FRIEDEWALD'S LDL-CHOLESTEROL ESTIMATION FORMULA IN A JAPANESE AMERICAN POPULATION*

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Friedewald's formula is often used to estimate low density lipoprotein cholesterol (LDL-c) when direct measurement is not available. In this equation, the ratio of triglyceride (TG): cholesterol (C) in very low density lipoprotein (VLDL) is assumed to be 5 : 1. Recently it has been reported that in native Japanese the formula provided a better fit if this ratio is taken to be 4 : 1. The application of the formula was therefore examined in a sample of 229 second-generation Japanese American (Nisei) men. In this population, the 5 : 1 ratio of TG : C in VLDL was found to be appropriate. Thus the findings reported for native Japanese do not appear to be generally applicable to all Japanese populations.

FRIEDEWALD'S low density lipoprotein cholesterol (LDL-c) estimation formula is often used to determine LDL-c from measurements of total cholesterol (TC), triglyceride (TG), and high density lipoprotein cholesterol (HDL-c)¹:

$$\text{LDL-c} = \text{TC} - (\text{HDL-c} + \text{TG}/k).$$

This formula assumes that TC is found only in LDL, very low density lipoprotein (VLDL), and HDL, and that TG is carried only by VLDL. Based upon the assumption that the ratio of TG : C is 5 : 1 in VLDL, k is usually taken to be 5.

Recently, Hata and Nakajima² have reported that the TG : C ratio in VLDL is not 5 : 1 among Japanese, and that the formula provided a better fit with $k = 4$ rather than $k = 5$. Furthermore, they reported that a better estimation was gained if $k = 3$ for those with TG < 150 mg/dl, $k = 4$ for those with TG 150–299 mg/dl, and $k = 5$ for

those with TG 300–400 mg/dl.

In view of this report, we have examined Friedewald's formula in a group of second-generation Japanese American (Nisei) men to determine whether the observations of Hata and Nakajima are also relevant to this population.

SUBJECTS AND METHODS

A total of 229 Nisei men ranging in age from 45–74 yrs who were participants in a study of diabetes mellitus and cardiovascular disease were examined. The recruitment and characteristics of these subjects have been described in detail previously.³ Mean age ($\pm$ SEM) was 61.5 ± 0.4 yrs. Seventy-nine men had normal glucose tolerance, 72 impaired glucose tolerance (IGT), and 78 type 2 diabetes. Subjects were also grouped by their TG levels as follows: 132 had TG < 150 mg/dl, 78 had TG 150–299 mg/dl, and 19 had TG $\geq$ 300 mg/dl.

Venous blood samples were collected into tubes containing EDTA (1.5 mg/ml) following a 10–12 hr overnight fast, and blood was kept at

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TABLE I MEAN VALUES FOR FRIEDEWALD CONSTANT (k)

	n	k	SD
Total Sample	229	5.35	1.57
Normal glucose tolerance	79	5.47	1.97
IGT	72	5.27	1.31
Diabetes	78	5.31	1.34

4°C until plasma was separated within 60 min of collection. Fractions containing VLDL and LDL plus HDL were isolated by ultracentrifugation at 105,000g, 10°C, for 18 hrs.⁴ HDL was separated by precipitation of the other lipoproteins with dextran-Mg⁺⁺.⁵ C and TG were quantified in plasma and lipoprotein fractions by enzymatic methods on the Abbott ABA 200 bichromatic analyzer.⁵ LDL-c was calculated by difference. Thus following ultracentrifugation, subtracting HDL-c from C in the LDL plus HDL fractions yielded LDL-c.

From the Friedewald equation, k was determined as follows:

$$k = TG \div (TC - HDL-c - LDL-c)$$

RESULTS

Results of the calculation of k for the entire group of men, for men with normal glucose tolerance, IGT, or diabetes, and for men with TG < 150 mg/dl, TG 150–299 mg/dl, and TG ≥ 300 mg/dl are shown in Tables I and II. In all cases, k was very close to 5. Notably, k did not increase but rather, appeared to decrease slightly with increasing TG.

DISCUSSION

Using the Friedewald equation and measurements of TC, TG, HDL-c, and LDL-c, we have calculated k for a group of Japanese American men and found k to approximate 5. This result suggests that Friedewald's original k = 5 is indeed appropriate for estimating LDL-c in plasma of Japanese American subjects. Furthermore, k was not found to increase with increasing TG.

These observations are quite different from the results of Hata and Nakajima² that prompted the present analysis. Friedewald's formula assumes that the ratio of TG : C is 5 : 1 in VLDL. This ratio was derived from subjects in the United States. Hata and Nakajima have reported

TABLE II MEAN VALUES FOR FRIEDEWALD CONSTANT (k) BY TG LEVEL

	n	k	SD
TG < 150 mg/dl	132	5.66	1.87
TG 150–299 mg/dl	78	4.99	0.91
TG ≥ 300 mg/dl	19	4.67	0.82

this ratio to be 4 : 1 in Japanese subjects and have suggested that the discrepancy may be due to the different composition of the Japanese diet. If this is indeed the basis for their findings, then our observations would tend to support this since the nutritional background of Japanese Americans is generally more similar to the usual western diet than it is to the native Japanese diet.^{6,7}

In conclusion, Friedewald's formula with k = 5 appears to be appropriate for application in the Japanese American population. Although the observations of Hata and Nakajima may be relevant to the native Japanese population, they do not appear to be generally applicable to all Japanese populations.

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