# Hypercholesterolaemia in a rural white population and its relationship with other coronary risk factors

H. J. STEENKAMP, P. L. JOOSTE, J. E. ROSSOUW, A. J. S. BENADÉ
A. S. P. SWANEPOEL

## Summary

The risk factor and dietary associations of hypercholesterolaemia were analysed. Twenty per cent of the 6 332 respondents aged 20 - 64 years in the Coronary Risk Factor Study (CORIS) were considered hypercholesterolaemic (i.e. above the 80th percentile). In this sample only 13,4% of men and 6,7% of women were on treatment, and only 32,7% and 37,1% respectively had 'desirable' high-density lipoprotein cholesterol levels.

Hypercholesterolaemia was significantly associated with a personal or family history of coronary heart disease, hypertension, smoking, obesity and hyperuricaemia. Analysis of the dietary intakes of a 15% subsample of the total population revealed no significant differences between high- and low-risk subjects in intake of dietary fats and cholesterol. However, high-risk subjects consumed significantly more animal protein and significantly less dietary fibre than those with a low cholesterol level.

These findings reflect a subpopulation at high risk of coronary heart disease. Their risk can be reduced to some extent by population strategies towards healthier lifestyles; ultimately the high-risk individuals have to be identified and appropriately treated.

**Research Institute for Nutritional Diseases of the South African Medical Research Council, Parowvallei, CP**
H. J. STEENKAMP, M.SC. (CLIN. EPIDEMIOL.)
P. L. JOOSTE, PH.D., B.SC. HONS (CLIN. EPIDEMIOL.)
A. J. S. BENADÉ, D.SC.
**National Heart, Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland, USA**
J. E. ROSSOUW, F.C.P. (S.A.), M.D.
**Department of Health Services and Welfare Administration, House of Assembly, Pretoria**
A. S. P. SWANEPOEL, M.SC.

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Reprint requests to: The Director, Research Institute for Nutritional Diseases of the South African Medical Research Council, PO Box 70, Tygerberg, 7505 RSA.

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Epidemiological studies have firmly established that a raised serum total cholesterol (TC) level is a precursor of coronary heart disease (CHD), and that the degree of hypercholesterolaemia is directly related to the rate of development of clinical CHD both within and among populations.[1-3] Furthermore, results of prospective epidemiological studies conducted in several countries have usually demonstrated an inverse association between high-density lipoprotein cholesterol (HDL-C) levels and CHD incidence and mortality rates.[4,5]

Interpopulation comparisons indicate that diet (particularly the quantity and type of fat consumed) plays an important role in determining plasma TC.[6,7] Populations with high fat consumption have high incidences of CHD and hypercholesterolaemia. However, cross-sectional studies within populations have found either weak or no associations between the diets of individuals and their plasma TC levels.[2]

The high serum TC levels described in the baseline report of the cross-sectional Coronary Risk Factor Study (CORIS),[8] together with the susceptibility of white South Africans to CHD,[9] prompted further analysis of the data to identify patterns of, and factors related to, hypercholesterolaemia in a large, predominantly Afrikaans-speaking study population.

## Study population and methods

The study population consisted of 7 188 white predominantly Afrikaans-speaking participants aged 15 - 64 years who took part in the community Coronary Risk Factor Study (CORIS) in the south-western Cape Province. Sampling procedures and laboratory methods have been described previously.[8] For the purpose of this article participants younger than 20 years of age were excluded from the analyses, since they were mainly schoolchildren whose risk factor status will be addressed in a separate report.

Non-fasting blood samples were taken and the serum separated within 2 hours. It was then analysed manually on the same day for TC and HDL-C in the field laboratory. The Boehringer CHOD-PAP enzymatic method and dextran sulphate-magnesium chloride precipitation[10] were used and reference standards (Ortho Diagnostics and Boehringer Precilip) were included in each run. Inter- and intra-run variation was less than 3%. The remaining serum was analysed for uric acid (Boehringer Uric Acid Uricaquant method). Other measurements included blood pressure, height, weight and a resting 12-lead ECG. All subjects completed a risk factor questionnaire and a London School of Hygiene questionnaire for chest pain by interview, as well as a self-administered Bortner Short Rating Scale for type A behaviour.

As recommended by the *ad hoc* committee of the Heart Foundation of Southern Africa,[11] the age- and sex-specific 80th percentiles of the TC levels of the CORIS population[12] were used as cut-off points to identify those at high risk of developing CHD owing to their serum TC level. In the present analysis, those subjects on medical and/or dietary treatment for hypercholesterolaemia but who had TC levels below the 80th percentile were also classified as having high-risk TC levels. Respondents below the 20th percentile were identified as having low-risk TC levels, and the prevalences of other known coronary risk factors (personal and family history of CHD, hypertension, smoking, obesity, type A behaviour and hyperuricaemia) in these subjects were compared with those of the high-risk subjects, using the chi-square test. HDL-C levels above 1,2 mmol/l for men and above 1,5 mmol/l for women were considered 'desirable'. These cut-off points represent the 60th percentile of the HDL-C levels of the CORIS population, which approximates the 50th percentile of the Lipid Research Clinics Program.[12]

Food intake was determined in a 15% subsample of the total population by the 24-hour dietary recall method. The means of nutrient intakes in high- and low-risk subjects were calculated and compared using the unpaired *t*-test. The diet score[13] (Keys score) was calculated as $1,26\ (2S\text{-}P) + 1,5\ \sqrt{1\,000\ C/E}$, where $S$ = % of total energy (%E) obtained from saturated fatty acids; $P$ = %E from polyunsaturated fatty acids; $C$ = dietary cholesterol (mg/d); and $E$ = daily energy intake (kcal). The Keys score gives an indication of the saturated and polyunsaturated fat (as well as the cholesterol) content of the diet, and therefore reflects its atherogenic potential.

## Results

Table I shows the age- and sex-specific prevalences of subjects with high-risk TC levels, the percentage of these subjects on medical and/or dietary treatment for hypercholesterolaemia, the percentage of those on treatment whose TC was controlled, and the percentage of high-risk subjects with desirable HDL-C levels. By definition, the prevalence of high-risk TC levels

**TABLE I. PREVALENCE OF HYPERCHOLESTEROLAEMIA, TREATMENT STATUS AND PROTECTIVE HDL-C LEVELS OF THE STUDY POPULATION**

| | Age groups (yrs) | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | 20 - 24 | | 25 - 34 | | 35 - 44 | | 45 - 54 | | 55 - 64 | | 20 - 64 | |
| Variable | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| **Men** | | | | | | | | | | | | |
| Hypercholesterolaemia (TC > 80th percentile) | 40 | 20,8 | 128 | 20,2 | 130 | 20,3 | 155 | 22,0 | 173 | 23,3 | 626 | 21,5 |
| Total on treatment and/or diet* | 1 | 2,5 | 4 | 3,1 | 15 | 11,5 | 27 | 17,4 | 37 | 21,4 | 84 | 13,4 |
| TC controlled with treatment/diet† (TC < 80th percentile) | 1 | 100,0 | 2 | 50,0 | 3 | 20,0 | 13 | 48,2 | 24 | 64,9 | 43 | 51,2 |
| Protective HDL-C level (HDL-C > 1,2 mmol/l)* | 12 | 30,0 | 32 | 25,0 | 42 | 32,3 | 62 | 40,0 | 57 | 33,0 | 205 | 32,7 |
| **Women** | | | | | | | | | | | | |
| Hypercholesterolaemia (TC > 80th percentile) | 49 | 20,0 | 144 | 20,1 | 165 | 20,3 | 176 | 20,8 | 169 | 21,0 | 703 | 20,5 |
| Total on treatment and/or diet* | 1 | 2,0 | 4 | 2,8 | 13 | 7,9 | 14 | 8,0 | 15 | 8,9 | 47 | 6,7 |
| TC controlled with treatment/diet† (TC < 80th percentile) | 0 | 0,0 | 1 | 25,0 | 2 | 15,4 | 6 | 42,9 | 10 | 66,7 | 19 | 40,4 |
| Protective HDL-C level (HDL-C > 1,5 mmol/l)* | 19 | 38,8 | 53 | 36,8 | 57 | 34,6 | 73 | 41,5 | 59 | 34,9 | 261 | 37,1 |

*Of hypercholesterolaemics.
†Of total on treatment and/or diet.

was about 20% in the different age groups. Of the hypercholesterolaemic men, 13,4% were on medical and/or dietary treatment for hypercholesterolaemia; only 6,7% of women were on treatment. TC levels were controlled (i.e. < 80th percentile) in 51,2% of men and 40,4% of women on treatment, although the actual numbers were small. Desirable HDL-C levels were present in 32,7% of the high-risk men and in 37,1% of the high-risk women.

The prevalences of other coronary risk factors in high- and low-risk subjects are shown in Table II. Men and women with high-risk TC levels had significantly higher prevalences of a personal and family history of CHD, hypertension, smoking, obesity and hyperuricaemia than the low-risk group ($P < 0,01$). The prevalence of the coronary-prone type A behaviour did not differ significantly between high- and low-risk subjects.

The nutrient intakes of high- and low-risk members of the 15% subsample are compared in Table III. High-risk subjects of both sexes consumed significantly more animal protein and significantly less dietary fibre per 4,2 MJ than those at low risk ($P < 0,05$). High-risk women also consumed significantly more total protein per 4,2 MJ than the low-risk women and had a higher Keys score but a significantly lower energy intake ($P < 0,05$).

## Discussion

The mean TC levels of this study population, as reported previously,[12] are typical of a high-risk westernised population, which is reflected by a distribution skewed towards high values.[14] It is disturbing to note that a mere 13,4% and 6,7% of hypercholesterolaemic men and women respectively were on any treatment for hypercholesterolaemia, treatment rates being lowest for the younger subjects. Not only were few of the hypercholesterolaemic subjects treated, but also when such treatment was attempted, and levels falling under the 80th percentile were regarded as adequate, at best only two-thirds (older men and women) were adequately treated.

The significantly higher prevalence of personal evidence of CHD or a family history of CHD in the high-risk individuals accords with the well-established relationship between TC and CHD incidence and mortality.[2,3,15]

Hypertension and hypercholesterolaemia are considered to be two of the primary CHD risk factors, and the Framingham Study[16] showed these two factors to have a powerful interaction in producing CHD. In the present study almost twice as many high-risk subjects as low-risk subjects had hypertension. This is probably due to a combination of existing risk factor profiles

**TABLE II. MEAN AGE (± SD) AND PREVALENCES OF CORONARY RISK FACTORS IN MEN AND WOMEN WITH HIGH- AND LOW-RISK TC LEVELS**

| | Men | | Women | |
|---|---|---|---|---|
| | Low-risk | High-risk | Low-risk | High-risk |
| **No.** | **576** | **626** | **680** | **703** |
| **Age (yrs)** | **43,3 ± 12,8** | **44,7 ± 12,2** | **42,9 ± 12,4** | **44,0 ± 12,3** |
| **Personal history of CHD†** | **6,6%** | **15,7%*** | **4,4%** | **8,5%*** |
| **Family history of CHD** | **36,5%** | **46,7%*** | **44,7%** | **57,3%*** |
| **Hypertension (> 160/95 mmHg and/or on treatment)** | **22,2%** | **41,1%*** | **24,0%** | **38,6%*** |
| **Smoking** | **51,0%** | **55,3%** | **17,4%** | **21,5%** |
| **Obesity (BMI > 30 kg/m²)** | **10,6%** | **24,0%*** | **14,3%** | **24,8%*** |
| **Type A behaviour (Bortner > 55)** | **40,5%** | **43,8%** | **39,4%** | **36,4%** |
| **Hyperuricaemia (> 416 μmol/l in men, > 339 μmol/l in women)** | **18,6%** | **31,6%*** | **14,6%** | **25,3%*** |

*$P < 0,01$ compared with low-risk group.
†Positive history of chest pain and/or an ECG finding suggestive of CHD (Minnesota codes 1.1 and 1.2).

**TABLE III. MEAN AGE AND NUTRIENT INTAKE (± SD) OF MEN AND WOMEN WITH HIGH- AND LOW-RISK TC LEVELS***

| | Men | | Women | |
|---|---|---|---|---|
| | Low-risk | High-risk | Low-risk | High-risk |
| **No.** | **64** | **85** | **109** | **133** |
| **Age (yrs)** | **35,2 ± 10,1** | **37,3 ± 9,4** | **37,1 ± 9,0** | **36,8 ± 9,6** |
| **Energy intake (MJ) (/d)** | **12,0 ± 4,0** | **10,9 ± 3,7** | **7,3 ± 2,5** | **6,4 ± 2,6**** |
| **Protein (g/4,2 MJ)** | | | | |
| **Total** | **37,4 ± 7,8** | **40,3 ± 11,6** | **37,2 ± 9,7** | **40,1 ± 11,1**** |
| **Animal** | **26,5 ± 9,1** | **30,8 ± 13,0*** | **25,8 ± 10,7** | **29,6 ± 12,1**** |
| **Fat (g/4,2 MJ)** | | | | |
| **Total** | **39,5 ± 7,9** | **41,7 ± 8,6** | **39,1 ± 7,7** | **40,7 ± 7,0** |
| **Saturated** | **14,5 ± 3,3** | **14,9 ± 3,6** | **14,0 ± 3,7** | **15,0 ± 3,4** |
| **Polyunsaturated** | **6,2 ± 3,0** | **7,0 ± 3,7** | **6,9 ± 2,9** | **6,7 ± 3,5** |
| **Dietary cholesterol (mg/4,2 MJ)** | **195 ± 129** | **192 ± 129** | **177 ± 149** | **199 ± 144** |
| **Keys score** | **45,8 ± 10,4** | **45,5 ± 11,8** | **42,7 ± 12,5** | **46,4 ± 12,8**** |
| **Dietary fibre (g/4,2 MJ)** | **8,5 ± 4,4** | **7,2 ± 3,7**** | **11,1 ± 4,6** | **9,8 ± 4,4**** |

*From the 15% subsample.
**$P < 0,05$ compared with low-risk group.

of hypercholesterolaemic subjects and the adverse lipid effects of antihypertensive therapy.[16]

Obesity increases the risk of CHD, primarily because of its association with hyperlipidaemia, hypertension, hyperuricaemia, sedentary habits and diabetes.[3] In the present study the prevalence of obesity in the high-risk group was almost double that in the low-risk group. Also, the prevalence of hyperuricaemia was significantly higher in the high-risk group. It is therefore possible that the high prevalence of obesity in the high-risk group could have contributed, at least in part, to their higher TC, blood pressure and uric acid levels. There were also more smokers of both sexes in the high-risk than in the low-risk groups, although this difference was not significant. Smoking, especially heavy smoking, has been associated with higher TC levels in various populations — a relationship found to be independent of confounders such as body weight or age.[17] Thus, in this study population, smoking may have contributed to the previously described higher TC levels of smoking individuals.[18]

In the present study there was no significant difference in dietary intakes of fats or cholesterol between subjects with a high and those with a low serum TC level, as shown previously by Wolmarans *et al.*[19] Several other cross-sectional population studies have also failed to show statistically significant correlations between dietary cholesterol and fat intake and plasma cholesterol level.[13,20] Although there was no difference in cholesterol intake between the high-risk and the low-risk groups, the high mean intake of both these groups (well above the recommended 111 mg/4,2 MJ[19]) reflected general consumption of an unfavourable Western-type diet by the population. Clinical trials, however, have clearly indicated that an elevation in serum TC results from an increase in dietary fat intake.[6,7] The difficulty in demonstrating the expected positive correlation between dietary fats and plasma TC in a cross-sectional study can be explained by methodological problems. These have been examined and extensively reviewed,[21] and the 24-hour dietary recall method in particular has been questioned. Because of large intra-individual variations in the lipid composition of the diet from day to day, single values for individuals may not reflect true relationships between the diet and blood composition of the individual, whereas mean values for groups of individuals are far more likely to reflect a true relationship.[21]

Dietary protein on its own has generally been considered to be of less importance than saturated fat in the causation of hypercholesterolaemia and atherosclerosis in humans. However, evidence that dietary protein has a significant influence on human plasma cholesterol is accumulating, and there are reports of lower plasma cholesterol levels in vegetarians than in the population as a whole.[22] The higher intake of animal protein by hypercholesterolaemic subjects in the present study could therefore have played a role in the causation of their high serum TC levels — an issue that needs further investigation. Similarly, the low fibre intake in the high-risk group may have contributed to their TC levels. The prevalence of CHD appears to be low in populations consuming diets high in dietary fibre. For instance, in the Zutphen study[23] the incidence of CHD was clearly negatively correlated with dietary fibre intake in univariate analysis.

The coronary risk profile of the hypercholesterolaemic subjects in the present study reflects a subgroup at great risk of CHD. It should be stressed, however, that persons with cholesterol levels below the 80th percentile could still be at moderate risk of CHD. The US Lipid Research Clinic Coronary Primary Prevention Trial[15] has shown that CHD mortality in high-risk groups can be lessened by reducing serum cholesterol. It is therefore important to identify the high-risk individuals in a community and treat those with persistent hypercholesterolaemia. Clinical decisions should be influenced by the presence of other coronary risk factors, and the ultimate aim of treating hypercholesterolaemic persons should be a net reduction of CHD risk. Although the population strategy, which is aimed at lowering mean cholesterol levels in whole populations, will reduce the number of high-risk individuals, there will always be some who require more active management.

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