Current State of and Recent Trends in Serum Lipid Levels in the General Japanese Population

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Key words; Hyperlipidemia, cholesterol, triglyceride, life style, coronary heart disease

Abstract

To determine the recent serum lipid levels and other serum variables in the general Japanese population and trends in their changes over the past 40 years, a nationwide survey of serum lipid levels was conducted in 36 institutes from various districts around Japan. The total number of subjects was 12,839 consisting of 7,658 men and 5,179 women aged 4 through 99 years. The mean total cholesterol level was 201 mg/dl; 202 mg/dl in men and 200 mg/dl in women. The mean HDL-cholesterol level was 59 mg/dl; 55 mg/dl in men and 65 mg/dl in women. The mean LDL-cholesterol level was 118 mg/dl; 121 mg/dl in men and 115 mg/dl in women. The mean triglyceride level was 118 mg/dl; 136 mg/dl in men and 92 mg/dl in women. The total cholesterol level was slightly increased by 5 mg/dl in 10 years. Although the triglyceride level in women was not changed, the triglyceride level in men was increased in 10 years, especially in the 30s through 70s, indicating a possible increase in the metabolic syndrome in the future. The present results will become the standard serum lipid level data for the Japanese people, and succeeding 10-year surveys will clarify the trends of lipid levels in this country.

Introduction

It has been well established that hyperlipidemia is a major risk factor for coronary heart disease (CHD) (1; 2). Numerous studies have shown that the reduction of serum lipid levels by dietary or drug treatment results in a decrease in both the incidence of and the mortality from CHD (3-7). In contrast to the sharp decline in both serum cholesterol and the mortality from CHD in the United States and Western Europe, remarkable increases in serum cholesterol levels as well as CHD mortality have been anticipated in the Asian-Pacific area due to industrialization and modernization of the lifestyle. Epidemiological studies indicate that changes in lifestyle have a great influence on the risk factors for atherosclerosis (8-10). Among the Asian-Pacific countries, Japan was found to have lower serum cholesterol values and a correspondingly lower incidence of CHD. Japanese in the 1960s consumed very little dietary fat, and both in cholesterol levels and the incidence of CHD were low. Japanese who migrated to Hawaii and California, however, showed higher levels of serum cholesterol and a higher incidence of CHD than people in Japan (10). Thus, dietary habits and other environmental factors rather than genetic background affect serum cholesterol levels and CHD mortality in the population. In the United States, during the period of 1900 through 1991, many changes in nutritional lifestyle and medical therapeutic factors may have decreased serum total cholesterol levels among American adults (11). On the other hand, Japanese have adopted mixed dietary habits of a traditionally low fat and low cholesterol diet and a western style diet of relatively high fat and high cholesterol. As a result the serum cholesterol levels in the Japanese populations were found to have gradually increased over the 30 years from 1960 to 1990 by the

10-year-interval national surveys of serum cholesterol levels conducted in 1960, 1970, 1980, and 1990 (12-14). This study is the fifth survey and reveals the most recent serum lipid levels as well as fasting glucose, hemoglobin A1c (HbA1c), insulin, and uric acid levels in the Japanese general population and the trends of serum lipid levels over the 40 years from 1960 to 2000.

Methods

Designs and Data Collection

The Research Group on Serum Lipid Level Survey 2000 in Japan organized the members of 36 institutes from various areas around Japan. The project was designed to produce representative data of serum lipid, , insulin, and uric acid plasma glucose and HbA1c levels in the civilian Japanese population. The subjects were people receiving annual health examinations in general community, companies, and schools, and not patient-visiting hospitals. The total number of subjects was 12,839, consisting of 7,658 men and 5,179 women. (Two of them were unknown for sex.)

Laboratory Methods

All serum and plasma samples were obtained in the fasting state except participants less than 20 years old, because it was hard to obtain permission of blood drawing in a fasting state in children. All lipid and other analyses were conducted on venous blood samples within one week of collection at BML (Saitama, Japan). Serum cholesterol and triglyceride levels were measured by enzymatic assay. HDL-cholesterol and LDL-cholesterol were measured enzymatically by a kit from Daiichi Kagaku Co. Ltd. (Tokyo, Japan). The results of lipid analyses in the four surveys were indirectly standardized according to the criteria of the CDC Lipid Standardization Program (11). There were

no differences between the data obtained by Zak-Henly's method in 1960 and 1970, and those by the enzymatic methods used in 1980 through 2000. Thus, the cholesterol levels in these five surveys appear to be comparable. In the present survey, we also measured remnant like particles (RLP)-cholesterol by a kit from Japan Immunoresearch Laboratories (Takasaki, Japan). Plasma glucose was determined enzymatically and HbA1c was determined by a kit from Kyowa Medics Co.Ltd (Tokyo, Japan). Serum insulin was determined by immunoradiometric assay (Abbott Diagnostics Division, Abbot Park, IL).

Data Analyses

The statistical analyses of the present data were performed by SAS statistical. The study was designed by the Research group, which organized 36 institutions from various districts of Japan from the extreme North (Hokkaido) to the furthest South (Okinawa) islands.

Results

Table 1 shows the age-specific means and standard deviations of serum total cholesterol levels by age group in all the participants as well as in men and women. The mean total cholesterol level in this survey was 201 mg/dl, which is 5 mg/dl higher than that in 1990. In men, the age-specific mean serum cholesterol levels gradually increased from 185 mg/dl in the 0- to 9-year-old age group to 207 mg/dl in the 50- to 59-year-old age group. There was a slight decrease after age 60. In women, the mean cholesterol levels gradually rose from 186 mg/dl in the 0- to 9-year-old age group to 218 mg/dl in the 50- to 69-year-old age groups, and fell to 208 mg/dl after age 80.

Table 2 shows the age-specific means and standard deviations of serum triglyceride levels in all the participants as well as in men and women. The mean triglyceride level in this survey was 118 mg/dl, which was 13 mg/dl higher than that in 1990. The age-specific mean triglyceride values in men increased from 53 mg/dl in the 0- to 9-year-old age group to 150 mg/ dl in the 40- to 49-year-old age group, followed by a decline to 88 mg/dl above 80 years old. In women, the age-specific mean triglyceride levels increased gradually from 59 mg/dl in the 0- to 9-year-old age group to 117 mg/dl in the 60- to 69-year-old age group, and then declined to 105 mg/dl above 80 years of age. Although the triglyceride level in women was not changed in ten years, the triglyceride level in men was markedly increased, especially 30- to 39-year-old to 70- to 79-year-old age group in the last ten years.

Table 3 shows the age-specific means and standard deviations in serum HDL-cholesterol levels in all the participants as well as in men and women. The mean HDL-cholesterol level in this survey was 59 mg/dl, which is 5 mg/dl higher than that in 1990. The age-specific mean HDL-cholesterol levels in men gradually decreased from 70 mg/dl in the 0-to 9-year-old age group to 54 mg/dl in the 30- to 39-year-old age group, and remained at this level up to 89 years old age. The mean HDL-cholesterol levels in woman remained constant from the 0- to 9-year-old age group to the 50- to 59-year-old age group, and gradually decreased thereafter.

Table 4 shows the age-specific means and standard deviations in serum LDL-cholesterol levels in all the participants as well as in men and women. LDL-cholesterol was measured directly, not by Friedewald equation. The mean LDL-cholesterol level in this survey was 118 mg/dl, which is

almost the same as that in 1990. The age-specific mean LDL-cholesterol levels in men gradually

increased from 101 mg/dl in the 0- to 19-year-old age group to 125 mg/dl in the 50- 59-year-old age

group. The age-specific mean LDL-cholesterol level in women increased from 93 mg/dl in the 20-

to 29-year-old age group to 135 mg/dl in the 60- to 69-year-old age group, and then decreased

slightly thereafter.

Table 5 shows the age-specific means and standard deviations in serum RLP-cholesterol

levels in all the participants as well as in men and women. The mean RLP-cholesterol level in this

survey was 4.5 mg/dl. The mean RLP-cholesterol level in men was significantly higher than that in

women, and the tendency in age-specific means was similar to the triglyceride level. Fig. 1

summarizes the recent trend of the mean cholesterol level in young and middle-aged men and

women from 1960 to 2000. The trend indicates a gradual increase in the total cholesterol level in

men and women in almost all generations over the last 40 years in Japan.

Table 6 shows the age-specific means and standard deviations in plasma fasting glucose

levels in all the participants as well as in men and women. The mean fasting glucose level in this

survey was 95 mg/dl. The mean glucose level was slightly higher in men than in women. The

glucose level had a tendency gradually increasing according to age in both men and women. HbA1c

levels also had a tendency gradually increasing according to age in both men and women. However,

the mean HbA1c levels in men and women were almost the same in each age group (Table 7). We

also measured the serum insulin level in this survey. The serum insulin level was almost constant

except in the 20- to 29-year-old age group and the mean insulin level in this survey was 7 μU/ml

(Table 8).

Finally, we determined uric acid levels. The mean uric acid level in this survey was 5.4 mg/dl. The mean uric acid level was significantly higher in men than in women. Although the level of uric acid in men was almost constant in all age groups, the uric acid level in women was gradually increased according to age.

Discussion

In this survey we found that the mean total cholesterol level in Japanese general population increased by 5 mg/dl in the last 10 years. This increase, however, is attributed to the increase in HDL-cholesterol, but not to LDL-cholesterol. The triglyceride level is also increased in the last 10 years. This increase is attributed to the increase in middle-aged men, making us anticipate a further increase in the incidence of hypertriglyceridemia in the future. The significance of triglyceride as a risk factor for CHD has recently obtained more attention world-wide, and its relationship with hyperinsulinemia and glucose intolerance is emphasized (15; 16). In the analysis by Yamamoto et al on the survey in 1990, they concluded that the most important cause of hypertriglyceridemia would be overweight. According to the survey conducted by the Ministry of Health, Labor, and Welfare the body mass index is increasing from 1980 to 2000 only in men. Therefore, as clinicians we need to encourage life style changes, such as more exercise and Japanese food instead of western diet to the Japanese general population, especially men. Unless we can change our life style in Japan, more people will die from cardiovascular disease in the 21st century.

Guidelines for the proper management of risk factors, targeting the prevention and treatment of atherosclerotic disease, have been established in the United States (17; 18) and Europe (19). The Japan Atherosclerosis Society also published a guideline for the management of hyperlipidemia for the prevention of CHD in 2002. As the American and European guidelines, the Japanese guideline also emphasized the importance of the management of high risk patients, such as patients with multiple risk factors or diabetes as well as those with established CHD. Although our survey shows no increase in LDL-cholesterol level, the triglyceride level was significantly increased in the last 10 years. Especially, the male mean triglyceride level in their 40s is 150 mg/dl, indicating about half of the participants have hypertriglyceridemia. Because hypertriglyceridemia is one of the criteria of the metabolic syndrome, our result implies that the number of the patients with the metabolic syndrome will increase in Japan. Therefore, in the next survey in 2010, we will investigate the incidence of the metabolic syndrome in Japanese .general population after establishing a guideline of the metabolic syndrome for Japanese. This survey also indicates that we as the members of the Japan Atherosclerosis Society have to make every effort to call more clinical attention for the management of dyslipidemia for the prevention of CHD.

Currently approximately 4 million people are taking statins for hyperlipidemia in Japan. In this survey about 5% of the participants were turned out to take lipid-lowering drug, most of which are supposed to be statins. The mean total cholesterol level of the participants without lipid lowering drugs was 209 mg/dl, which is slightly higher than the mean total cholesterol levels of all the participants. In this sense, the participants in this survey represent the general population in

Japan. Use of lipid-lowering drugs, such as statins would be more important for the treatment of high risk patients to prevent CHD.

In 2000, another survey was done at the same time, conducted by the Ministry of Health, Labor, and Welfare. In this study, more subjects were selected from rural, agricultural, and mountain areas, and there was no rise in serum cholesterol in the last 10 years (from 1990 to 2000). In this study carried out by the members of the Japan Atherosclerosis Society more subjects from urban areas were included. In both studies, the cholesterol levels used to be significantly lower in the districts including wider agricultural and mountain areas than in the districts including large cities like Tokyo and Osaka in 1980. In 1990, the difference in serum cholesterol levels was no longer significant between urban, rural, and mountain village areas. Therefore, it is not clear why these studies show a different trend in the cholesterol level.

In this survey we also determined fasting glucose, insulin, and HbA1c levels of approximately 10,000 participants. We think that this is the largest survey for glucose metabolism in Japan. Our data indicate that the glucose and HbA1c levels are gradually increasing according to age in both sexes. However, the plasma insulin levels are almost constant in all age groups. We also showed that the uric acid level is significantly higher in men than in women. This is consistent with the data that the incidence of hyperuricemia and gout is higher in males than in females. Alcohol consumption would contribute to the higher level of uric acid in men. According to the database from the Ministry of Health, Labor, and Welfare (http://www.mhlw.go.jp/toukei/), the incidence of hyperuricemia in men and women is increasing in Japan. Because hyperuricemia is related to

obesity, hypertension, and insulin resistance, and eventually to the incidence of CHD, controlling the uric acid level would be important for the prevention of CHD in Japan.

Thus this report tells us the importance of the prevention and treatment of hyperlipidemia for the prevention of CHD in Japan. We need to establish a guideline for the life style change to prevent the further increase of dyslipidemia in the future.

Acknowledgements

Appendix

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other Societies on Coronary Prevention. Atherosclerosis 140:199-270, 1998

Figure legends

Fig. 1

Trends of serum cholesterol levels in Japanese in 40 years from 1960 to 2000. Results of the

surveys carried out by the members of Japan Atherosclerosis Society. The mean cholesterol level in

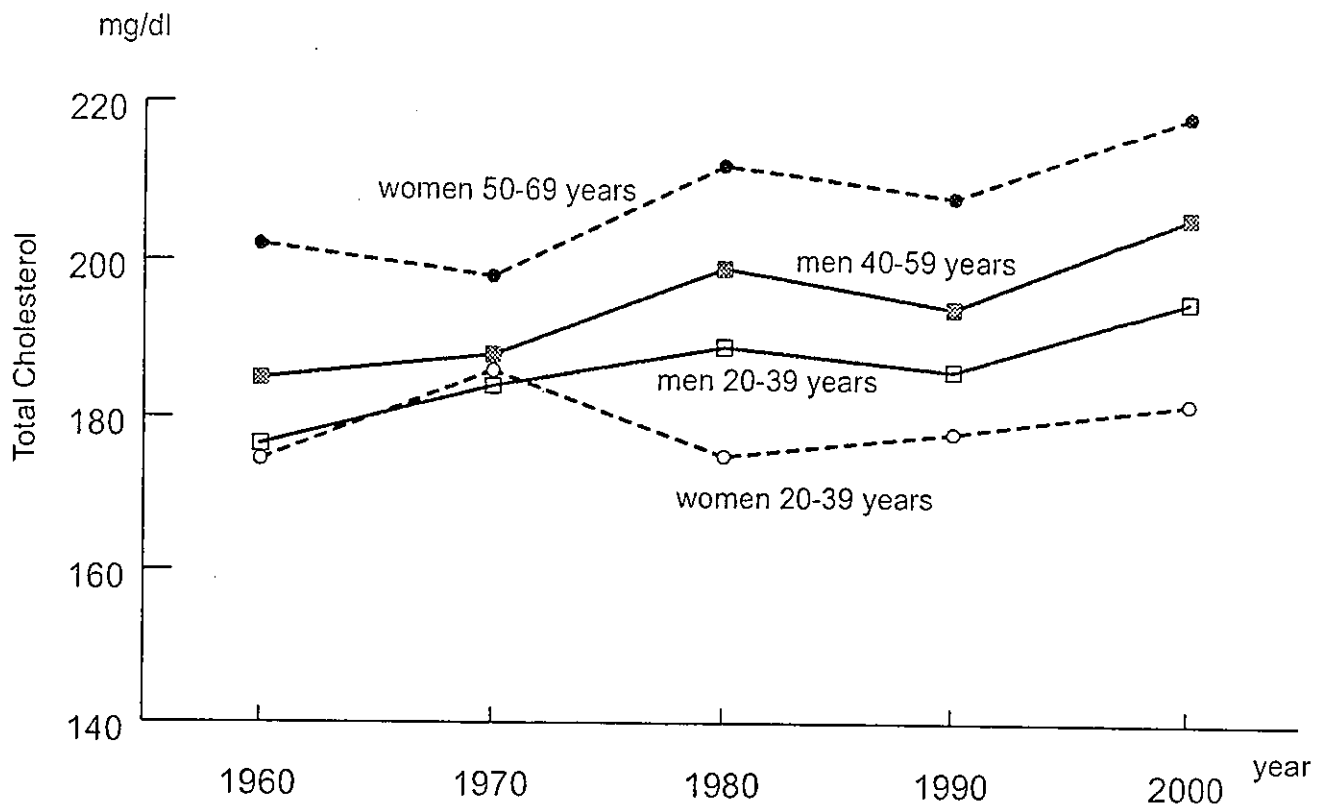men and women of 20-39 years, men of 40-59 years, and women of 50-69 years.

Fig. 1

mg/dl

Total Cholesterol

220

200

180

160

140

women 50-69 years

men 40-59 years

men 20-39 years

women 20-39 years

1960   1970   1980   1990   2000   year

Table 1. Serum total cholesterol (mg /dl) for each 10-year group in Japanese

Age	all			men			women		
	N	mean	S.D.	N	mean	S.D.	N	mean	S.D.
0-9	216	186	27	102	185	26	114	186	27
10-19	465	181	28	196	178	28	269	183	27
20-29	1,256	180	31	394	181	32	861	180	31
30-39	1,642	195	34	1,101	200	34	541	185	31
40-49	3,564	201	33	2,399	204	32	1,165	195	32
50-59	3,467	211	34	2,328	207	33	1,139	218	34
60-69	1,625	209	34	844	200	34	780	218	32
70-79	551	206	33	271	198	32	280	214	32
80-89	53	197	33	23	181	29	30	208	32
Total	12,839	201	34	7,658	202	34	5,179	200	35

Table 2. Serum triglyceride (mg /dl) for each 10-year group in Japanese

Age	all			men			women		
	N	mean	S.D.	N	mean	S.D.	N	mean	S.D.
0-9	216	56	30	102	53	30	114	59	30
10-19	465	67	36	196	66	39	269	68	33
20-29	1,256	83	65	394	105	74	861	73	58
30-39	1,642	118	109	1,101	142	123	541	70	42
40-49	3,564	129	103	2,399	150	112	1,165	87	63
50-59	3,467	129	102	2,328	139	115	1,139	108	66
60-69	1,625	123	83	844	128	98	780	117	64
70-79	551	118	63	271	123	67	280	113	59
80-89	53	100	44	23	93	38	30	105	47
Total	12,839	118	96	7,658	136	109	5,179	92	62

Table 3. Serum HDL-cholesterol (mg/dl) for each 10-year group in Japanese

Age	all			men			women		
	N	mean	S.D.	N	mean	S.D.	N	mean	S.D.
0-9	216	69	15	102	70	15	114	68	16
10-19	465	65	14	196	63	14	269	66	13
20-29	1,255	64	14	393	56	13	861	68	14
30-39	1,637	58	15	1,096	54	14	541	67	14
40-49	3,545	58	15	2,380	55	14	1,165	65	15
50-59	3,434	59	16	2,295	56	15	1,139	65	16
60-69	1,614	57	14	833	55	14	780	60	14
70-79	551	57	15	271	55	15	280	60	15
80-89	53	58	16	23	54	12	30	61	18
Total	12,770	59	15	7,589	55	14	5,179	65	15