

Plasma Vitamins A, C and E in the General Population of Singapore, 1993 to 1995

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Abstract

The National University of Singapore Heart Study measured cardiovascular risk factors, including selected plasma vitamins, on a random sample of the general population aged 30 to 69 years.

Plasma vitamins A and E were normal and similar by ethnic group. Mean plasma vitamin A levels were: Chinese (males 0.68 and females 0.52 mg/L), Malays (males 0.67 and females 0.54 mg/L), and Indians (males 0.66 and females 0.51 mg/L). Mean plasma vitamin E levels were: Chinese (males 12.6 and females 12.6 mg/L), Malays (males 13.6 and females 13.3 mg/L), and Indians (males 12.9 and females 12.8 mg/L). No person had plasma vitamin A deficiency (<0.01 mg/L) and only 0.1% had vitamin E deficiency (<5.0 mg/L).

In contrast, plasma vitamin C was on the low side and higher in Chinese than Malays and Indians. Mean plasma vitamin C levels were: Chinese (males 6.3 and females 8.4 mg/L), Malays (males 5.1 and females 6.4 mg/L), and Indians (males 5.7 and females 6.9 mg/L). Likewise, the proportions with plasma vitamin C deficiency (<2.0 mg/L) were lower in Chinese (males 14.4 and females 0.7%), than Malays (males 19.7 and females 7.2%), and Indians (males 17.8 and females 11.0%). Relatively low levels of plasma vitamin C may contribute to the high rates of coronary heart disease and cancer in Singapore. In particular, lower plasma vitamin C in Malays and Indians than Chinese may contribute to their higher rates of coronary heart disease. However, plasma vitamin C does not seem to be involved in the higher rates of cancer in Chinese than Malays and Indians. The findings suggest a relatively low intake of fresh fruits and a higher intake is recommended. Also, food sources of vitamin C may be destroyed by the high cooking temperatures of local cuisines, especially the Malay and Indian ones.

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Introduction

The current disease pattern in Singapore (an island state of 3.3 million people composed of 76% Chinese, 14% Malays, 7% Asian Indians and 3% Others) is dominated by non-communicable diseases. There have been increasing trends, though with recent declines, for coronary heart disease (CHD)¹ and cerebrovascular disease.² Cancer has also been increasing.³ Cardiovascular diseases and cancer are now the commonest causes of death.⁴ Coronary heart disease (CHD) rate is highest in Indians, followed by Malays and then Chinese.⁵ Cancer incidence, on the other hand, is highest in Chinese, followed by Malays and then Indians, with ethnic differences for the different types of cancer.³ These trends and ethnic differences may be due to changes and differences in lifestyles, such as diet.

There is strong evidence that oxidative free-radicals have a role in the development of degenerative diseases,

including CHD and cancer.⁶ Antioxidants in the diet include vitamins A, C and E. There is evidence, though inconclusive, that antioxidant vitamins are beneficial.^{7,8} In particular, there is evidence for the benefits of consumption of fresh fruits and vegetables.⁹ However, no benefits have been found for vitamins A and E supplements on cardiovascular disease or cancer in the Alpha-Tocopherol, Beta Carotene (ATBC) Cancer Prevention Study,¹⁰ the Physicians' Health Study,¹¹ and the Beta-Carotene and Retinol Efficacy Trial (CARET).¹² However, these trials were of short duration and examined the possible benefits of vitamin supplementation rather than the possible harmful effects of a low vitamin intake. A prospective study in Finland found that vitamin C deficiency (assessed by low plasma levels) was a risk factor for CHD.¹³

It is important to know the current blood levels of vitamins in Singapore, and to examine their possible role

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in the high rates of cardiovascular diseases and cancer, with ethnic differences. The National University of Singapore Heart Study measured cardiovascular risk factors, including newer ones not studied in the previous Singapore Thyroid and Heart Study.¹⁴ This paper examines levels and ethnic differences of plasma vitamins A, C and E, which may be important in the risk of CHD and cancer.

Materials and Methods

Sample

The National University of Singapore Heart Study is a cross-sectional survey of a random sample of persons aged 30 to 69 years from the general population of Singapore. The sample was obtained from two sources, the Singapore Thyroid and Heart Study,¹⁴ and electoral registers of 5 divisions from different parts of the island (north, south, east, west and centre). There was disproportionate sampling by ethnic group to obtain an equal number of subjects in each of the 6 main gender-ethnic groups. The required sample was 180 subjects in each gender-ethnic group giving a total of 1080 subjects. Assuming that 20% of the subjects would not be recruitable because of death, migration, infirmity, and relocation (which is high in Singapore due to massive urban redevelopment) and a response rate of 75%, a total of 1800 persons were selected. Of these, 419 (23.3%) were found not to be recruitable and 983 responded giving a response rate of 71.2%. Of the 983 subjects, 22 were 70 years or over and were excluded, leaving 961 persons aged between 30 and 69 years. Of these 961 persons, 4 refused to give blood. A further 16 did not have plasma vitamin assessments due to the unavailability of the technician on their clinic days, but this was in a purely random way. Hence, plasma vitamin assessments were performed on 941 persons, composed of 468 males (158 Chinese, 144 Malays and 166 Indians) and 473 females (165 Chinese, 142 Malays and 166 Indians).

Procedures

All clinics were held between 0900 and 1200 hours (from June 1993 to December 1995) with subjects from the two genders and three ethnic groups seen concurrently. The subjects were asked to fast from 2100 hours the previous evening. A questionnaire was administered by the same investigator trained in interview techniques and included questions on age, gender, and ethnic group (classification previously described⁵).

Venous blood specimens were taken with the subject in a sitting position using venoject vacuum containers with minimum venous stasis. Vacutainers containing ethylene diamine-tetra-acetate (EDTA) and heparin as anticoagulants were covered with aluminium foil to prevent admission of light and transported on ice to the laboratory, where the blood was centrifuged and meas-

urements made on plasma by automated high performance liquid chromatography. On the EDTA tubes, measurements of plasma vitamin C (ascorbic acid)¹⁵ were performed immediately. On the heparinised tubes, measurements of plasma vitamin A (retinol)¹⁶ and vitamin E (alpha-tocopherol)¹⁶ were performed in batches within two weeks after storing at -70°C.

Analysis

The mean ages of the subjects were similar by gender and ethnic group. Nevertheless there was age-adjustment; for means by analysis of covariance using the GLM procedure of SAS and for prevalences by direct standardisation to the total population of the sample with significance testing by the Z test. All significance testing was two-tailed. Cigarette smoking is known to reduce plasma vitamin C,⁶ and hence levels of this vitamin were also compared by ethnic group in non-smokers and smokers (the latter was not done in females as the proportion who smoke was only 2.3%). For the prevalences of plasma vitamin deficiencies, the cut-off levels were vitamin A <0.01 mg/L,¹⁷ vitamin E <5.0 mg/L,¹⁸ and vitamin C <2.0 mg/L.¹⁹ As there was disproportionate sampling by ethnic group, the prevalence rates of plasma vitamin C deficiency in Singapore for the two genders were estimated by applying the age/ethnic group specific rates to the population for 1995.²⁰

Results

All 6 distributions for each of the vitamins were unimodal with slight skewing to the right. Table I shows the mean plasma levels of the vitamins. Plasma vitamin A levels were higher in males than females, but were similar in the ethnic groups. No one had plasma vitamin A deficiency. Plasma vitamin E levels were similar in the males and females. Plasma vitamin E concentrations were highest in Malays, followed by Indians, and then Chinese for both genders, though only the differences between Chinese and Malays were statistically significant. Only one person (an Indian male) had plasma vitamin E deficiency.

Mean plasma vitamin C levels were much higher in females than males (Table I). Plasma vitamin C levels also showed ethnic differences, being higher in Chinese than Malays or Indians for both genders, with little difference between Malays and Indians (Table I). For males, plasma vitamin C was the higher in Chinese than Malays by 1.2 mg/L and higher than Indians by 0.6 mg/L. While for females, the differences were 2.0 mg/L and 1.5 mg/L, respectively. Levels for non-smoking males were higher than for all males (smokers and non-smokers) with the same ethnic differences. Levels in male cigarette smokers were lower than in non-smokers and ethnic differences were no longer present. Levels in female non-smokers were the same as for all females (only 2.3%

TABLE I: MEAN LEVELS (95% CONFIDENCE INTERVALS) OF VITAMINS, AGE-ADJUSTED BY ANALYSIS OF COVARIANCE, BY GENDER AND ETHNIC GROUP FOR AGE-GROUP 30 TO 69 YEARS, 1993 TO 1995

		Chinese (C)	Malays (M)	Indians (I)	Significance, <i>P</i> value		
					C vs M	C vs I	M vs I
Plasma vitamin A (mg/L)	Males	0.68 (0.66-0.70)	0.67 (0.65-0.69)	0.66 (0.64-0.68)	0.70	0.34	0.58
	Females	0.52 (0.50-0.54)	0.54 (0.52-0.56)	0.51 (0.49-0.53)	0.39	0.63	0.19
Plasma vitamin E (mg/L)	Males	12.6 (12.0-13.2)	13.6 (13.0-14.2)	12.9 (12.4-13.4)	0.02	0.46	0.11
	Females	12.6 (12.0-13.1)	13.3 (12.7-13.9)	12.8 (12.3-13.3)	0.08	0.67	0.18
Plasma vitamin C (mg/L)	Males	6.3 (5.8-6.8)	5.1 (4.6-5.6)	5.7 (5.2-6.2)	<0.01	0.09	0.12
	Females	8.4 (7.9-8.9)	6.4 (5.8-7.0)	6.9 (6.4-7.4)	<0.01	<0.01	0.20
	Males*	7.3 (6.8-7.8)	5.6 (5.1-5.7)	6.1 (5.6-6.6)	<0.01	0.01	0.35
	Females*	8.4 (8.1-8.7)	6.4 (6.1-6.7)	6.8 (6.5-7.1)	<0.01	<0.01	0.21
	Males**	3.7 (2.7-4.7)	4.3 (3.5-5.1)	4.7 (3.9-5.5)	0.33	0.11	0.47

* Non-smokers; **Cigarette smokers

TABLE II: PREVALENCE RATES(%) [95% CONFIDENCE INTERVALS] OF DEFICIENCY OF PLASMA VITAMIN C (<2.0 mg/L), AGE-ADJUSTED BY DIRECT STANDARDISATION, * BY GENDER AND ETHNIC GROUP FOR AGE-GROUP 30 TO 69 YEARS, 1993 TO 1995

	Chinese (C)	Malays (M)	Indians (I)	Significance, <i>P</i> value		
				C vs M	C vs I	M vs I
Males	14.4 (8.8-20.0)	19.7 (13.3-26.2)	17.8 (11.9-23.7)	0.21	0.40	0.66
Females	0.7 (0.0-3.5)	7.2 (3.6-12.8)	11.0 (6.2-15.8)	<0.01	<0.01	0.26
Males**	5.3 (1.9-11.3)	12.2 (6.1-21.1)	9.7 (4.0-16.8)	0.10	0.21	0.59
Females**	0.7 (0.0-3.6)	6.6 (3.1-12.1)	11.2 (6.3-16.0)	<0.01	<0.01	0.16
Males***	40.1 (25.3-56.6)	30.0 (18.8-43.2)	35.1 (23.4-48.7)	0.28	0.60	0.55

* To the total sample population

** Non-smokers; ***Cigarette smokers

of females were smokers).

The proportion of the males with plasma vitamin C deficiency was highest in Malays, followed by Indians and then Chinese, though the differences were not statistically significant (Table II). The proportion of females with plasma vitamin C deficiency (less than for males in all three ethnic groups) was highest in Indians, followed Malays, and then Chinese, with statistical significance for the differences between Indians and Chinese (10.3%) and between Malays and Chinese (6.5%).

Discussion

This study is the first to report on plasma levels of vitamins A, E and C in the general population of Singapore, and examine the possible roles of these antioxidants in the differential incidence of CHD and cancer between Chinese, Malays and Indians. An individual's plasma levels of vitamins will vary with changes in dietary intake, though 96.8% of the subjects in this study had been fasting for at least 10 hours. Despite any individual variation, on a population basis this study will measure ethnic differences in plasma levels, which reflect dietary intake.

As plasma lipids influence tocopherol concentrations, the plasma vitamin E to cholesterol ratio is sometimes used to measure plasma vitamin E level.²¹ However,

total cholesterol levels are similar in the three ethnic groups in Singapore,²² so that this correction is not needed for ethnic comparisons. Plasma vitamin A and E levels were similar by ethnic group. Levels of plasma vitamins A and E are comparable to those reported in US populations.^{17,18} No one had plasma vitamin A deficiency and only one person (0.1%) had plasma vitamin E deficiency. Vitamin A largely comes from foods of animal origin, vegetables and fruits¹⁷ and vitamin E largely from vegetables and grains.¹⁸ Dietary intakes of vitamins A and E from these foods in Singapore are adequate. Furthermore, vitamins A and E do not seem to contribute to the occurrence and ethnic differences of CHD or cancer in Singapore.

Lower plasma levels of vitamin C with cigarette smoking have been found in males. This could not be examined in females due to the small proportion of female smokers (2.3%). Lower plasma levels of vitamin C in smokers are due to both a lower intake and a higher metabolic turnover.¹⁹ Plasma levels of vitamin C were higher in females than males, which is consistent with findings elsewhere, despite similar dietary intakes.¹⁹

Plasma levels of vitamin C were lower in Malays and Indians than Chinese for both genders, both in all persons and in non-smokers. Similarly, the proportions with plasma vitamin C deficiency were higher in Malays

and Indians than Chinese, though statistical significance was present only for females. However, this ethnic difference was not present in male cigarette smokers. Most vitamin C in the diet comes from fruits and vegetables.¹⁹ Probably, Indians and Malays take less of these food than Chinese. Also, unlike vitamins A and E, vitamin C is water soluble and easily destroyed by heat treatment.²³ Prolonged cooking at higher temperatures are usually required in Indian and Malay dishes such as curry compared to the typical fast stir-fried dishes in Chinese cooking. Hence, more vitamin C will be destroyed in Indian and Malay cooking resulting in lower blood levels. Lower vitamin C may contribute to Indians and Malays having higher rates of CHD than Chinese,⁵ but vitamin C does not seem to be involved in the higher rates of cancer in Chinese than Malays and Indians.³

Mean levels of plasma vitamin C for all three ethnic groups in Singapore are lower than have been reported for US population, and are at the lower end of the normal range of 4.0 to 15.0 mg/L.¹⁹ Using age/ethnic group specific rates it is estimated that the overall rates of plasma vitamin C deficiency for the 30 to 69 years age group in Singapore are 14.5% for males and 2.2% for females, while without cigarette smoking the rate in males would be reduced to 6.2%. The relatively low levels for plasma vitamin C compared to the normal levels for plasma vitamins A and E suggest that in Singapore there is a relatively low intake of fresh fruits and that food is generally over-cooked. These relatively low levels of plasma vitamin C may contribute to the relatively high occurrence of CHD and cancer in Singapore.⁴ It should be noted that, in Finland, vitamin C deficiency (defined as plasma ascorbate <2.0 mg/L, as in this study) has been identified as a risk factor for CHD.¹³

In this study there were no measurements of dietary vitamin supplements. However, a food consumption survey in Singapore in 1993 did include questions on vitamin supplements [Food and Nutrition Department. Food consumption study 1993. Singapore: Ministry of Health, 1994 (unpublished data)]. Table III shows the proportions of the three ethnic groups aged between 18 and 69 years who were regularly taking vitamin supplements. Only a small proportion of Singaporeans were taking vitamins A and E, with slightly more taking vitamin C and multi-vitamins, suggesting that Singaporeans are getting slightly less vitamin C from their diet than plasma levels indicate.

In conclusion, if plasma vitamin C is established as being protective against CHD and cancer, relatively low plasma levels of this antioxidant could contribute to risk of these diseases in Singapore. Lower levels also could contribute to the higher risk of Indians and Malays having CHD compared to Chinese, but not to the relatively higher risk of Chinese having cancer. Intake of fresh fruits would seem to be inadequate in Singapore

TABLE III: PROPORTIONS (%) TAKING VITAMIN SUPPLEMENTS, BY GENDER AND ETHNIC GROUP FOR AGE GROUP 18 TO 69 YEARS, 1993

		Chinese	Malays	Indians	All
Vitamin A	Males*				1.1
	Females*				0.6
Vitamin E	Males*				1.1
	Females	4.0	0.0	1.4	2.5
Vitamin C	Males	5.9	8.5	1.8	4.5
	Females	6.3	1.4	6.9	5.3
Vitamin B Co	Males	0.7	1.8	3.6	1.5
	Females	1.1	2.7	1.4	1.6
Multi-vitamins	Males	3.9	0.0	7.3	3.8
	Females	0.6	2.7	2.8	1.6

Source: Food and Nutrition Department. Food consumption study 1993. Singapore: Ministry of Health, 1994 (unpublished data).

* Numbers are too small to be broken down by ethnic group

and should be increased. A further reason for the relatively low levels of plasma vitamin C, especially in Indians and Malays, is probably its destruction by cooking at high temperatures. Plasma vitamins A and E are at normal levels with no important ethnic differences.

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