# IRON-DEFICIENCY ANAEMIA AND SERUM FERRITIN LEVELS IN MALAYSIAN WOMEN

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## SUMMARY

Serum ferritin and blood haemoglobin levels were studied in 229 women attending a family planning clinic. Ferritin values ranged from 2 to 438  $\mu$ g/l and was skewed with an arithmetic mean of 41.8 and geometric mean of 23.4  $\mu$ g/l; 26.6% were iron-deficient (ferritin < 12  $\mu$ g/l). Heamoglobin values were normally distributed with a mean of 11.7 g/dl but 59% were anaemic (Hb < 12 g/dl). The correlation between ferritin and haemoglobin values was poor (r = 0.147) but almost all women with a haemoglobin below 10 g/dl were iron-deficient. This study reaffirms the need for monitoring iron-deficiency anaemia in apparently healthy women seeking contraception.

#### INTRODUCTION

Ferritin is the major iron storage protein in the body and is found largely in the reticulo-

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M. Hariharan, MBBS, MPath Associate Professor Department of Pathology Faculty of Medicine University of Malaya 59100 Kuala Lumpur, Malaysia endothelial system. Its concentration in serum is small but as this accurately mirrors changes in body iron stores, its measurement provides a sensitive and reliable tool for epidemiological studies.<sup>1,2,3</sup> In Caucasian populations, serum ferritin levels range from 12 - 300  $\mu$ g/l with mean values of 29-43  $\mu$ g/l in women and 52 -112  $\mu$ g/l in men;<sup>1-5</sup> this reflects the sex differences in iron stores.

We have measured serum ferritin concentrations in a cohort of healthy young Malaysian women in order to study their distribution pattern and their relationship to blood haemoglobin values.

#### MATERIALS AND METHODS

Subjects were recruited at their first consultation visit to the family planning clinic based at the University Hospital, Kuala Lumpur. They were regularly menstruating women with no significant systemic or pelvic disease. Women who had been pregnant, been on the oral contraceptive pill or who had used intrauterine devices in the previous two months were excluded as were those who had had depot progestogen injections in the last six months or iron therapy in the preceding three months.

Venous blood samples were taken from an antecubital vein with the aid of a tourniquet, mostly between 1400 and 1600 hours. Sera for ferritin measurement were immediately separated and stored at  $-20^{\circ}$ C prior to assay in batches

using an immunoradiometric method;<sup>6</sup> the  $I^{12.5}$ Ferritin-Roche Kit was used. The between-run coefficient of variation was 5.8% and 10.5% at concentrations of 10 and 100  $\mu$ g/l respectively, and within-run 9.5% and 35  $\mu$ g/l.<sup>7</sup> Blood haemoglobin concentration was measured using the cyanmethaemoglobin method. The paired t-test was used for statistical comparison except where otherwise indicated and p > 0.05 is considered not significant.

# RESULTS

The study population consisted of 229 women with a mean age (SD) of 28.5 (4.7) years and mean parity (SD) of 3 (1.6). For various technical reasons, haemoglobin results were available for only 226 women and for ferritin in 220. The distribution of ferritin levels showed a large range (2-438  $\mu$ g/l) and was skewed with a preponderance of low values (Fig. 1); the arithmetic mean was 41.8  $\mu$ g/l and geometric mean 23.4  $\mu$ g/l while in 58 women (26.6%) it was less than 12  $\mu$ g/l, the level considered iron-deficient.<sup>1</sup> Because of this skewed distribution, geometric rather than arithmetic means were used for statistical comparisons.

Haemoglobin values showed a more normal distribution (Fig. 2) with a mean of 11.7 g/dl and median of 11.8 g/dl. Using the WHO standard of 12 g/dl,<sup>9</sup> 58% would be considered anaemic and even where the haemoglobin was normal about 14% were iron-deficient (Table I). The correlation between ferritin and haemoglobin values was small and not significant (r = 0.147). However, with a rise in haemoglobin, there was an increase in mean ferritin levels and a corresponding decrease in the proportion of anaemic women. The proportion of iron-deficient women also decreased significantly with rising haemoglobin levels up to 11 - 11.9 g/dl (Table I). Comparing the latter with those whose haemoglobin was 12 g/dl or more, the respective rates of irondeficiency of 20.5% and 14.4% were not signicantly different.



Fig. 1 Distribution of serum ferritin values.



Fig. 2 Distribution of blood haemoglobin levels.

TABLE !
RELATIONSHIP BETWEEN HAEMOGLOBIN CONCENTRATION,
SERUM FERRITIN LEVEL AND IRON-DEFICIENCY

Hb (g/dl)	Number	Mean ferritin (μg/l)	Iron-deficiency (ferritin $\leq 12$ //a/l)	
			Number	(%)
≤ 9.9	16	6.1	15	93.8+
10 — 10.9	34	37.3	14	*41.2+
11 – 11.9	78	41.1	16	*20.5
≥12	90	49.9	13	14.4
Total	218	41.8	58	26.6

+ se = 15.0; P < 0.001. \* se = 9.1; p < 0.05.

The Chinese ethnic group had higher mean haemoglobin and ferritin levels than the Malays

and Indians but only in the latter were the differences statistically significant (Table II).

Ethnic gro	ыр	Hb (g/dl +)	SD	Number	Ferritin (μg/dl*) (geometric)	SD	Number
Malay (M)		12.0	1.4	42	27.5	1.98	· 43
Indian (I)		11.5	1.13	111	16.3	3.29	108
Chinese (C	:)	12.03	1.09	71	36.6	2.35	66
+ M - 1	t = 2.28	df = 151	p < .05	<u> </u>	* M – I t = 16.2	df = 149	р < .001
I — C	t = 3.13	df = 180	p < .01		I – C t = 14.7	df = 172	р < .001
M — C	t = 0.13	df = 111	(not significant)		M - C t = 9.4	df = 107	р < .001

TABLE II MEAN HAEMOGLOBIN AND FERRITIN LEVELS BY ETHNIC GROUP

While ferritin levels were comparable between Indians and Malays, mean haemoglobin concentration was significantly higher in Malays.

Eighteen percent of subjects were in social classes<sup>8</sup> I and II, 31% in class III and 51% in classes IV and V. Their respective serum arithmetic (geometric) mean ferritin levels were 41 (26.1), 35.4 (22.1) and 44.9 (23.1)  $\mu$ g/I. None of these differences were significant. Mean haemoglobin concentrations were respectively 12.2, 11.5 and 11.8 g/dl; social classes I and II had a significantly higher haemoglobin level than class III (t = 2.88, df = 108, p = 0.005); it was not significantly different between class III and classes IV and V.

### DISCUSSION

Studies on iron-deficiency anaemia have largely been based on haemoglobin measurements.<sup>9</sup> However, as the haemoglobin level does not fall till after iron depletion, it is not a sensitive indicator of iron stores especially within the physiological range.<sup>3</sup> It was therefore not unexpected to find a lack of significant correlation between ferritin and haemoglobin levels. Nevertheless, a haemoglobin of 10 g/dl appears to be an important and practical reference point as almost all women whose haemoglobin was below this value were iron-deficient.

Of the methods currently available for determining iron stores, serum ferritin measurement appears to be the optimal in being simple noninvasive and accurate.<sup>2,3</sup> To our knowledge, this study is the first in which ferritin levels have been measured in a sizeable population of non-pregnant Malaysian women. The mean level of  $42 \mu g/l$  which is equivalent to an iron store of 336 mg<sup>5</sup> is comparable to published figures for Caucasian women.<sup>1-5</sup> However, low values were common, which confirms our earlier findings in a smaller study.<sup>7</sup> Though this is primarily nutritional in origin,<sup>9</sup> other factors may be contributory. Many women had delivered within the preceding year and may not have had sufficient time to replenish their iron stores. Even in Caucasian women who are presumably on better diets, it may take up to two years for prepregnancy levels of iron stores to be regained.<sup>11</sup> Conversely, repeated childbearing at close intervals and prolonged lactation may have aggravated the situation though it is difficult to quantitate their relative significance.

Menstrual blood loss is a major determinant of iron status in women of reproductive age.<sup>12</sup> As copper-bearing intrauterine devices increase menstrual losses substantially, there may be an increased risk of subsequent anaemia.<sup>9,10,12</sup> A fall in ferritin levels may also occur after sterilization<sup>7,13</sup> whereas the oral contraceptive pill and progestogen-releasing intrauterine devices tend to improve iron stores.<sup>9,12,14</sup> The high incidence of anaemia in women attending the family planning clinic and the increased risk of subsequent anaemia with certain contraceptive methods re-affirm the need for careful follow-up of these women. Furthermore many are young and of low parity and may be expected to conceive again after a brief interval of contraception, thus placing further demands on the body's iron stores.

The haematological status of the Chinese was better than the Indians while the Malays were intermediate. Similar ethnic differences were previously reported in late pregnancy when haemoglobin, serum and red cell folate levels were studied.<sup>15</sup> The higher gravidity among Indian and Malay women and differences in diet and food preparation were suggested as the reasons for these observations. Social class did not seem to have a major effect on ferritin and haemoglobin levels. However, as other influences which may have a bearing on haematological status were not considered in a multivariate analysis, no definite conclusion can be drawn at this stage.

# REFERENCES

- <sup>1</sup> Jacobs A, Worwood M. Ferritin in serum. N Engl J Med 1975; 292: 951 - 956.
- <sup>2</sup> Cook J D, Lipschitz D A, Miles L E M, Finch C A. Serum ferritin as a measure of iron stores in normal subjects. *Am J Clin Nut* 1974; 27: 681-7.
- <sup>3</sup> Editorial. Serum ferritin. Lancet 1974; 1 : 1263-5.
- <sup>4</sup> Addison G M, Beamish M R, Hales C N, Hodgkins M, Jacobs A, Llewellin P. An immunoradiometric assay for ferritin in the serum of normal subjects and patients with iron deficiency and iron overload. *J Clin Path* 1972; 25 : 326-9.

- <sup>5</sup> Walters G O, Miller F M, Worwood M. Serum ferritin concentration and iron stores in normal subjects. J Clin Path 1973; 26: 770-2.
- <sup>6</sup> Halliday J W, Gera K L, Powell L W. Solid-phase radioimmunoassay for serum ferritin. *Clin Chem Acta* 1975; 58: 207–14.
- <sup>7</sup> Goh T H, Hariharan M. Effect of laparoscopic sterilization and insertion of Multiload Cu 250 and Progestasert IUDs on serum ferritin levels. *Contraception* 1983; 28: 329–36.
- <sup>8</sup> Susser M W, Watson W. Theories and indices of social class. In : *Sociology in Medicine* (2nd ed). London : Oxford University Press, 1977 : 105-127.
- <sup>9</sup> Royston E. The prevalence of nutritional anaemia in women in developing countries: a critical review of available information, *World Health Statistics Quarterly* No. 2 World Health Organization, Geneva 1982.
- <sup>10</sup> Goh T H, Hariharan M, Chan G L. Anaemia and menstrual blood loss studies in women using Multiload Cu 250 and Progestrasert IUDs. *Contraception* 1984; 29: 359–366.
- <sup>11</sup> Taylor D J, Mallen C, McDougall N, Lind T. Serum ferritin in women of reproductive age. Br J Obstet Gynaecol 1982; 89: 1000 - 5.
- <sup>12</sup> Cohen B J B, Gibor Y. Anaemia and menstrual blood loss. Obstet Gynaecol Survey 1980; 35: 597-618.
- <sup>13</sup> Letchworth A T, Filer S, Anthony F, Slattery M, Barnett M D. Serum ferritin levels following female sterilization. *J Obstet Gynaecol* 1980; 1:46-8.
- <sup>14</sup> WHO Special Programme of Research, Development and Research Training in Human Reproduction --9th Annual Report: 42-62. Geneva WHO, 1980.
- <sup>15</sup> Hibbard B M, Hibbard E D. Anaemia and folate status in late pregnancy in a mixed Asiatic population. J Obstet Gynaecol Br Commonwealth 1972; 79 : 584 – 91.