# Serum Ferritin and Iron Status in the General Population of Singapore, 1993 to 1995

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**Abstract**

***The National University of Singapore Heart Study is a cross-sectional survey of cardiovascular risk factors in persons aged 30 to 69 years from the general population of Singapore, with 957 persons having measurements of serum ferritin. For males aged 30 to 69 years, mean serum ferritin concentrations were highest in Chinese (236 μg/L), followed by Malays (175 μg/L) and then Indians (132 μg/L). For females aged 30 to 49 years (pre-menopausal), mean levels were higher in Chinese (61 μg/L) and Malays (55 μg/L) than Indians (30 μg/L), and likewise for the 50 to 69 years age group (post-menopausal) where the mean values were 144 μg/L for Chinese, 141 μg/L for Malays, and 85 μg/L for Indians. The proportions with iron deficiency (serum ferritin <12 μg/L) were low in males aged 30 to 69 years (1.9%) and in females aged 50 to 69 years (2.6%), but fairly high in females aged 30 to 49 years and was highest in Indians (23.0%), followed by Malays (15.6%), and then Chinese (7.8%). The much lower ferritin in Indians is maybe partly due to their more vegetarian diet and binding of dietary iron by phytates, but other mechanisms probably exist. Only 0.4% of males and no females had serum ferritin ≥1000 μg/L. Levels of serum ferritin were somewhat higher than that reported in the USA. The overall iron status in Singapore seems to be satisfactory, although pre-menopausal females (especially Indians) have a fairly high rate of iron deficiency and these females need to be identified and treated with iron supplementation.***

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***Key words: Coronary heart disease, Diet, Ethnic, Indians, Pro-oxidants***

## Introduction

Iron, a dietary constituent, is an essential element. Body iron stores can be measured by haemoglobin, serum ferritin, transferrin saturation, and erythrocyte protoporphyrin.[1] However, serum ferritin is the single most important indicator of iron stores, both clinically to diagnose iron deficiency anaemia and epidemiologically to assess the iron status of a population.[2] Each microgram of ferritin per litre (μg / L) of serum equals to about 10 μg stored iron.[3]

Iron deficiency is the most common nutritional disorder, which is not limited to developing countries, and is the main cause of anaemia in developed countries.[4] Furthermore, iron deficiency is a systemic condition with non-haematological effects; it impairs physical endurance, infant development, intellectual performance, and the immune system, and increases the risk of prematurity, low birth weight and perinatal mortality.[5-8] Correction of iron deficiency in adolescent girls improved cognition and memory.[9] Serum ferritin forms a single distribution curve;[1] the cut-off point for iron deficiency has been set at <12 μg / L,[1,2] while <16 μg / L is considered below normal by the Department of Laboratory Medicine, National University Hospital, Singapore.

Conversely, high levels of iron are also of concern. Iron is a pro-oxidant and thus a possible risk factor for coronary heart disease (CHD). It has been proposed that the gender difference in CHD is due to differences in blood ferritin levels.[10] However, it has been concluded on present evidence that the role of iron in CHD is undecided.[11] Furthermore, in certain diseases, levels of serum ferritin may be elevated (≥1000 μg / L) out of proportion to iron stores.[12]

There is therefore a need for monitoring of the iron status of a population, looking for both iron deficiency and iron repletion.[1] This will help set regulatory policies for iron fortification of foods and iron supplementation with tablets.

Singapore is an island state of 3.3 million people comprising of 76% Chinese, 14% Malays, 7% Asian Indians and 3% Others. Cardiovascular disease and cancer are now the commonest causes of death.[13] The National University of Singapore Heart Study has measured cardiovascular risk factors in the general popula-

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tion, including the newer ones not studied in the previous Singapore Thyroid and Heart Study.[14] This paper examines levels and ethnic differences in serum ferritin.

## 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.[15] In brief, 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. There was a response rate of 71.2%. Of the 961 responders, 4 refused to give blood and hence serum ferritin measurements were performed on 957 persons, composed of 474 males (160 Chinese, 145 Malays, and 169 Indians) and 483 females (169 Chinese, 142 Malays, and 172 Indians).

### *Procedures*

All clinics were held on weekday mornings 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 described[16]).

Venous blood specimens were taken with the subject in a sitting position using venoject vacuum containers with minimum venous stasis. Serum ferritin was measured on blood specimens collected in plain vacutainers, in the Department of Laboratory Medicine, National University Hospital, Singapore. Measurements were performed by microparticle enzyme immunoassay (MEIA) using Abbott IMX in batches weekly after storing at -20°C.

### *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. Apart from the 30 to 69 years age group, ferritin levels were also examined separately in those aged 30 to 49 years and 50 to 69 years, as pre-menopausal and post-menopausal females differ in their iron stores because of loss with menstruation. As there was disproportionate sampling by ethnic group, the estimated means and prevalence rates of iron deficiency in Singapore for the two genders were obtained by applying the age-ethnic group specific rates to the population for 1995.[17]

## Results

All 6 distributions for serum ferritin were uni-modal with slight skewing to the right. Table I shows that mean serum ferritin levels were considerably higher in males than females for all three ethnic groups and age groups. While ferritin levels in females increase considerably after menopause they are still less than males in the 50 to 69 years age group. There were also marked ethnic differences (Table I). For males in all age groups, Indians had much lower mean levels than Chinese and Malays, with Malays lower than Chinese. For males in the overall 30 to 69 years age group, ferritin levels for Indians were less than those for Chinese and Malays by 104 μg / L and 43 μg / L, respectively, while Malays had lower values than Chinese by 61 μg / L. For females, Indians had lower levels than Chinese and Malays whose levels were not very different. For females in the overall 30 to 69 years age group, ferritin levels for Indians were less than those for Chinese and Malays by 42 μg / L and 35 μg / L, respectively.

TABLE I: MEAN CONCENTRATIONS [95% CONFIDENCE INTERVALS (CI)] OF SERUM FERRITIN (μg/L), AGE-ADJUSTED BY ANALYSIS OF COVARIANCE, BY GENDER, ETHNIC GROUP AND AGE-GROUP

| | | Chinese (C) | Malays (M) | Indians (I) | Significance, *P* value | | |
|---|---|---|---|---|---|---|---|
| | | Mean concentration (95% CI) | | | C v M | C v I | M v I |
| 30 to 49 years | Males | 197 (180 - 214) | 178 (161 - 195) | 136 (121 - 151) | 0.13 | <0.01 | <0.01 |
| | Females | 61 (46 - 76) | 55 (38 - 72) | 30 (15 - 45) | 0.65 | 0.01 | 0.04 |
| 50 to 69 years | Males | 302 (271 - 333) | 168 (133 - 203) | 124 (91 - 157) | <0.01 | <0.01 | 0.08 |
| | Females | 144 (113 - 175) | 141 (104 - 178) | 85 (52 - 118) | 0.91 | 0.01 | 0.03 |
| 30 to 69 years | Males | 236 (221 - 251) | 175 (158 - 192) | 132 (117 - 147) | <0.01 | <0.01 | <0.01 |
| | Females | 92 (77-107) | 85 (68 - 102) | 50 (35 - 65) | 0.54 | <0.01 | <0.01 |

TABLE II: PREVALENCE RATES % [95% CONFIDENCE INTERVALS (CI)] OF SERUM FERRITIN <12.0 μg/L (IRON DEFICIENCY), BY GENDER, ETHNIC GROUP AND AGE-GROUP

| | | Chinese (C) | Malays (M) | Indians (I) | Significance, *P* value | | | Singapore* |
|---|---|---|---|---|---|---|---|---|
| | | Prevalence rate % (95% CI) | | | C v M | C v I | M v I | |
| 30 to 49 years | Males | 3.1 (0.6 - 8.7) | 1.0 (0.0 - 5.7) | 0.9 (0.0 - 5.0) | 0.31 | 0.27 | 0.71 | 2.7 |
| | Females | 7.8 (3.5 - 14.9) | 15.6 (9.0 - 24.5) | 23.0 (15.2 - 30.8) | 0.06 | <0.01 | 0.12 | 9.9 |
| 50 to 69 years | Males | 0.0 (0.0 - 5.8) | 4.1 (0.5 - 14.0) | 0.0 (0.0 - 6.0) | 0.19 | 0.99 | 0.19 | 0.4 |
| | Females | 3.0 (0.4 - 10.4) | 0.0 (0.0 - 7.7) | 1.7 (0.0 - 9.1) | 0.34 | 0.54 | 0.56 | 2.6 |
| 30 to 69 years** | Males | 2.0 (0.5 - 5.5) | 2.1 (0.4 - 5.9) | 0.6 (0.0 - 3.3) | 0.92 | 0.28 | 0.25 | 1.9 |
| | Females | 6.1 (3.1 - 10.8) | 10.0 (4.9 - 15.0) | 15.4 (10.0 - 20.8) | 0.19 | <0.01 | 0.13 | 7.2 |

* Obtained by applying the age-ethnic group rates to the population of Singapore for 1995[17]

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

TABLE III: PREVALENCE RATES % [95% CONFIDENCE INTERVALS (CI)] OF SERUM FERRITIN <16.0 μg/L (LOW IRON), BY GENDER, ETHNIC GROUP AND AGE-GROUP

| | | Chinese (C) | Malays (M) | Indians (I) | Significance, *P* value | | | Singapore* |
|---|---|---|---|---|---|---|---|---|
| | | Prevalence rate % (95% CI) | | | C v M | C v I | M v I | |
| 30 to 49 years | Males | 3.1 (0.6 - 8.7) | 1.0 (0.0 - 5.7) | 2.8 (0.6 - 7.8) | 0.31 | 0.60 | 0.35 | 2.8 |
| | Females | 14.7 (7.8 - 21.6) | 21.9 (14.1 - 31.5) | 30.1 (21.6 - 38.5) | 0.13 | <0.01 | 0.11 | 16.7 |
| 50 to 69 years | Males | 0.0 (0.0 - 5.8) | 6.1 (1.3 - 16.9) | 5.0 (1.0 - 13.9) | 0.08 | 0.11 | 0.55 | 1.1 |
| | Females | 4.5 (0.9 - 12.5) | 0.0 (0.0 - 7.7) | 6.8 (1.9 - 16.5) | 0.20 | 0.42 | 0.09 | 4.1 |
| 30 to 69 years** | Males | 2.0 (0.5 - 5.5) | 2.9 (0.9 - 7.0) | 3.6 (1.3 - 7.6) | 0.61 | 0.38 | 0.73 | 2.2 |
| | Females | 11.0 (6.3 - 15.6) | 14.0 (8.2 - 19.8) | 21.7 (16.3 - 28.7) | 0.41 | <0.01 | 0.05 | 12.1 |

* Obtained by applying the age-ethnic group rates to the population of Singapore for 1995[17]

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

The proportions with iron deficiency (serum ferritin <12 μg / L) were low in all three ethnic groups for males and post-menopausal (50 to 69 years) females, with estimates for the Singapore population of 1.9% and 2.6% respectively (Table II). However, the proportions in pre-menopausal females (30 to 49 years) were quite high. They were higher in Indians than Chinese and Malays by 15.2% and 7.4%, respectively, and higher in Malays than Chinese by 7.8% (Table II). The estimated proportion of pre-menopausal females in Singapore with iron deficiency was 9.9%.

The proportions with low iron (serum ferritin <16 μg / L) showed a similar pattern, though as expected the values were higher (Table III). However, they were still relatively low for males and post-menopausal females, with estimates for the Singapore population of 2.2% and 4.1%, respectively. However, the proportions in pre-menopausal females were quite high. They were higher in Indians than Chinese and Malays by 15.4% and 8.2% respectively, and higher in Malays than Chinese by 7.2% (Table III). The estimated proportion of pre-menopausal females in Singapore with low iron stores was 16.7%.

Only 0.4% of the males (two Chinese men in their sixties) had elevated serum ferritin levels ≥1000.0 μg / L.

## Discussion

This population-based study in Singapore has measured mean concentrations of serum ferritin (and thus stored iron) among Chinese, Malays and Indians. It has also measured the prevalences of iron deficiency (serum ferritin <12 μg / L[1,2]) and a low iron level (serum ferritin <16 μg / L and a low iron level (serum ferritin <16 μg / L). The latter is considered as below normal by the Department of Laboratory Medicine, National University Hospital, Singapore). This study will contribute to the continued monitoring of iron status in Singapore.

Serum ferritin was noted to be lower in females than males. This is most probably due to menstrual loss of iron. However, post-menopausal women still had lower levels than males. This finding has been observed elsewhere.[18]

Of the males, 0.4% (2 Chinese men in their sixties) had very high serum ferritin concentrations (≥1000 μg / L), which may indicate some underlying disease;[12] no females had such levels.

Indians had much lower mean serum ferritin concentrations than Chinese and Malays for both genders, while for males but not females, Malays had lower levels than Chinese. Iron deficiency (serum ferritin <12 μg / L)

and a low iron level (serum ferritin <16 μg/L) were uncommon in males and post-menopausal females with no important ethnic differences. However, for pre-menopausal females, iron deficiency and low iron were not uncommon (estimated in the Singapore population to be 9.9% and 16.7%, respectively) and were highest in Indians, followed by Malays, and then Chinese.

The lower levels of ferritin in Indians could be due to reduced dietary intake or impaired absorption of iron. It was found in a study of females in Britain, that Indians had lower levels of serum ferritin than Whites, Blacks and Orientals, which was considered probably due to reduced iron intake.[19]

Dietary iron is obtained mainly from meat (mainly red meat) and some vegetables.[18] Absorption of non-haem iron is inhibited by binding with phytates which are present in some vegetables and cereals.[18] Iron stores in vegetarians may be reduced, especially with a diet based on unleavened unrefined cereals (phytates in wheat flour are hydrolysed during leavening and bread baking).[20] A food consumption survey carried out in Singapore in 1993 on a random sample of the general population aged 18 to 69 years, found that 7.8% of Indians but no Chinese or Malays were strict vegetarians, with a further 5.1% of Indians and only 0.9% of Chinese and 0.8% of Malays having a red meat-free diet.[21] The combination in Indians of a more vegetarian diet and consumption of chapatis (unleavened bread) would result in lower ferritin levels.

Vitamin C facilitates iron absorption.[20] The National University of Singapore Heart Study has found that Indians and Malays have lower plasma levels of vitamin C than Chinese, probably due to a lower intake of fresh fruits and destruction of dietary vitamin C by the more prolonged cooking at high temperatures in Indian and Malay cuisines.[15] Lower vitamin C is maybe another reason for lower ferritin in Indians, and also a reason for the slightly lower levels in Malays compared to Chinese.

However, it is unlikely that a more vegetarian diet, and a slightly lower vitamin C in Indians can explain their much lower levels of serum ferritin, other factors probably operate.

The health effects of lower ferritin in Indians are not clear. In Singapore, CHD is highest in Indians, followed by Malays, and then Chinese.[16] Blood ferritin levels cannot play a role in this ethnic difference in CHD; if anything the lower levels among Indians would be protective. One of the effects of iron deficiency is the increase in the risk of low birth weight.[7] In Singapore, low birth weight has been found to be highest in Indians, followed by Malays, and then Chinese.[22] Iron deficiency could contribute to this ethnic difference, although iron deficiency during pregnancy in Singapore would probably be detected and treated.

Levels of serum ferritin in the USA have been reported from the Second National Health and Nutrition Examination Survey (NHANES II).[1] Mean concentrations were: 113 μg/L for males aged 18 to 64 years, 37 μg/L for females aged 18 to 44 years, and 78 μg/L for females aged 45 to 64 years. Prevalence rates of iron deficiency (serum ferritin <12 μg/L, as in this study in Singapore) were: 1.6% for males aged 18 to 64 years, 21.3% for females aged 18 to 44 years, and 5.9% for females aged 45 to 64 years. Hence in Singapore, mean levels of serum ferritin were higher and proportions with iron deficiency generally lower than in the USA, except for Indian females who had comparable values. The health implications of this are not clear.

The food consumption survey in Singapore studied the regular taking of nutritional supplements and found that only 0.4% of males and 0.6% of females were taking iron tablets (Unpublished data—Food and Nutrition Department. Food consumption study 1993. Singapore: Ministry of Health, 1994).

In conclusion, Indians have much lower blood ferritin (stored iron) levels than Chinese and Malays, which is probably partly due to a more vegetarian diet and binding of non-haem iron by dietary phytates, though other mechanisms probably exist. Generally, the iron status in Singapore seems to be satisfactory, and there does not seem to be a need to radically change public health policy with regards to iron. However, this study has found that quite a fair proportion of pre-menopausal females (especially Indians) has iron deficiency and these females need to be identified and given iron supplementation.

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REFERENCES

1. Cook J D, Skikne B S, Lynch S R, Reusser M E. Estimation of iron sufficiency in the US population. Blood 1986; 68:726-31.
2. Cook J D, Skikne B S. Iron deficiency: definition and diagnosis. J Intern Med 1989; 226:349-55.
3. Herbert V. Everyone should be tested for iron disorders. J Am Diet Assoc 1992; 92:1502-9.
4. Cook J, Finch C. Assessing iron status of a population. Am J Clin Nutr 1979; 32:2115-9.
5. Oski F A. The nonhaematologic manifestations of iron deficiency. Am J Dis Child 1979; 133:315-22.
6. Cook J D, Lynch S R. The liabilities of iron deficiency. Blood 1986; 68:803-9.
7. Dallman P R. Iron deficiency: does it matter? J Intern Med 1989; 226:367-72.
8. Baynes R D, Bothwell T H. Iron deficiency. Ann Rev Nutr 1990; 10:133-48.
9. Bruner A B, Joffe A, Duggan A K, Casella J F, Brandt J. Randomised study of cognitive effects of iron supplementation in non-anaemic iron-deficient adolescent girls. Lancet 1996; 348:992-6.

10. Sullivan J L. Iron and the sex difference in heart disease risk. Lancet 1981; i:1293-4.

11. Burt M J, Halliday J W, Powell L W. Iron and coronary heart disease. BMJ 1993; 307:575-6.

12. Lee M H, Means R T. Extremely elevated serum ferritin levels in a university hospital: associated diseases and clinical significance. Am J Med 1995; 98:566-71.

13. Registry of Births and Deaths. Report on Registration of Births and Deaths 1995. Singapore: National Registration Department.

14. 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.

15. Hughes K, New A L, Lee B L, Ong C N. Plasma vitamins A, C and E in the general population of Singapore, 1993 to 1995. Ann Acad Med Singapore 1998; 27:149-53.

16. 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.

17. Department of Statistics. Yearbook of Statistics Singapore, 1995. Singapore: Ministry of Trade & Industry, 1995:24.

18. Fairbanks V F. Iron in medicine and nutrition. In: Shils M E, Olson J A, Shike M, editors. Modern Nutrition in Health and Disease. Philadelphia: Lea & Febiger, 1994:185-213.

19. Godsland I, Seed M, Simpson R, Broom G, Wynn V. Comparison of haematological indices between women of four ethnic groups and the effect of oral contraception. J Clin Pathol 1983; 36:184-91.

20. Craig W J. Iron status of vegetarians. Am J Clin Nutr 1994; 59(5 Suppl):1233S-7S.

21. Food and Nutrition Department. Food Consumption Study 1993. Singapore: Ministry of Health, 1994:13.

22. Hughes K, Tan N R, Lun K C. Low birthweight of live singletons in Singapore, 1967-1974. Int J Epidemiol 1984; 13:465-71.