HIGH MORTALITY LIPOPROTEIN AND TOTAL SERUM CHOLESTEROL LEVELS IN A GROUP OF BRITISH COLUMBIA NATIVE INDIANS*1

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ABSTRACT

High density lipoprotein (HDL) and total serum cholesterol levels were evaluated in 282 members of the Nisquall Nation, a native Indian people residing on the British Columbia (B.C.) coast. Cholesterol was measured enzymatically in non-fasting serum, and HDL cholesterol was measured ultracentrifugally in non-fasting serum, and HDL cholesterol was measured ultracentrifugally. Serum cholesterol levels averaged 202.2 ± 23.7 mg/dl, and HDL cholesterol levels averaged 39.5 ± 17.3 mg/dl. At expected, cholesterol levels were positively correlated with body mass index (r = .52, p < .001) and body mass index (r = .35, p < .05), and HDL cholesterol correlated negatively with body mass index (r = -.25, p < .01). An unexpected result of the study was that HDL cholesterol levels in Nisquall men were not different from those in women, but were higher than average values for sale for males. This observation could not be explained on the basis of data obtained in the study; it may be a feature in the low survival mortality rate for B.C. registred Indians.

KEY WORDS: Cholesterol; HDL-Cholesterol; Sex differences; Indians, North American

INTRODUCTION

Mortality due to coronary heart disease appears to be significantly lower in British Columbia (B.C.) native Indians than in the Canadian population as

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Larger. In 1977, the Canadian death rate due to cardiovascular disease was 55.7 per 100,000 population (11), as compared to a death rate of 131 per 100,000 among U.S. registered Indians (9). Similar findings have been noted previously for southwestern American Indians, who were found to have an overall prevalence of myocardial infarction and electrocardiographic evidence of ischemic heart disease that was only 23% of that of the population studied in Framingham (11). In contrast, with lower rates of coronary disease, the southwestern American Indians were also found to have lower serum cholesterol levels than the American Caucasian population (1,3), and to have relatively higher levels of high density lipoprotein (HDL) cholesterol and lower levels of low density lipoprotein (LDL) cholesterol (6). Higher levels of HDL cholesterol are associated with a decreased risk of coronary disease (7-9), whereas elevated LDL cholesterol levels are known to be atherogenic (10).

Relatively few data exist on serum cholesterol levels in B.C. native people. The Nutrition Canada National Survey found that although median cholesterol levels in Canadian native Indians and the general population were not substantially different, lower native people had cholesterol levels above standards indicating a high risk for heart disease (12). Another report indicates that serum cholesterol levels in B.C. native people are slightly greater than those of the Canadian population (12). HDL cholesterol levels in B.C. native people do not appear to have been reported. Thus, although the data are incomplete, the lower coronary mortality in B.C. native people, in comparison to the general population, may not be associated with substantially lower cholesterol levels. This contrasts with the observations in the southwestern American Indians.

Coronary heart disease is also reported to be relatively rare among the B.C. First Nations people (13), and it has been suggested that this may be due to consumption of marine oils containing large amounts of omega-3 fatty acids (14,15). These fatty acids appear to lower both plasma cholesterol and triglyceride levels (16), and to have antiplatelet effects which are likely mediated through an influence on platelet lipoprotein composition and function (17). Significant amounts of omega-3 fatty acids are found in Pacific salmon (18), which have traditionally served as a prominent food for many groups of B.C. native Indians, particularly those residing in coastal communities.

Moderate use of alcohol appears to favorably alter coronary mortality (19), and to result in elevated HDL cholesterol levels (20,21). The mechanism by which alcohol has its effects on lipid levels and coronary mortality in these people is presently unknown. Changes in liver function, as assessed by liver enzyme levels, have been related to changes in both lipid levels and alcohol consumption (22). Alcohol use by Canadian native people, as reported by Nutrition Canada, appears to be highest among males aged 20 to 44 (23).

The present study was designed to evaluate the levels of HDL and total serum cholesterol in the people of the Nisga'a Nation, a native Indian community on the B.C. coast. The associations of cholesterol levels with age, body mass index (BMI), and activity of glucose-6-phosphate dehydrogenase (G6PD), a liver enzyme, were also assessed.
SUBJECTS

In May, 1983, a nutrition and health assessment was made available to the people of the Hauxalk Nation living in Bella Coola, British Columbia (24). Bella Coola is located on the central BC coast at the head of a deep sea inlet. Of the 202 Bella Coola-resident band members, a total of 388 individuals of all ages participated in the health assessment. Participation rates were similar among different age groups.

PROCEDURES

Non-fasting blood samples were obtained from 302 of the 226 participants aged 13 years and over. Specimens were centrifuged at 4°C to obtain the serum, and were stored in polypropylene tubes at -20°C prior to conducting the analyses. Non-fasting samples were taken in order to enhance participation, as it is generally accepted that serum total and HDL cholesterol levels are not acutely affected following the ingestion of normal meals (25,26). Chylomicronemia was not evident in any samples.

Serum cholesterol levels were determined using a well-established enzymatic procedure (27), with reagents obtained from Boehringer Mannheim, and HDL cholesterol levels were determined enzymatically in the supernatant following precipitation of low and very low density lipoproteins with polyethylene glycol (28). Intraclass and inter-assay coefficients of variation for these assays were less than 5%.

The activity of gamma-glutamyl transferase was assayed colorimetrically in serum using Boehringer Mannheim reagents (29). Height and weight measurements were completed by a single individual, using a stadiometer and a beam balance. These measurements were used to calculate body mass index (BMI = kg/m²).

STATISTICAL ANALYSIS

Data analysis was conducted using SPSS 13.0. Statistical procedures included analysis of variance, t-tests, Pearson correlation analysis, and partial correlation (31).

RESULTS

Serum total and HDL cholesterol levels are presented by sex and age in Table 1. The average serum cholesterol level for the entire group was 203.4 mg/dl, whereas HDL cholesterol averaged 57.5 mg/dl. Analysis of variance of the data revealed no sex effects for either total or HDL cholesterol (p=0.516 and 0.483 respectively). An age effect was found for total cholesterol (p<0.001), but not for HDL cholesterol (p=0.260). No age-by-sex interactions were detected in the results for either HDL or total cholesterol.
<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>Sex</th>
<th>n</th>
<th>Serum Cholesterol (mg/dL)</th>
<th>HDL Cholesterol (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 - 19</td>
<td>Male</td>
<td>21</td>
<td>152.4 ± 7.8a</td>
<td>53.3 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>29</td>
<td>146.1 ± 6.5</td>
<td>54.3 ± 2.8</td>
</tr>
<tr>
<td>20 - 29</td>
<td>Male</td>
<td>29</td>
<td>201.5 ± 9.8</td>
<td>61.9 ± 3.5</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>35</td>
<td>196.3 ± 8.7</td>
<td>60.7 ± 3.1</td>
</tr>
<tr>
<td>30 - 39</td>
<td>Male</td>
<td>23</td>
<td>205.9 ± 7.4</td>
<td>55.6 ± 2.6</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>18</td>
<td>210.1 ± 16.0</td>
<td>60.4 ± 4.0</td>
</tr>
<tr>
<td>40 - 59</td>
<td>Male</td>
<td>26</td>
<td>232.1 ± 8.6</td>
<td>59.7 ± 4.2</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>25</td>
<td>218.4 ± 9.2</td>
<td>56.6 ± 4.9</td>
</tr>
<tr>
<td>&gt; 60</td>
<td>Male</td>
<td>16</td>
<td>260.3 ± 26.6</td>
<td>61.5 ± 13.4</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>12</td>
<td>232.6 ± 9.1</td>
<td>51.1 ± 6.2</td>
</tr>
<tr>
<td>All Ages</td>
<td>Male</td>
<td>103</td>
<td>205.1 ± 8.7</td>
<td>58.2 ± 1.3</td>
</tr>
<tr>
<td></td>
<td>Female</td>
<td>47</td>
<td>202.2 ± 8.5</td>
<td>56.8 ± 1.7</td>
</tr>
</tbody>
</table>

*Results are expressed as mean ± S.E.M.*

Pearson product-moment correlation coefficients were calculated to examine the associations of age, GGT activity and body mass index with total and HDL cholesterol levels, as shown in Table 2. It can be seen that significant positive correlations existed between serum total cholesterol and all three of these variables, HDL cholesterol levels, in contrast, correlated negatively with body mass index, and were not significantly associated with age. GGT activity correlated positively with HDL cholesterol levels, although the association was not significant (*r* = 0.06).

As is obvious from the data presented in Table 2, the independent variables also correlated positively with one another. Partial correlation coefficients were therefore calculated to examine the association of each of the independent variables with total and HDL cholesterol while simultaneously controlling for the effects of the other independent variables. These results, presented in Table 3, indicate that significant positive correlations persisted between total cholesterol and each of age and body mass index, whereas the correlation between GGT and total cholesterol was no longer significant. In contrast, GGT activity was significantly correlated with HDL cholesterol levels when age and body mass index were controlled.
TABLE 2
Product-Moment Correlation Coefficients
Among HDL and Total Cholesterol, Body Mass Index, Age and GGT

<table>
<thead>
<tr>
<th></th>
<th>HDL</th>
<th>Body Mass Index</th>
<th>Age</th>
<th>GGT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol</td>
<td>( r = 0.159 )</td>
<td>( r = 0.365 )</td>
<td>( r = 0.326 )</td>
<td>( r = 0.191 )</td>
</tr>
<tr>
<td></td>
<td>( p = 0.013 )</td>
<td>( p &lt; 0.001 )</td>
<td>( p &lt; 0.001 )</td>
<td>( p = 0.003 )</td>
</tr>
<tr>
<td>HDL</td>
<td>( r = 0.265 )</td>
<td>( r = 0.001 )</td>
<td>( r = 0.111 )</td>
<td>( p = 0.060 )</td>
</tr>
<tr>
<td></td>
<td>( p = 0.002 )</td>
<td>( p = 0.137 )</td>
<td>( p = 0.019 )</td>
<td></td>
</tr>
<tr>
<td>Body Mass Index</td>
<td>( r = 0.479 )</td>
<td>( r = 0.166 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>( p &lt; 0.001 )</td>
<td>( p = 0.018 )</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
<td>( r = 0.154 )</td>
<td>( p = 0.013 )</td>
</tr>
</tbody>
</table>

TABLE 3
Partial Correlations of Age, BMI and GGT with Total and HDL Cholesterol Levels

<table>
<thead>
<tr>
<th>Partial Correlation With:</th>
<th>Cholesterol</th>
<th>HDL, Cholesterol</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>( r = 0.417 )</td>
<td>( r = 0.091 )</td>
</tr>
<tr>
<td></td>
<td>( p &lt; 0.001 )</td>
<td>( p = 0.104 )</td>
</tr>
<tr>
<td>BMI</td>
<td>( r = 0.174 )</td>
<td>( r = 0.055 )</td>
</tr>
<tr>
<td></td>
<td>( p = 0.008 )</td>
<td>( p = 0.001 )</td>
</tr>
<tr>
<td>GGT</td>
<td>( r = 0.116 )</td>
<td>( r = 0.155 )</td>
</tr>
<tr>
<td></td>
<td>( p = 0.055 )</td>
<td>( p = 0.032 )</td>
</tr>
</tbody>
</table>

Controlling for BMI and GGT
Controlling for age and GGT
Controlling for age and BMI
There are relatively few appropriately rigorous data to which the results of the present study may be compared. The Nutrition Canada National Survey obtained data on non-fasting serum cholesterol levels in a total of 1806 native Indians, 286 of whom were members of four bands in the Pacific region (11). In this survey, median serum cholesterol levels were similar in the Indian and National (largely European) components of the study. However, variability in the native Indian group must have been lower, as fewer native Indians were classified as being at high risk for heart disease on the basis of having serum cholesterol levels above age and sex-specific standards. In contrast, greater proportions of Northwest native people would be classified as being at high risk on the basis of these standards, as is shown in Figure 1. Caution must be exercised in interpreting these results, as some samples sizes are small. M excess in the case of the Pacific region results of the Nutrition Canada Indian Survey, and 199 in the present study. However, it does appear that a greater proportion of the Northwest native people have elevated cholesterol levels than did individuals studied by Nutrition Canada, irrespective of which group the results are compared to.

**FIG. 1**

Percentage of participants with serum cholesterol levels classified as high risk using Nutrition Canada interpretive standards. These levels were > 230 mg/dl for women aged up to 59; > 230 mg/dl for women aged 60 to 59; > 230 mg/dl for men up to 59 years of age; and > 230 mg/dl for men 60 and over and women 55 and over. For participants in the Nutrition Canada National Survey (11), age ranges to which interpretive standards were applied and for which data are displayed were 20-54 years, 60-64 years, and 65 years and over.
Several factors may explain the apparent discrepancy between the Nutrition Canada results and those of the present study. Firstly, the response rate among those initially selected for the Nutrition Canada Indian survey was 30% (31) compared to a 42% response rate by the Muskil population. The possibility that exists that native Indians with higher average cholesterol levels were less likely to have participated in the Nutrition Canada Survey. Second- ly, there may be variability among bands, even within a region. Support for this is provided by data on plasma cholesterol levels at 9.2% native Innuw buildings on the Naknek and Abashut reserves (32). Mean native cholesterol levels for individuals over 35 years of age were 220 mg/dl and 245 mg/dl for Naknek and Abashut residents, respectively, as compared to a mean level of 202.6 mg/dl for Muskil people of similar age.

The lack of a sex difference in HDL cholesterol levels in these subjects was surprising. Given the usual finding of higher levels in women than in men (33,34). The method used for HDL cholesterol determinations could acciden- tally detect a sex difference when one existed: a small in-house study on similarly-treated blood samples from male and female Caucasians revealed a significant (p<0.05) sex difference (unpublished data). The Muskil men included in this study had a mean HDL cholesterol level of 59.2 mg/dl, not significantly different from the average of 54.8 mg/dl in the women. The level in men is substantially higher than average levels in a Caucasian population. The Lipid Research Clinic Prevalence Study reported rounded mean values of 35 mg/dl and 50 mg/dl in men aged 15 to 44 and 45 or older, respec- tively (35). In contrast, the average level in the Muskil men was similar to the UHC averages, which are 55 mg/dl and 60 mg/dl in men aged up to 39 years and over 40, respectively (36). There are few reports in the literature of HDL cholesterol levels in native Indian populations. A group of ten southeastern American Indians was found to have HDL cholesterol levels averag- ing 56 mg/dl, although no conclusion could be reached concerning sex differ- ences as there were only three women in this group (4). Plasma and HDL choles- terol levels of the Tarahumara Indians of Mexico have also been reported (37). These people consume a very low cholesterol, low fat, high fibre diet, and have levels of both total and HDL cholesterol that are low, averaging 125 ± 36 mg/dl and 25 ± 8 mg/dl respectively. Although it was reported that gender differences did not exist, only six nonpregnant women between 19 and 70 years of age were studied, as compared to 30 men in the same age range. Finally, the only other expert located in the literature which did not detect a sex difference in HDL cholesterol was a study done in New Zealand, which reported that full-blooded Maori males and females had similar HDL cholesterol levels (39). However, this study was confined to adolescents.

There is no obvious explanation for the relatively elevated HDL choles- terol levels in the Muskil men. Body mass index correlated negatively with HDL cholesterol levels in the subjects in the present study, a relationship which has been reported in studies of other groups (9,33,35). However, the average body mass index of the Muskil men, at 27.8 kg/m², was higher than the mean of 25.2 kg/m² calculated from Nutrition Canada data for adult men (11). On the basis of the regression equation relating body mass index to HDL choles- terol developed on data from the LHC study (37), one would have expected the mean HDL cholesterol level in the Muskil men to be 2.4 mg/dl lower than the LHC average, instead of approximately 10 mg/dl higher. It is clear that direct comparisons of the Muskil data to the LHC data are not totally appro- priate, due to differences between the populations; however, it is equally clear that the higher HDL cholesterol levels in the Muskil men cannot be explained on the basis of a lower-than-average body mass index.
It is also unlikely that dietary factors contribute to the relatively elevated HDL cholesterol levels in the Nunavik men. As a coastal people, the Nunavik do incorporate salmon into their diets on a frequent basis, and some recent studies have indicated that omega-3 fatty acids found in marine oils may elevate HDL cholesterol levels (38, 39). However, a diet with salmon and salmon oil fed to healthy volunteers did not influence HDL cholesterol, although significant reductions in total cholesterol and triglyceride levels were observed (40). It should be noted that the amount of salmon and salmon oil used in this study (up to one pound of salmon and 3-6 tablespoons of salmon oil per day) was considerable. The Nunavik people may consume a similar amount of salmon seasonally, but they do not use salmon oil as a dietary condiment (40). Furthermore, blood samples for this study were obtained in the spring, whereas the peak salmon season is in late summer. Thus, the relatively elevated HDL cholesterol levels in Nunavik men would not appear to be accounted for by consumption of large amounts of omega-3 fatty acids from salmon. Obligatory fat in a traditional source of fat included in the Nunavik diet, but this is a largely unsaturated fat which contains only 15 polyunsaturated (41). Finally, irrespective of any possible effects of traditional foods on serum lipid levels, there are no data to support (nor any reason to suspect) differential uses of these foods by men and women (42).

Alcohol is felt to be one of the major determinants of HDL cholesterol, and strong positive relationships between alcohol intake and HDL cholesterol levels have been demonstrated (26, 29). In this study, accurate data on alcohol consumption were not obtained. However, HDL cholesterol levels were correlated with GGT activity (Table 1), and the activity of this enzyme has previously been found to be elevated in alcoholics as compared to control populations (22, 42). It is not possible, however, that use of alcohol would account for the lack of an expected male-female difference of approximately 10 mg/dl in HDL cholesterol: The average HDL cholesterol level for subjects in the highest quintile for GGT activity was only 6.5 mg/dl greater than the average for those in the lowest quintile, whereas the difference in GGT activity was 88 IU/L (data not shown). Because the main difference in GGT activity between the Nunavik men and women was only 15 IU/L (unpublished observation), GGT activity as an indicator of alcohol use would not be a major factor in explaining the relatively elevated HDL cholesterol levels in the Nunavik men. It remains possible that a more valid estimate of alcohol intake would show a stronger relationship to cholesterol levels, but it has been estimated that the maximum proportion of variance accounted for by alcohol use, given a valid and reliable indicator of consumption, would be no more than 10% (42). Thus, the lack of a sex difference in mean HDL cholesterol levels is not likely to be entirely due to greater alcohol use by the men. Furthermore, it must be remembered that there is a male-female differential in alcohol use in the Caucasian population as well (23), despite the lower HDL cholesterol levels found in Caucasian men as compared to women.

In conclusion, the results of this study indicate that HDL cholesterol levels in Nunavik men are similar to levels in Nunavik women, and are substantially higher than mean levels reported for Caucasian populations. These findings would not be explained by the biology of body mass index nor by the use of GGT activity as an index of alcohol use. While the results of this study reflect data gathered from only a single community of B.C. native people, it is tempting to suggest that the elevated HDL cholesterol levels found in men contribute to the low coronary mortality rates observed in the B.C. native Indian population. Studies of other native people living both on and off
reserves would be desirable to support this hypothesis, so further information on lifestyle and metabolic variables that may influence HDL cholesterol levels.

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