are compared to one another.

Background

The incidence of cardiovascular disease is increasing likely in relation to the increasing prevalence of the metabolic syndrome in adults. The metabolic syndrome is a constellation of health factors that has been shown to put people at increased risk cardiovascular disease. It is defined as having three of more of the following characteristics:

1) Abdominal obesity: waist circumference > 102 cm in men and >88 cm in women;
2) Hypertriglyceridemia: ≥ 150 mg/dl;
3) Low high-density lipoprotein (HDL) cholesterol: < 40 mg/dl in men and < 50 mg/dl in women;
4) High Blood Pressure: ≥ 130/85 mm Hg;
5) High Fasting Glucose: ≥ 110 mg/dl.

According to population-based studies, the prevalence of metabolic syndrome among US adults is high[1]. The Third National Health and Nutrition Examination Survey showed that it was prevalent in 6.7% of adults aged 20 through 29 and with prevalence of 43.5% in participants aged 60 to 69 years. Mexican Americans showed highest age-adjusted prevalence of MS 31.9%. The age adjusted prevalence was similar between men and women. In this study, 11.9% of Whites, 15.1% of African Americans, 20% of Mexican Americans, and 14.3% of "Other" had High Fasting Glucose or Medication Use.[1]

South Asian is defined as people who originate from India, Sri Lanka, Bangladesh, Nepal, Pakistan, Bhutan, and Maldives. The US Census Bureau states that as of 2000, there were two million people of South Asian Ancestry living in the US. The largest populations of South Asians reside in the metropolitan areas surrounding New York City, Chicago, Baltimore/Washington, D.C., Los Angeles, and San Francisco. Of the entire population, Hispanics comprise the largest minority group at more than 15% of the total US population (45.5 million of the 301.6 million at the time of the census). Whites comprise 199.1 million or 66% of the population and Blacks are 40.7 million with Asians totaling 15.2 million. While South Asians are a small minority in the US, they carry a high disease burden globally and also in the US. It is important to study this group in context of the discussion below.

South Asians are a minority in the US and have been studied amongst each other and as compared to Whites. There have been few studies evaluating disease burden in South Asians compared to other major minority groups in the US. South Asians have been shown to have a high cardiovascular disease burden, especially at a younger age.[1,2,3] In Canada, a study of coronary heart disease mortality in Canada showed that over a 15-year period, South Asians had the highest CHD mortality compared with individuals of Chinese and European descent. In global studies, it has been purported that South Asian ethnicity is an independent predictor of cardiovascular disease.[3]

It is thought that impaired glucose metabolism, specifically diabetes, is a major culprit in the progression of vascular disease. Unlike other traditional risk factors, type 2 diabetes is higher in South Asians than in other ethnic populations.[4] In fact, the prevalence of insulin resistance in healthy, young, lean Asian Indian men is three- to four times higher than lean men in other ethnic groups. In a study of Asian Indian (South Asian) people living in Atlanta, GA, the prevalence of diabetes mellitus was 18.3% in the survey group. This is higher than estimates of diabetes prevalence in other ethnic groups.[4,5] Direct comparison to other studies cannot be performed, however, because study composition, technique, and time-period were different.

Additionally, it has been suggested that South Asians are at higher risk for central adiposity at lower BMI. This may support a relationship of glucose intolerance with body fat pattern. A study comparing South Asian men and women with European men and women showed that at similar body mass index the South Asians had higher mean waist-hip ratio and trunk skinfolds were thicker. Also, a prospective study has shown that central adiposity is related to insulin resistance in Mexican Americans – another group at high risk of metabolic syndrome and cardiovascular disease.[6]

The median age of the US population is 36.6 according to the US Census Bureau. Twenty five percent of the population is younger than 18 years old. In studying the trajectory of disease burden, it is important to consider screening younger individuals especially when related to preventable disease. Because glucose intolerance and its progression to diabetes hold a central role in cardiovascular disease formation, and because South Asians have an especially high disease burden, I have chosen to assess younger adults and also to include South Asians specifically in the ethnic mix. [7]

In a population based screen of glucose tolerance in adolescents, grades 5-12, it was found that 7.3% of post-pubertal males and 4.1% of post-pubertal females studied had impaired carbohydrate [glucose] tolerance. The post-pubertal stage of growth most similarly represents our goal population.[9]

The ADA recommends opportunistic testing of at-risk asymptomatic children.[10,11] A review of WHO and ADA recommendations evaluated rationale for screening asymptomatic children and adolescents for diabetes.[10] It stated that the risk of MI is 14-fold higher in young adults (ages 18 to 44) diagnosed with type 2 diabetes than their non-diabetic control subjects. Interventions regarding lifestyle have also been shown to prevent the onset or delay the onset of diabetes in patients with impaired glucose tolerance. The prevention of diabetes may also lower risks of developing microvascular and cardiovascular complications.[12] Thus, it is possible to argue that while broad spectrum screening for diabetes among adolescents may be not warranted, opportunistic screening of at-risk youngsters is recommended in order to intervene and prevent long-term outcomes. At-risk adolescents include those who may be obese, have a strong family history of diabetes, and/or they are of ethnic minority origin.[10]

The aim of this study builds on the fact that certain ethnic groups may be at higher risk of developing impaired glucose tolerance and diabetes. If we are able to identify that certain groups have a higher prevalence of impaired glucose tolerance, then we may intervene early and prevent future morbity and mortality in those groups. Specifically, we are studying South Asians as compared to other ethnic groups given the significance and severity of disease burden in this minority population.

Study Design and Statistical Procedures

This observational study involves recruitment of adolescent subjects, consent, survey of baseline characteristics, and data collection including a standard glucose tolerance test.

Study subjects are individuals, aged 18-25, men and women, with no prior diagnosis of diabetes, impaired glucose tolerance, or impaired fasting glycemia. The goal is to recruit at least 2000 subjects and at least 500 from each ethnic group in order to achieve expected statistical differences in percentage of each ethnic group with impaired glucose tolerance. For the purposes of setting power, it was hypothesized that 10% of South Asians would have previously undetected impaired glucose tolerance while only 5% of the Caucasian would have impaired glucose tolerance. Given these numbers, 500 subjects are needed in each group to achieve power, and when all groups are included, 2000 total subjects are needed.

Study subjects would be recruited via flyers, email, and word-of-mouth on local university campuses in New York City. Subjects would be asked to identify themselves within specific criteria before inquiring about inclusion in the study. A recruitment flyer would advertise the purpose of the study and the fact that study subjects should be between the ages of 18 to 25. They should self-identify as part of a particular ethnic group based on the ethnicity of all four grandparents. A sample recruitment sentence on the flyer may state, “How would each of your four grandparents identify themselves? If all four identify as the same ethnic group, please consider participation in this study. We are recruiting men and women, aged 18 to 25, from the

following ethnic backgrounds: White/Caucasian, Hispanic/Latino, Black/African American, and Asian (specifically South Asian)."

The Recruitment process would include an IRB-approved consent form stating the risks and benefits of the study (discussed below). After consent is obtained, subjects will fill out a questionnaire asking them to provide information on the following: Name, age, gender, ethnic background (as identified by all four grandparents), education level, health status of relatives – ie: Do any of your parents, siblings, etc. have any of the following diseases – diabetes, hypertension, etc. And for each disease state, the subject will identify from a drop-down menu the family member who has each of the diagnoses.

At the time of data-collection, the subject will have weight, height, abdominal circumference, and blood pressure recorded. Fasting glucose and lipid panel will be obtained. An oral glucose load will be administered – 1.75 gm/kg glucose up to maximum 75 gm glucose. The subject will be asked to wait two hours for the follow up blood glucose level. During the two-hour wait time, the subject will be provided with educational materials about diabetes, metabolic syndrome, and guidelines on physical activity and diet.

Once the data points are obtained from the survey and laboratory measures, they will be entered into Excel and appropriate statistical software. Baseline characteristics based on the survey and measures of blood pressure, BMI (as calculated from height/weight), abdominal circumference, and fasting glucose and fasting lipids will be recorded.

The result of the glucose tolerance test will be recorded, and for purposes of analysis, secondarily categorized as Normal, Impaired Glucose Tolerance, and Diabetes Mellitus. These values will be: Normal Glucose Tolerance: Less than 140 mg/dl, Impaired Glucose Tolerance: Greater than or equal to 140 mg/dl but less than 200 mg/dl, and Diabetes Mellitus: equal to or greater than 200 mg/dl.

Chi-squared analysis would be used to assess percentage of participants with impaired glucose tolerance in each ethnic group. Also, analyses will be done controlling for BMI, blood pressure, and abdominal girth. We also aim to identify Metabolic Syndrome in any of the study subjects and assess the prevalence in this study population. Metabolic Syndrome is defined as 3 or more of the following criteria: Abdominal obesity: waist circumference > 102 cm in men and >88 cm in women; Hypertriglyceridemia: ≥ 150 mg/dl; Low high-density lipoprotein (HDL) cholesterol: < 40 mg/dl in men and < 50 mg/dl in women; High Blood Pressure: ≥ 130/85 mm Hg; High Fasting Glucose: ≥ 110 mg/dl.

The data obtained is confidential within the realm of HIPAA practices. Study subjects may obtain the results of their blood-work and baseline characteristics during the study. Subjects with abnormal results will be notified and encouraged to seek further medical care.

Potential risks of the study include the risks associated with travel to and from the study-site and the risks associated with two blood draw. The administration of the oral glucose challenge is relatively safe, but there may be a risk of choking or unforeseen adverse reaction to the glucose

load. Also, there is a potential risk of a false-positive diagnosis for various health parameters including glucose tolerance,

Potential benefits of the study include access to health information as measured by healthcare professionals and access to data regarding lipid profile, fasting glucose, and response to glucose challenge. Also, study participants will have access to other educational materials during the process.

Alternatives to this study may include broader inclusion criteria, especially to look at all Asian groups, or increased data collection such as other baseline characteristics – homocysteine levels, etc. However, the aim of this study is to evaluate glucose tolerance in context with ethnic and other baseline characteristics.

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