Lipoprotein lipids and the prevalence of hyperlipidaemia in rural India

Rajeev Gupta, Hari P. Gupta, Neeta Kumar*, Anil K. Joshi and Vijay P. Gupta[†]

Background: The prevalence of hyperlipidaemias has been inadequately studied in rural populations of developing countries. No significant data exist on the population levels of serum cholesterol, cholesterol subclasses or triglycerides in these countries. **Methods:** We studied fasting blood samples of 300 apparently healthy adults (202 men and 98 women, age range 20–73 years) randomly selected from a larger sample of 3148 individuals during a comprehensive cardiovascular risk-factor survey in Rajasthan, India. Levels of serum total cholesterol, its subfractions [low-density-lipoprotein (LDL) cholesterol, very-low-density-lipoprotein cholesterol and high-density-lipoprotein (HDL) cholesterol] and triglycerides were measured and correlated with age and anthropometric data.

Results: The mean ±SD serum total-cholesterol levels were 4.39±1.0 mmol/l in men and 4.37 ± 1.0 mmol/l in women, the mean LDL-cholesterol levels 2.51 ± 1.0 mmol/l in men and 2.62±0.9 mmol/l in women, the mean HDL-cholesterol levels 1.15±0.4 mmol/l in both men and women and the mean fasting serum triglyceride levels 1.63±0.6 mmol/l in men and 1.48±0.7 mmol/l in women. Age correlated positively with total-cholesterol, LDL-cholesterol, HDL-cholesterol and triglyceride levels in both men and women. Levels of the cholesterol subtypes did not differ between the sexes (P > 0.01), although triglyceride levels were significantly higher in men (P<0.01). Lipoprotein lipids did not correlate significantly with height, weight, body-mass index or waist: hip ratio. When classified according to the recommendations of the US National Cholesterol Education Program for the determination of the prevalence of hyperlipidaemia, 43 individuals (14.3%; men 14.4% and women 14.3%) had borderline high cholesterol levels (5.20-6.18 mmol/l) and 24 (8%; men 7.9% and women 8.2%) had high cholesterol levels (≥6.21 mmol/l). Forty-five participants (15%) had borderline high LDL-cholesterol levels (3.36-4.11 mmol/l) and 20 (6.7%) had high LDL-cholesterol levels (≥4.14 mmol/l); low HDL-cholesterol levels (< 0.9 mmol/l) were found in 89 (29.7%). Eighteen participants (6%) had mild hypertriglyceridaemia (2.82-5.64 mmol/l) and two (0.7%) had severe hypertriglyceridaemia (>5.64 mmol/l).

Conclusion: Total-cholesterol and LDL-cholesterol levels are low in a rural Indian population, although an atherogenic lipid profile is present in a significant proportion.

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Introduction

Cholesterol and its lipoprotein subclasses play a major role in cardiovascular risk. Both primary [1-3] and sec-

ondary [4,5] prevention trials have shown the importance of plasma total-cholesterol and low-density-lipoprotein (LDL)-cholesterol levels in the causation of coronary heart disease (CHD). Conversely, high-density-

From the Departments of Medicine and *Pathology, Monilek Hospital and Research Centre, Jawahar Nagar, Jaipur, and the †Department of Statistics, University of Rajasthan, Jaipur, India.

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Requests for reprints to Dr Rajeev Gupta, Department of Medicine, Monilek Hospital and Research Centre, Sector 4, Jawahar Nagar, Jaipur 302004, India.

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lipoprotein (HDL) cholesterol is important in the prevention of atherosclerosis [6,7].

Recent studies among Indians have shown a rise in the prevalence of CHD in both urban [8,9] and rural [9-12] populations. The cause of this rise is poorly understood but may be related to changing lifestyle, faulty dietary habits and lack of physical activity. Studies have also shown a very high prevalence of CHD in individuals from southern Asia who have settled abroad [13]. In these studies, it has been shown that apart from totalcholesterol levels, increased serum triglyceride levels are also important. These studies have also described a state of insulin resistance (hyperinsulinaemia, glucose intolerance and truncal obesity) among south Asians who have CHD [14,15]. High total- and LDL-cholesterol and low HDL-cholesterol levels may also be important [16]. To determine the population levels of cholesterol, its major subclasses and triglycerides, we studied a randomized sample of the adult population of villages in central Rajasthan. We also analysed the prevalence of abnormal lipid profiles in this population.

Methods

The detailed methodology, including a full description of the proforma and statistical analyses, has been described elsewhere [12]. In short, a detailed proforma was prepared according to suggestions published by the World Health Organization [17], the US National Institutes of Health [18] and in a review of previous national studies of the prevalence of CHD and coronary risk factors [19]. The proforma included details of various social factors as well as conventional risk factors.

The study was designed to include villages that are at a substantial distance from a major town. To this end, various areas in Rajasthan were assessed where enthusiastic and willing medical personnel, both doctors and technicians, were available. After detailed enquiries and pilot surveys, a cluster of villages in the Parbatsar county in the Nagaur district of Rajasthan were identified. These villages are 155 km from Jaipur and 65 km from Ajmer, the major towns in the area. Adults aged 20 years and over in the three adjoining villages of Bagoth, Badoo and Janjila were examined. According to census data, 2188 men and 1968 women over 20 years of age inhabited these villages; we examined 90.6% of the men and 59.2% of the women.

The physical examination included measurements of blood pressure and body-mass index (BMI). Blood pressure was measured using a standard mercury manometer. BMI was calculated by dividing the subject's weight (measured in kilograms with the subject dressed in normal indoor clothing) by the square of their height (measured in metres with the subject barefoot). The maximum supine waist circumference and the standing hip circumference at the inter-trochanteric level were measured to determine the waist: hip ratio.

Fasting blood samples from a randomly selected 10% of the total study population were sought for analysis. To achieve this, 12% of the people in each of the age groups were offered the blood test. The response rate was lower in the younger age groups than in the older ones (Table 1). The overall response rate was 87% in men and 71% in women. In those aged 20–29 years, the response rate was lower than the target of 10%.

Table 1. Response to the request for a blood test in the various age groups.

Age		Mer	ו	Women			
(years)	Total	Offered	Accepted	Total	Offered	Accepted	
20–29	571	68	40 (59%)	382	46	18(39%)	
30–39	495	59	52 (88%)	342	41	25 (61%)	
40-49	336	40	39 (98%)	212	25	27 (108%)	
50-59	288	32	38 (119%)	127	15	13 (87%)	
≥60	292	34	33 (97%)	103	12	15(125%)	
Total	1982	233	202 (87%)	1166	139	98 (71%)	

The response rate exceeded 100% in some groups because of the number of people volunteering for the test.

Serum samples were separated and kept at 4°C. All the samples were analysed within 48 h of their collection at our laboratory. Proper standardization techniques were used. Total-cholesterol levels were estimated using cholesterol oxidase-phenol 4-aminophenazone peroxidase and HDL-cholesterol levels using a precipitation enzymatic method after the precipitation of non-HDL cholesterol with manganese-heparin substrate. Triglyceride levels were measured using the glycerol phosphate oxidase-peroxidase enzymatic method. LDLcholesterol and very-low-density-lipoprotein-cholesterol levels were derived from the above using Freidewald's formula.

Statistical analysis

Data are means ± SD. Pearson's coefficient of correlation (r) was first calculated for numerical variables in order to detect any linear association between lipoprotein lipid subtypes and anthropometric data such as height, weight, BMI and waist : hip ratio; no significant correlation emerged after univariate analysis, so multivariate analysis was not performed. Non-parametric statistical analysis was performed using a commercially available statistics package (SPSS version 4.0, SPSS Inc., Chicago, Illinois, USA). Analysis of variance (ANOVA) was used to analyse the above-mentioned variables, treating each lipoprotein lipid subtype as a dependent variable. When no significant F-values emerged, a multiple classification analysis was performed within the ANOVA. This determined multiple R- and R2-values, the significance of which was determined using standard tables. Differences

were considered significant when the two-tailed *P*-value was less than 0.05.

Results

A total of 3148 people were examined in the prevalence study, and blood samples were collected from 311 (9.9%). The results from 11 of these samples were inadequate for the analysis and were excluded.

Table 2 shows the lipoprotein lipid composition according to age group and sex. The mean \pm SD serum total-cholesterol levels were $4.39 \pm 1.0 \text{ mmol/l}$ in men (range 2.17-6.75) and $4.37 \pm 1.0 \text{ mmol/l}$ in women (range 2.61-12.05), the mean LDL-cholesterol levels 2.51 \pm 1.0 mmol/l in men (range 0.31-4.99) and 2.62 \pm 0.9 mmol/l in women (range 0.49-8.71), the mean HDL cholesterol levels 1.15 \pm 0.4 mmol/l in men (range 0.54-2.51) and 1.15 \pm 0.4 mmol/l in women (range 0.5-2.56) and the mean fasting serum triglyceride levels 1.63 \pm 0.6 mmol/l in men (range 0.42-4.29) and 1.48 \pm 0.7 mmol/l in women (range 0.52-5.78). Levels of total cholesterol, LDL-cholesterol and triglycerides tended to increase with increasing age (Fig. 1).

Age correlated significantly with total-cholesterol level ($R^2 = 0.23$ for men and 0.25 for women), LDL-cholesterol level ($R^2 = 0.25$ for men and 0.28 for women), triglyceride level ($R^2 = 0.18$ for men and 0.23 for women) and HDL-cholesterol level ($R^2 = 0.15$ for men

Table 2. Lipoprotein lipid concentrations (mmol/l) in various age groups	Table 2.	Lipoprotein	i lipid co	ncentrations	(mmol/l) ir	various ag	e groups.
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and 0.34 for women). No significant differences between the sexes emerged for total-cholesterol, LDLcholesterol or HDL-cholesterol levels (P>0.1), although triglyceride levels were significantly higher in men (P < 0.01). Univariate correlation coefficients were calculated separately for each of the lipoprotein lipid subtypes and anthropometric indices. No significant correlations between height, weight, BMI or waist : hip ratio and total-, LDL-cholesterol or triglyceride levels were found in either men or women. The HDL-cholesterol level correlated significantly with BMI in women (r=0.34, P<0.05). Non-parametric analyses were performed using ANOVA for various lipoprotein lipids and anthropometric variables but no significant effects were observed. The multiple classification analysis also confirmed the absence of any significant multiple R- or R²-values.

The participants in our study were classified according to the recommendations of the US National Cholesterol Education Program [20] for the determination of the prevalence of hyperlipidaemia (Table 3). Borderline high cholesterol levels (5.20–6.18 mmol/l) were present in 43 participants (14.3%; men 14.4% and women 14.3%), and high cholesterol levels (\geq 6.21 mmol/l) in 24 (8%; men 7.9% and women 8.2%). Borderline high LDL-cholesterol levels (3.36–4.11 mmol/l) were found in 45 participants (15%), and high LDL-cholesterol levels (\geq 4.14 mmol/l) in 20 (6.7%); low HDL-cholesterol levels (<0.9 mmol/l) were found in 89 (29.7%). Mild hypertriglyceridaemia (2.82–5.64 mmol/l) was found in

	Number of participants	Total cholesterol	LDL cholesterol	HDL cholesterol	Triglycerides
Age 20–29 years				···	
Men	40	4.00±0.9	2.28 ± 0.7	1.10±0.3	1.37 ± 0.5
Women	18	4.19±0.9	2.45 ± 0.8	1.19±0.5	1.20 ± 0.6
Age 30–39 years					
Men	52	4.42±1.1	2.49±1.1	1.23 ± 0.4	1.61±0.8
Women	25	4.03 ± 0.9	2.37 ± 1.0	1.01 ± 0.2	1.51 ± 1.0
Age 40-49 years					
Men	39	4.36±1.1	2.34 ± 1.0	1.21 ± 0.4	1.82±0.9
Women	27	4.56 ± 1.2	2.78 ± 1.0	1.15±0.4	1.65 ± 0.6
Age 50-59 years					
Men	38	4.58±1.1	2.70±1.1	1.09 ± 0.3	1.81±0.6
Women	13	4.46±0.7	2.80 ± 0.7	1.14±0.4	1.63 ± 0.5
Age ≥60 years					
Men	33	4.63±1.1	2.82 ± 0.9	1.07 ± 0.3	1.56±0.6
Women	15	4.76±0.9	2.84 ± 0.7	1.31 ± 0.4	1.32 ± 0.6
Means					
Men	202	4.39±1.0	2.51 ± 1.0	1.15±0.4	1.63 ± 0.6
Women	98	4.37±1.0	2.62 ± 0.9	1.15 ± 0.4	1.48±0.7
Overall	300	4.38±1.0	2.55±1.0	1.15±0.4	1.58±0.7

Data are means±SD unless otherwise indicated. LDL, low-density lipoprotein; HDL, high-density lipoprotein.

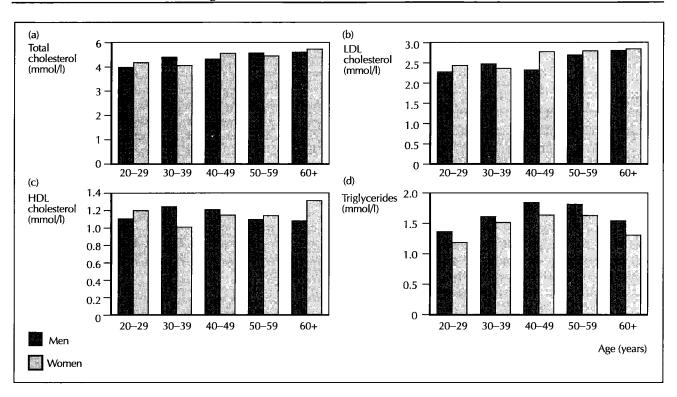


Fig. 1. A composite diagram showing the mean levels of lipoprotein lipids according to age.

18 (6%) and severe hypertriglyceridaemia (>5.64 mmol/l) in two of the participants (0.7%).

Table 3. Prevalence of hyperlipidaemia.

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Lipoprotein lipids	Men	Women	Total	
Total cholesterol (n	nmol/l)			
< 5.20	157 (77.7%)	76 (77.5%)	233 (77.7%)	
5.20-6.18	29 (14.4%)	14 (14.3%)	43 (14.3%)	
≥6.21	16 (7.9%)	8 (8.2%)	24 (8.0%)	
LDL cholesterol (m	mol/l)			
< 3.36	165 (81.7%)	70(71.4%)	235 (78.3%)	
3.36-4.11	29 (14.4%)	16(16.3%)	45 (15.0%)	
≥4.14	8 (3.9%)	12(12.3%)	20 (6.7%)	
HDL cholesterol (n	nmol/l)			
<0.9	49 (24.2%)	40 (40.8%)	89 (29.7%)	
Triglycerides (mmo	I/I)			
< 2.82	189 (93.6%)	91 (92.9%)	280 (93.3%)	
2.82-5.64	12 (5.9%)	6(6.1%)	18(6.0%)	
>5.64	1 (0,5%)	1 (1.0%)	2(0.7%)	

LDL, low-density lipoprotein; HDL, high-density lipoprotein.

Discussion

The present study shows that the mean total-cholesterol, LDL-cholesterol and HDL-cholesterol levels in a rural Indian population are lower than, and triglyceride values are as high as, those in developed countries. Subgroup analysis showed that an atherogenic lipid profile is present in a significant proportion of the population.

Recent studies from developing countries such as China [21] and Costa Rica [22] have shown that cholesterol and other lipid levels are lower in these than in developed countries such as the USA [23] and Norway [24]. A comparison of mean lipoprotein lipid levels from these countries is shown in Table 4. In China, mean cholesterol levels (4.55 mmol/l in men and 4.52 mmol/l in women) are similar to those in the present study (4.40 mmol/l in men and 4.37 mmol/l in women), both much lower than the latest US data (NHANES III) [23], which show total-cholesterol levels in adults of 5.30 mmol/l for men and 5.35 mmol/l for women. LDL-cholesterol levels in Chinese populations (2.69 mmol/l in men and 2.61 mmol/l in women) are similar to those in the present study (2.51 mmol/l in men and 2.61 mmol/l in women), both much lower than those in US and Norwegian populations. The HDLcholesterol level in Chinese men is 1.32 mmol/l and 1.42 mmol/l in women, both of which are marginally higher than our data (1.15 mmol/l). The triglyceride levels in the present study (1.64 mmol/l in men and 1.48 mmol/l in women) are much higher than those in Chinese men and women (1.17 mmol/l in men and 1.14 mmol/l in women) and are similar to the US data. The raised triglyceride levels may be related to the high intake of carbohydrate by Indians as part of their routine diet [12,13]. However, the Chinese also consume a high level of carbohydrate but have lower triglyceride

	Total cholesterol		LDL cholesterol		HDL cholesterol		Triglycerides	
Country	Men	Women	Men	Women	Men	Women	Men	Women
USA (NHANES III)	5.30	5.35	3.39	3.26	1.20	1.44	_	-
Norway (Tromsø)	5.69	5.48	3.77	3.77	1.37	1.63	1.42	0.99
China (Rural)	4.55	4.52	2.69	2.59	1.32	1.42	1.17	1.14
Costa Rica (Rural)	4.47	4.89	2.71	3.00	1.06	1.16	1.69	1.49
New Delhi	4.14	3.88	2.66	2.30	0.78	0.85	1.44	1.31
Present study	4.40	4.37	2.51	2.61	1.14	1.14	1.64	1.48

Table 4. International comparisons of lipoprotein lipid levels (mmol/l).

LDL, low-density lipoprotein; HDL, high-density lipoprotein; NHANES, National Health and Nutrition Examination Survey; -, data not available.

levels than the Indians in our study. Further studies are therefore needed to confirm this finding.

The mean lipoprotein lipid levels of 200 people from Delhi reported by Gandhi [25] are lower than those in the present study (Table 4). In contrast, results from a recent study in rural Delhi [26] (cholesterol 4.65 mmol/l, HDL cholesterol 1.13 mmol/l and triglycerides 1.02 mmol/l) are similar to ours. This contrast may reflect a change in the levels of various lipoprotein lipids in the Indian population.

The absence in the present study of differences between the sexes in total-cholesterol and HDL-cholesterol levels is noteworthy. Studies from developed countries have shown that women have higher HDL-cholesterol levels than men [23], a fact that is related to sex differences including high oestrogen levels in premenopausal women. Previous Indian studies have also shown no significant sex-related differences in HDL-cholesterol levels [25]. (The International Clinical Epidemiology Network study of cardiovascular risk factors in developing countries [27] reported the data in men only and is thus not comparable.) The reason for this finding is not clear, but may be related to the overall low total- and HDL-cholesterol levels in the study population.

Analysis of the prevalence of atherogenic lipid profiles indicates that hypercholesterolaemia (>5.20 mmol/l) is present in 22.3% of our study population compared with 55% of the adult US population [28]. LDL hypercholesterolaemia (>3.36 mmol/l) is present in 21.7% and low HDL-cholesterol levels (<0.9 mmol/l) in 29.7% of the population. The prevalence of significant hypertriglyceridaemia is low (6.7%). The population-based classification of cholesterol levels in India according to the guidelines of the US National Cholesterol Education Program has not been reported, and it is therefore difficult to comment on the comparative prevalence of hyperlipidaemias in different regions of the country.

No significant determinants of cholesterol level and levels of cholesterol subtypes were identified in the present study. With both linear and non-parametric statistical analysis, we were unable to find any significant correlation between lipoprotein subtypes and any of the anthropometric factors such as height, weight, BMI and waist : hip ratio. International data have confirmed the positive correlation between total- and LDL-cholesterol levels and weight, BMI [29] and waist : hip ratio [30]. A larger sample size is probably required to evaluate these results. Also, we have not analysed the dietary history in detail and thus cannot comment on this factor, although dietary intake is similar in all classes of persons in rural India [31] and this variable may therefore not be of great importance.

General awareness of the importance of cholesterol subtypes as major risk factors for coronary atherosclerosis is low among the Indian population [32] and the country's doctors [33]. Our data indicate that an atherogenic lipid profile is present in a significant proportion of a rural population in India. Public education measures should be able to achieve a realistic reduction in population cholesterol levels [34], thus helping to reduce the rising incidence of CHD in the country.

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