

Serum Selenium in the General Population of Singapore, 1993 to 1995

K Hughes,*^{DM (Oxford), FRCP, FFPHM (UK)}, L H Chua,**^{MT}, C N Ong,**^{PhD (Manc), MSc (Lond), BSc (Nan)}

Abstract

Selenium is a trace element which plays a vital role in many metabolic functions and in particular is an integral part of the antioxidant enzyme glutathione peroxidase. It may be involved in the prevention of a number of diseases including cardiovascular diseases and cancer, which are the main causes of death in Singapore with ethnic differences. The National University of Singapore Heart Study measured cardiovascular risk factors, including serum selenium, in a random sample of the general population aged 30 to 69 years from 1993 to 1995. Mean serum selenium was higher in Chinese (males 126 and females 119 µg/L) and Malays (males 122 and females 122 µg/L) than Indians (males 117 and females 115 µg/L). These levels (with an estimated mean of 122 µg/L in Singapore) are lower than those in the USA but higher than those in Western Europe. The proportions with serum selenium <80 µg/L (classified as low values) were low, though highest in Indians (males 1.2% and females 1.2%), then Chinese (males 0.6% and females 1.3%) and then Malays (males 0.0% and females 0.0%), but the differences were not statistically significant. The overall estimate for the prevalence of low selenium in Singapore was 0.8%. It is concluded that levels of serum selenium in Singapore are satisfactory and no action with regard to dietary supplementation is needed. Serum selenium levels are slightly lower in Indians than in Chinese and Malays (probably due to a more vegetarian diet) and this may make a small contribution to Indians' higher rates of coronary heart disease compared to Chinese and Malays.

Ann Acad Med Singapore 1998; 27:520-3

Key words: Anti-oxidants, Cancer, Coronary heart disease, Diet, Ethnic

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 with cancer also increasing.³ Cardiovascular diseases and cancer are now the commonest causes of death.⁴ Coronary heart disease is highest in Indians, followed by Malays, and then Chinese.⁵ Cancer, on the other hand, is highest in Chinese, followed by Malays, and then Indians, with ethnic differences in the frequencies of the different types of cancer.³ These trends and ethnic differences must, at least partially, be due to changes and differences in lifestyles, such as diet.

Selenium, a trace element, is a key component of a number of functional selenoproteins required for normal health. In particular, selenium is an integral part of the antioxidant enzyme glutathione peroxidase, which removes hydroperoxides generated *in vivo* by free radi-

cals and which lead to lipid peroxidation, atherosclerosis, DNA damage, and production of carcinogens.⁶ There is epidemiological evidence for the beneficial effect of selenium on CHD particularly from Finland,⁷ though it is considered inconclusive.⁸ However, a recent editorial concluded that low levels of selenium probably increase cardiovascular diseases and cancers, and also hypothyroidism and subfertility.⁹

Selenium enters the food chain through plants and dietary intakes show a large geographical variation depending on the selenium content in soil. There is evidence that selenium levels are falling in some parts of the world, partly due to changes in bread making technology.⁹

It is important to know the current levels of blood selenium in Singapore. The National University of Singapore Heart Study measured cardiovascular risk factors, including newer ones not studied in the previous Singapore Thyroid and Heart Study.¹⁰ This paper examines levels and ethnic differences of serum selenium, which may be important in the risk of CHD and cancer.

* Associate Professor

** Medical Technologist

*** Professor

Department of Community, Occupational and Family Medicine
National University of Singapore

Address for Reprints: Associate Professor Kenneth Hughes, Department of Community, Occupational and Family Medicine, Faculty of Medicine, National University of Singapore, Lower Kent Ridge Road, Singapore 119260.

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. Details of the sampling have been described elsewhere.¹¹ In brief, the sample was obtained from two sources, the Singapore Thyroid and Heart Study,¹⁰ 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. There was a response rate of 71.2%. Of the 961 responders, 4 refused to give blood and another 8 had insufficient blood taken to include selenium measurements. Hence, serum selenium was measured on 949 persons aged between 30 and 69 years, composed of 471 males (158 Chinese, 146 Malays and 167 Indians) and 478 females (167 Chinese, 142 Malays and 169 Indians).

Procedures

All clinics were held between 0900 and 1200 hours (from June 1993 to December 1995) with 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. Serum selenium was measured on blood samples collected in plain vacutainers, in the Department of Community, Occupational and Family Medicine, National University Hospital, Singapore. Measurements were performed by Zeeman graphite atomic absorption spectrophotometry (ZAAS) in batches within 2 weeks after storing at -70°C . There was strict quality control. Precision of the method was measured by coefficients of variation, which were found to be 2.5% for within-day determinations and 4.4% for between-day determinations. Standardisation was carried out through the International Quality Control Programme of Canada (ICP-Canada). The mean bias between the laboratory and ICP-Canada was 4.8%.

Analysis

The mean ages 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. Fisher's Exact Test was used for comparisons of prevalences within age groups. All significance

testing was two-tailed. Serum selenium concentrations of $>100\ \mu\text{g/L}$ are considered to be required for optimal activity of glutathione peroxidase, and values $<80\ \mu\text{g/L}$ can be considered to be low.⁹ As there was disproportionate sampling by ethnic group the estimated means and prevalence rates of low levels of selenium in Singapore for the two genders were obtained by applying the age-ethnic group specific rates to the population for 1995.¹²

Results

All 6 distributions of serum selenium were normal. Table I shows that overall mean serum selenium was slightly higher in males than females, with no important changes with age. The estimated mean levels for Singapore were higher in males than females for the 30 to 49 years age group but not for the 50 to 69 years age group. The overall means in the 30 to 69 years age group were $125\ \mu\text{g/L}$ for males, $119\ \mu\text{g/L}$ for females, and $122\ \mu\text{g/L}$ for all persons.

Table I further shows that there were ethnic differences. For both genders and all age groups, mean levels of selenium were lower in Indians than in Chinese and Malays with the differences between Chinese and Malays being small and variable (Table I). In the overall 30 to 69 years age group for males, selenium level was highest in Chinese, followed by Malays, and then Indians, with Indians having lower levels than Chinese and Malays by $9\ \mu\text{g/L}$ and $5\ \mu\text{g/L}$ respectively, and Malays having a lower level than Chinese by $4\ \mu\text{g/L}$. In the overall age group for females, serum selenium was higher in Chinese and Malays than Indians, with differences of $4\ \mu\text{g/L}$ and $7\ \mu\text{g/L}$, respectively.

Table II shows that the proportions with low concentrations of serum selenium ($<80\ \mu\text{g/L}$) showed little gender difference, being slightly higher in females for the younger age group and slightly higher in males for the older age group. The proportions were very low for both genders and all three ethnic groups. It is estimated that the proportions with these low levels in Singapore were 0.5% of males, 1.2% of females and 0.8% of all persons. The proportions with these low values were higher in Indians than Chinese and Malays but the differences were small and not statistically significant.

Discussion

This is the first study on selenium in the general population of Singapore and the objective was to examine its possible role in the differential risk from CHD and cancer among Chinese, Malays and Indians.

Mean serum selenium levels were little different by age and just slightly higher in males than females. In the USA, average blood selenium levels have been found to range from 160 to 260 $\mu\text{g/L}$ with values in areas considered to have low and marginally adequate levels of soil

TABLE I: MEAN CONCENTRATIONS [95% CONFIDENCE INTERVALS (CI)] OF SERUM SELENIUM ($\mu\text{g/L}$), AGE-ADJUSTED BY ANALYSIS OF COVARIANCE, BY GENDER, ETHNIC GROUP AND AGE-GROUP

		Chinese (C)	Malays (M)	Indians (I)	Significance, <i>P</i> value			Singapore*
		Mean concentration (95% CI)			C v M	C v I	M v I	
30 to 49 years	Males	128 (125 - 131)	121 (118 - 124)	117 (114 - 120)	<0.01	<0.01	0.06	126
	Females	117 (114 - 120)	120 (117 - 123)	113 (110 - 116)	0.15	0.05	<0.01	117
50 to 69 years	Males	123 (119 - 127)	123 (118 - 128)	118 (114 - 122)	0.94	0.09	0.13	122
	Females	122 (118 - 126)	123 (118 - 128)	117 (113 - 121)	0.67	0.14	0.08	122
30 to 69 years	Males	126 (124 - 128)	122 (120 - 124)	117 (115 - 119)	0.02	<0.01	0.01	125
	Females	119 (117 - 121)	122 (120 - 124)	115 (113 - 117)	0.18	0.01	<0.01	119

* Obtained by applying the age-ethnic group means to the population of Singapore for 1995¹²

TABLE II: PREVALENCE RATES % [95% CONFIDENCE INTERVALS (CI)] OF LOW SERUM SELENIUM (< 80.0 $\mu\text{g/L}$), BY GENDER, ETHNIC GROUP AND AGE-GROUP

		Chinese (C)	Malays (M)	Indians (I)	Significance, <i>P</i> value			Singapore*
		Prevalence rate (95% CI)			C v M	C v I	M v I	
30 to 49 years	Males	0.0 (0.0 - 3.7)	0.0 (0.0 - 3.7)	0.9 (0.0 - 5.1)	0.99	0.52	0.52	0.1
	Females	2.0 (0.2 - 7.0)	0.0 (0.0 - 3.8)	1.8 (0.2 - 6.4)	0.25	0.64	0.28	1.7
50 to 69 years	Males	1.7 (0.0 - 8.9)	0.0 (0.0 - 7.3)	1.7 (0.0 - 9.1)	0.55	0.74	0.54	1.5
	Females	0.0 (0.0 - 5.4)	0.0 (0.0 - 7.7)	0.0 (0.0 - 6.2)	0.99	0.99	0.99	0.0
30 to 69 years**	Males	0.6 (0.0 - 3.5)	0.0 (0.0 - 2.5)	1.2 (0.1 - 4.3)	0.29	0.55	0.15	0.5
	Females	1.3 (0.2 - 4.4)	0.0 (0.0 - 2.6)	1.2 (0.1 - 4.2)	0.15	0.92	0.15	1.2

* Obtained by applying the age-ethnic group rates to the population of Singapore for 1995¹²

** Age-adjusted by direct standardisation to the total sample population

selenium being 119 and 134 $\mu\text{g/L}$, respectively.¹³ However in contrast, a range of 50 to 197 $\mu\text{g/L}$ with a mean of 79 $\mu\text{g/L}$ has been found in seven European Union countries.¹⁴ The overall mean level in Singapore for the 30 to 69 years age group, was estimated as 122 $\mu\text{g/L}$. Serum selenium concentrations of >100 $\mu\text{g/L}$ are considered to be required for optimal activity of glutathione peroxidase, and values <80 $\mu\text{g/L}$ can be considered to be low and may lead to reduced protection from oxidative damage.⁹ Concentrations <80 $\mu\text{g/L}$ were very uncommon in Singapore, with an overall proportion of 0.8%. The situation in Singapore with regards to selenium can be considered to be satisfactory.

Selenium intakes worldwide are highly variable, depending on the selenium content of the soil and the composition of the diet. Cereals are the primary source of selenium in most diets, with meat and seafood being the secondary source in omnivorous diets.¹³ It would seem that the selenium content of flour in Singapore is of moderate levels. A food consumption survey carried out in 1993 in Singapore of persons aged 18 to 69 years found that only a very small proportion of Singaporeans were taking selenium supplements; 1 male (0.4%) took selenium and 1 female (0.3%) took "mineral mixtures" (Unpublished data: Food and Nutrition Department. Food consumption study 1993. Singapore: Ministry of Health,

1994). While the role of selenium in degenerative diseases is not fully clear, its moderate levels suggest that it has no overall major role to play in the occurrence of CHD and cancer in Singapore.

Methods of increasing selenium intake are by adding sodium selenium to fertilisers as in Finland (which has low soil selenium) or possibly by adding selenium to bread flour as is done with calcium and iron. Action to increase selenium levels in Europe has been recommended.⁹ However, it would seem that action with regard to supplementation for selenium is not required in Singapore.

Nevertheless, it is interesting to note that Indians had consistently lower mean levels of serum selenium than Malays and Chinese in both genders. Indians also had slightly higher proportions with low selenium levels, although the differences were small and statistically insignificant. Vegetarian diets have a lower content of selenium than omnivorous diets.¹⁵ Furthermore, in a vegetarian diet, high amounts of phytates and fibre may reduce the absorption of selenium, though this has not been established.¹⁵ The food consumption survey in Singapore found that 7.8% of Indians were strict vegetarians but there were none among Chinese or Malays, with a further 5.1% of Indians and only 0.9% of Chinese and 0.8% of Malays having a red meat-free diet.¹⁶ The

more vegetarian diet among Indians is probably the explanation for their slightly lower serum selenium. Indians, together with Malays, have been found in Singapore to have lower levels of plasma vitamin C than Chinese, probably due to a lower intake of fresh fruits and the more prolonged cooking at high temperatures in their cuisines which would destroy dietary vitamin C.¹¹ It is possible that lower levels of selenium and vitamin C, both anti-oxidants, could be additive and even synergistic. Hence, lower levels of selenium in Indians could contribute to their greater susceptibility to CHD than Chinese and Malays, which has been found in Singapore.⁵ However, the magnitude of the difference suggests that this contribution can only be small.

In conclusion, the overall status with regard to selenium is satisfactory in Singapore. The slightly lower levels of serum selenium in Indians for both genders are probably due to a more vegetarian diet, and could play a small part in Indians' increased risk of CHD compared to Malays and Chinese.

Acknowledgements

The National University of Singapore Heart Study was funded by the National University of Singapore and the National Medical Research Council. Thanks go to Ms Alice Chew for interviewing and to Mr Ong Her Yam for laboratory assistance.

REFERENCES

1. Hughes K. Trends in mortality from ischaemic heart disease in Singapore, 1959 to 1983. *Int J Epidemiol* 1986; 15:44-50.
2. Hughes K. Trends in mortality from hypertensive and cerebrovascular diseases in Singapore, 1959 to 1983. *Int J Epidemiol* 1987; 16:18-24.
3. Chia K S, Lee H P, Seow A, Shanmugaratnam K. Trends in cancer incidence in Singapore 1968-1992. Singapore: Singapore Cancer Registry, 1996.
4. Registry of Births and Deaths. Report on registration of births and deaths 1995. Singapore: National Registration Department:68-9.
5. Hughes K, Lun K C, Yeo P B B. Cardiovascular diseases in Chinese, Malays, and Indians in Singapore. I. Differences in mortality. *J Epidemiol Community Health* 1990; 44:24-8.
6. Diplock A T. Antioxidants and disease prevention. *Molecular Aspects of Medicine* 1994; 15:295-376.
7. Salonen J T, Salonen R, Seppanen K, Kantola M, Parviainen M, Alfthan G, et al. Relationship of serum selenium and antioxidants to plasma lipoproteins, platelet aggregability and prevalent ischaemic heart disease in eastern Finnish men. *Atherosclerosis* 1988; 70:155-60.
8. Ascherio A, Willett W C. New directions in dietary studies of coronary heart disease. *J Nutr* 1995; 125(3 Suppl):647S-55S.
9. Rayman M P. Dietary selenium: time to act [editorial]. *BMJ* 1997; 314:387-8.
10. Hughes K, Yeo P B B, Lun K C, Thai A C, Sothy S P, Wang K W, et al. Cardiovascular diseases in Chinese, Malays, and Indians in Singapore. II. Differences in risk factor levels. *J Epidemiol Community Health* 1990; 44:29-35.
11. Hughes K, New A L, Lee B L, Ong C N. Vitamins A, C and E in the general population of Singapore, 1993 to 1995. *Annals Acad Med Singapore* 1998; 27:149-53.
12. Department of Statistics. Yearbook of statistics Singapore, 1995. Singapore: Ministry of Trade & Industry:24.
13. Levander O A, Burk R F. Selenium. In: Shils M E, Olson J A, Shike M, editors. *Modern Nutrition in Health and Disease*. Philadelphia: Lea & Febiger, 1994:242-51.
14. Alfthan G, Neve J. Reference values for serum selenium in various areas evaluated according to the TRACY protocol. *J Trace Elements Med Biol* 1996; 10:77-87.
15. Gibson R S. Content and bioavailability of trace elements in vegetarian diets. *Am J Clin Nutr* 1994; 59 (5 Suppl):1223S-32S.
16. Food and Nutrition Department. Food consumption study 1993. Singapore: Ministry of Health, 1994:13.