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Iron deficiency, general health and fatigue: Results from the Australian Longitudinal Study on Women's Health

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Abstract

Associations between self-reported 'low iron', general health and well-being, vitality and tiredness in women, were examined using physical (PCS) and mental (MCS) component summary and vitality (VT) scores from the MOS short-form survey (SF-36). 14,762 young (18–23 years) and 14,072 mid-age (45–50 years) women, randomly selected from the national health insurance commission (Medicare) database, completed a baseline mailed self-report questionnaire and 12,328 mid-age women completed a follow-up questionnaire 2 years later. Young and mid-age women who reported (ever) having had 'low iron' reported significantly lower mean PCS, MCS and VT scores, and greater prevalence of 'constant tiredness' at baseline than women with no history of iron deficiency [Differences: young PCS = −2.2, MCS = −4.8, VT = −8.7; constant tiredness: 67% vs. 45%; mid-age PCS = −1.4, MCS = −3.1, VT = −5.9; constant tiredness: 63% vs. 48%]. After adjusting for number of children, chronic conditions, symptoms and socio-demographic variables, mean PCS, MCS and VT scores for mid-age women at follow-up were significantly lower for women who reported recent iron deficiency (in the last 2 years) than for women who reported past iron deficiency or no history of iron deficiency [Means: PCS – recent = 46.6, past = 47.8, never = 47.7; MCS – recent = 45.4, past = 46.9, never = 47.4; VT – recent = 54.8, past = 57.6, never = 58.6]. The adjusted mean change in PCS, MCS and VT scores between baseline and follow-up were also significantly lower among mid-age women who reported iron deficiency only in the last 2 years (i.e. recent iron deficiency) [Mean change: PCS = −3.2; MCS = −2.1; VT = −4.2]. The results suggest that iron deficiency is associated with decreased general health and well-being and increased fatigue.

Key words: Fatigue, Iron deficiency, SF-36, Women

Introduction

Iron deficiency, before the onset of anaemia, can affect work performance, behaviour, immunity and thermoregulation [1–5]. The current prevalence of iron deficiency for Australian women on childbearing age is unknown, but baseline data from the Australian Longitudinal Study on Women's Health (ALSWH) suggest that one in three women have had diagnosed iron deficiency by the age of 45–50 years [6]. Despite this, surprisingly little is known about how the effects of iron deficiency relate to the lives of 'ordinary' women.

While it has been shown that work performance is reduced in iron deficient athletes and those engaged in manual labour, the ability to perform hard physical work is not necessarily important in the lives of many women in Australia. However, iron deficiency may result in reduced ability to perform daily tasks and exercise, which in turn may impact adversely on health. It has been shown that cognitive functioning is reduced in iron deficient infants and young children [7, 8], and a few studies suggest that adults may be similarly affected [9, 10]. Concentration and short-term memory are the two factors most impaired in iron deficiency [9], and both are crucial to daily

functioning. Decreased immunity and increased illness and infection, which have also been shown to be associated with iron deficiency, may also reduce well-being and performance in daily living [5].

Chronic tiredness or fatigue is a non-specific symptom often attributed to iron deficiency by both the general public and the medical community [11]. However, there is no convincing evidence to suggest that iron deficiency, before the onset of anaemia, causes tiredness. Links between iron deficiency and tiredness could however be postulated from current knowledge of the effects of iron deficiency on physical and mental performance [1–5].

The aim of this study was to explore associations between iron deficiency and general health and well-being from an epidemiological perspective. Specifically, baseline and follow-up data from the first two years of the ALSWH were used to examine associations between self-reported iron deficiency and general health and well-being, vitality and fatigue in Australian women.

Methods

The ALSWH is a national study designed to track the health and well-being of Australian women over a 20 year period. The study includes women in two age cohorts: 'young' women aged 18–23; and 'mid-age' women aged 45–50, at the time of the baseline survey in 1996.

The sampling frame for the study was the health insurance commission (HIC) database which includes all citizens and permanent residents of Australia. Based on pilot study response rates and target sample sizes for the cohorts, 39,000 young and 28,000 mid-age women were randomly selected from all females on the HIC database with birthdays in the ranges 1/4/74–31/3/78 (n = 759,680) and 1/4/47–31/3/51 (n = 734,155) respectively. After exclusion of responses from males, women who were not selected and those with invalid birthdays, the response rates for the young and mid-age cohorts were 42 and 54% respectively [12], giving total sample sizes of 14,762 young women and 14,072 mid-age women at baseline.

A requirement for use of the HIC database as a sampling frame was that the study team did not know the names or contact details of the women selected until they gave written informed consent to participate. This meant that many of the usual methods to encourage participation were not possible, that the women declining to participate could not be distinguished from those who did not receive the original invitation, and that a comparison of responders and non-responders was not possible. Nonetheless, the women were broadly representative of the women in these age groups in the Australian population (Australian Bureau of Statistics, unpublished data), but with over representation of women with tertiary education. Given the large sample size, chi squares showed statistically significant differences in all the socio-demographic variables (Table 1); these variables were therefore included in the final analysis as potential confounders.

All data were collected using mailed, self-report questionnaires. The baseline surveys included 100 questions on a broad range of health-related issues. The first 36 items comprised the Medical Outcomes Survey short form questionnaire (SF-36; see below) [13]. Two other questions from the baseline surveys were used in the present analyses: "Have you ever been told by a doctor that you have low iron?" (yes/no) and "In the last twelve months have you had any of the following: (long list of symptoms, including 'constant tiredness')?" (The responses were: never; rarely; sometimes; often). These questions were separated by at least 30 unrelated items in each of the questionnaires so that a positive response to iron deficiency was unlikely to influence responses about tiredness. Responses to questions about number of children under 19 years living at home, number of chronic conditions (e.g. diabetes, cardiovascular disease, asthma, bronchitis and osteoporosis) and symptoms (e.g. allergies, indigestion, headaches, heavy menstrual bleeding, constipation) were assessed for possible confounding influences.

Follow-up data for the mid-age cohort were collected in 1998 (response rate 91% of eligible, n = 12,328). Follow-up data for the young cohort will be collected in the year 2000. In the mid-age follow-up questionnaire, the SF-36 items were included in identical format, though the other two questions used in this analysis varied slightly between baseline and follow-up. The question about 'low iron' was varied to allow identification of women who had developed low iron since the

Table 1. Socio-demographic characteristics for the young and mid-age respondents and for women of the same age in the general population (ABS Census, 1996)

	Young (18–23 years)		Mid-age (45–50 years)	
	ALSWH (%)	ABS (%)	ALSWH (%)	ABS (%)
N	14,762	759,680	14,072	734,155
Main current employment status				
Employed full-time	31.3	32.4	36.1	36.0
Employed part-time	19.2	26.4	30.1	28.5
Worked (without pay)/employed (other)	1.9	1.3	7.0	2.0
Unemployed	6.4	10.5	1.9	4.0
Total not in labour force	39.4	26.3	21.6	27.0
Not stated	1.8	2.7	3.3	2.5
Highest qualification completed				
No post school qualification	69.8	69.3	63.1	61.8
Trade/apprenticeship	2.4	7.9	3.5	7.0
Certificate/diploma	15.1	6.0	15.9	8.7
University degree	12.1	7.7	16.3	11.6
Other (not stated, inadequately described)	0.6	9.1	1.2	10.8
Country of birth				
Australia	88.6	77.8	69.0	62.6
Other English speaking	3.5	4.1	13.9	11.6
Other European	1.3	1.6	8.7	11.0
Asian	3.6	10.6	4.3	8.2
Other/not stated	3.0	6.0	4.2	6.5
Present marital status				
Married/de facto	20.2	17.7	80.8	73.0
Separated/divorced	0.0	1.1	13.2	18.7
Widowed	0.0	0.2	2.1	2.7
Never married	79.0	89.8	3.9	5.6
Present housing situation				
House	74.3	79.4	84.7	89.2
Flat/apartment/unit	20.0	14.0	7.1	6.5
Caravan/cabin/houseboat	0.7	0.6	0.7	0.8
Other & not applicable	5.0	6.0	7.5	3.5

ALSWH – Australian Longitudinal Study on Women's Health; ABS – Australian Bureau of Statistics.
$p < 0.001$ for all socio-demographic variables using χ^2 to compare ALSWH and ABS proportions.

baseline survey: "Have you ever been told by a doctor that you have a low iron level (iron deficiency or anaemia)?" (yes, in the last 2 years/yes, more than 2 years ago). Women were able to choose one, both or neither of these responses. The question about 'tiredness' maintained the original format but the term 'constant' was replaced by 'severe' (after realising that it is not possible to have 'constant tiredness' rarely).

SF-36

The SF-36 contains 36 items which are scored as eight multi-item scales and two overall summary scores: the physical component summary score (PCS) and the mental component summary score (MCS). The eight scales are scored from 0 (low) to 100 (high). The summary scores are compared with norms for the reference population (in this case, women aged 18–22 and 45–54 from the Australian National Health Survey, 1995), such that the population average is set at 50. Thus for PCS and MCS scores, a score below 50 indicates worse physical or mental health, while a score above 50 indicates better health than the reference population. PCS and MCS are standardised and therefore exhibit strongly normal distributions. In this paper we have used these two summary scores

and the sub-scale scores for vitality (VT) which are also normally distributed, and directly related to the a priori hypothesis relating to iron deficiency and fatigue.

Data analysis

Student's *t*-tests and 95% confidence intervals (CIs) for the difference between two independent means were used to compare mean PCS, MCS and VT scores for women in each age group who answered 'yes' or 'no' to the question "Have you ever been told by a doctor that you have low iron?" at baseline. The effects of potential confounding variables were assessed using the least significant difference option of the analysis of variance procedure of SAS [14] to compare mean PCS, MCS and VT for the sub-groups of women shown in Table 2.

For women in the mid-age cohort, comparisons were made between those who reported recent iron deficiency (i.e. in the last 2 years), past iron deficiency (i.e. prior to 2 years ago, but not in the last 2 years) and for those who reported never having had iron deficiency, at follow-up. Mean change in PCS, MCS and VT scores for these three groups of women between 1996 and 1998 were compared using multiple linear regression with adjustment for the socio-demographic confounders shown in Table 1, as well as number of children at home, symptoms and chronic conditions (see Table 3). All confounding variables except number of symptoms were treated as categorical.

The mean scores were also adjusted for baseline scores. Means and confidence intervals were calculated for each iron deficiency category using the least square means option of the generalised linear models procedure of SAS [14].

Contingency tables and χ^2 analyses were used to compare the proportion of women in each of the three groups at follow-up who reported 'severe tiredness' sometimes or often.

Results

Baseline data

At baseline, the proportions of young and mid-age women who reported (ever) having had 'low iron' were 24 and 31% respectively. Mean scores for the vitality subscale and for the physical and mental component summary scores of the SF-36 were significantly lower for the women who reported (ever) having had 'low iron' than for those with no history of low iron (Table 2). The greatest contrast was in the vitality scores for both the young and mid-age women.

Table 2. Mean SF-36 physical component summary scores, mental component summary scores and vitality scores for the young and mid-age women at baseline (1996)

	Have you ever been told by a doctor that you have low iron?		Difference between means*	95% CI for the difference
	Yes	No		
Young	(n = 3675)	(n = 10,926)		
PCS	47.2	49.3	−2.2	−2.5; −1.9
MCS	41.9	46.8	−4.8	−5.2; −4.4
Vitality	50.3	58.9	−8.7	−9.3; −8.0
Mid	(n = 4442)	(n = 9447)		
PCS	48.7	50.0	−1.4	−1.6; −1.1
MCS	45.1	48.1	−3.1	−3.4; −2.7
Vitality	54.7	60.6	−5.9	−6.5; −5.3

*All *t*-tests $p < 0.0001$.

The proportion of women who reported sometimes or often experiencing constant tiredness was significantly higher in both cohorts for women who reported (ever) having had low iron than for those with no history of low iron [young: 67 and 45% respectively, difference = 22% (95% CI: 21–24%); mid: 63 and 48% respectively, difference = 15% (95% CI: 13–17%)]. Women without children had higher mean MCS and VT scores and lower mean PCS scores than women with two or more children, and mean PCS, MCS and VT scores for mid-age women decreased significantly as number of symptoms or chronic conditions increased (see Table 3).

Follow-up data

The question about iron deficiency in the mid-age follow-up questionnaire enabled comparisons to be made between women who had only experienced recent iron deficiency (i.e. in the last 2 years) (n = 959), women who reported having iron deficiency prior to 2 years ago (n = 3241) and those with no history of iron deficiency (n = 8018).

Table 3. Mean SF-36 physical component summary scores, mental component summary scores and vitality scores by potential confounders (number of children, symptoms and chronic conditions) for the mid-age women at baseline (1996)

	N[a]	PCS	MCS	Vitality
Children <19 at home[b]				
0	8540	49.0	47.5	59.1
1	3014	50.0	46.7	58.2
2+	2546	50.7	46.2	57.7
Symptoms[c]				
0–2	2027	53.6	54.0	72.6
3–5	3853	51.5	50.6	65.0
6–8	3940	49.7	46.9	57.6
9–11	2574	47.4	42.5	50.1
12–14	1222	43.9	39.5	44.4
15–23	449	41.1	34.8	37.6
Chronic conditions[c]				
0	5584	51.9	49.2	63.4
1	4548	49.9	47.3	58.8
2	2365	47.4	44.8	53.9
3+	1553	43.6	42.6	48.2

[a] Numbers vary due to missing values.
[b] Least significant differences significant for all comparisons (PCS), between 0 and 1 or 2+ children (MCS) and between 0 and 2+ children (vitality).
[c] Least significant differences significant for all comparisons.

Women who reported iron deficiency both in the last 2 years and prior to 2 years ago were excluded from this analysis (n = 41).

After adjustment for the socio-demographic characteristics shown in Table 1, as well as number of children, symptoms and chronic conditions, and baseline scores, mean VT, PCS and MCS scores at follow-up were lowest for women who reported recent iron deficiency and highest for those with no history of iron deficiency (Table 4).

Similarly, after adjusting for the confounding variables, significant decreases in the mean change in VT, PCS and MCS scores between 1996 and 1998 were found for women with a recent history of iron deficiency. PCS scores decreased significantly for all categories of iron deficiency, however the decreases were greatest among those who reported recent iron deficiency (Table 4).

Sixty eight percent of the women who reported recent iron deficiency also reported severe tiredness. In contrast, 56 and 46% of those with past or no history of iron deficiency reported this problem ($\chi^2 = 189$, df = 2, $p < 0.001$).

Discussion

There is a widely held belief, both among the medical community and the general public, that tiredness is a symptom of iron deficiency [11]. However, while anaemia is known to be associated with tiredness, and physical work capacity is reduced in iron deficient women [15], an association between tiredness and iron deficiency has not to our knowledge been demonstrated. Both the cross sectional and longitudinal data presented here provide evidence of such an association.

Analysis of the baseline ALSWH data found an association between answers to the question "Have you ever been told by a doctor that you have low iron?" and physical and mental component summary scores and vitality scores on the SF-36. Both the young and mid-age women who reported a history of low iron had lower scores than those who did not. Women who reported (ever) having had 'low iron' were also more likely to report 'constant tiredness.'

Analyses of the follow-up data from the mid-age women, which allowed identification of 'recent' and 'past' iron deficiency, suggested that general health and well-being and vitality were reduced when iron deficiency was recent (in the last 2 years). (We were not able to ascertain from the available data whether any of the women were currently iron deficient.)

The longitudinal data presented here provide reasonable (but not conclusive) evidence of a causal relationship between iron deficiency and reduced general health and well-being and vitality. Mean PCS, MCS and VT scores were significantly reduced from 1996 to 1998 among women who reported no history of iron deficiency at baseline, but who reported iron deficiency in the 2 years to follow-up, after adjustment for potential confounders such as socio-demographic variables, number of children or illness. One important limitation of these findings however, is the fact that the data were self-reported, and the history of iron deficiency could not be confirmed.

Another important consideration is whether or not the results represent a clinically significant decrease in physical and mental health with iron deficiency. Normative data from the 1995 Australian National Health Survey (ANHS) show that the presence of one serious physical condition

Table 4. Mean (95% CI) PCS, MCS and VT scores in 1998 and mean (95% CI) change in scores between baseline (1996) and follow-up (1998) for mid-age women who reported recent iron deficiency, past iron deficiency and no history of iron deficiency adjusted for number of children, number of symptoms, number of chronic conditions and the socio-demographic confounders shown in Table 1

	PCS Mean (95% CI)	MCS Mean (95% CI)	Vitality Mean (95% CI)
Mean for 1998			
Recent iron deficiency*	46.6 (45.7; 47.4)	45.4 (44.3; 46.5)	54.8 (53.0; 56.6)
Past iron deficiency	47.8 (47.1; 48.8)	46.9 (46.0; 47.9)	57.6 (56.0; 59.1)
Never iron deficient	47.7 (47.0; 48.4)	47.4 (46.5; 48.4)	58.6 (57.1; 60.1)
Mean change (1998 minus 1996)			
Recent iron deficiency*	−3.2 (−4.0; −2.4)	−2.1 (−3.2; −1.0)	−4.2 (−6.0; −2.4)
Past iron deficiency	−1.9 (−2.7; −1.2)	−0.5 (−1.5; 0.4)	−1.4 (−3.0; 0.2)
Never iron deficient	−2.1 (−2.8; −1.3)	0.0 (−1.0; 0.9)	0.4 (−1.9; 1.1)

* 1998 means and mean change for recent iron deficiency significantly different from those for past or no history of iron deficiency.

(e.g. cancer, heart disease, diabetes, hypertension, asthma, arthritis) results in decreases of PCS and MCS of 3.3 and 2.1 respectively, which are very similar to the decreases seen in this study with recent iron deficiency (PCS: 3.2; MCS: 2.1; see Table 4) [16]. The decrease in VT with iron deficiency was approximately two thirds of the ANHS decrease for one serious physical condition (4.2 cf. 6.4). Thus, it would appear that iron deficiency may result in clinically significant decreases in physical and mental functioning similar to those associated with a range of serious medical conditions.

To date, research on the effects of iron deficiency has focused on the objective measurement of physical and mental characteristics such as work performance, cognition, immunity and thermoregulation. The overall impact of these effects on general health and well-being has not been examined. However, in health research, the value of the 'patient's point of view' has been increasingly recognised. Scales such as the SF-36 have been developed to measure health-related quality of life, which includes concepts of functional status and well-being (the extent to which a person's behavioural functioning or well-being meets their needs or expectations) as well as individuals' perceptions of their own general health [14].

The SF-36 results indicate that for women who are iron deficient there may be implications for both work and social lives. PCS measures attributes such as a person's perceptions of their health, in regard to their own expectations and relative to those around them, ability to perform normal physical activities (such as walking various distances, climbing stairs, carrying groceries, bathing and dressing etc), role limitations due to physical difficulties (such as a reduction in the amount of time, or kind or amount of work performed or accomplished) and magnitude of bodily pain and the degree to which it interferes with normal work [13].

In relation to these 'physical' components of health, iron deficiency has been previously shown to reduce work performance, as a result of inadequate iron at a tissue level [1]. Iron is a critical component of many of the enzymes involved in the production of cellular energy, and these are affected in iron deficiency prior to the development of anaemia [17]. It is plausible therefore that inefficient energy production at a tissue level could underlie women's own perceptions of decreased ability to carry out the daily physical tasks of everyday life.

Mental health scores were also lower in women with iron deficiency. These scores measure attributes such as nervousness and sadness, role limitations due to emotional difficulties (such that a person is less careful or accomplishes less), the extent to which physical or emotional problems interfere with social activities, and levels of 'energy' and 'feeling full of life' [13]. Vitality scores were also lower in women who reported iron deficiency. Overall these results lend some support to previous research which has suggested that iron deficiency is associated with

'mental fatigue' which is associated with reduced short-term memory and attention span [8].

These results are important because they attempt to quantify women's own perceptions of vitality and well-being, and their impact on women's everyday lives. The 'load' of women's roles, in terms of paid work and family responsibilities is undoubtedly increasing [18], and our data suggest that these factors may affect vitality and well-being. However, if iron deficiency, which is easily diagnosed and readily treated, is compounding the problem, then strategies for the prevention, detection and treatment of iron deficiency may be indicated.

These data provide support for a relationship between iron deficiency and reduced physical and mental health and vitality. The data are limited by the fact that the iron deficiency could not be confirmed at the time of survey completion and it is possible that only those women who feel tired have their iron levels checked. One way to clarify the relationships suggested by the data presented here would be to see whether SF-36 measures return to pre-iron deficient levels with restoration of iron status. As an adjunct to this study, a clinical trial in which blood indices of iron status and general health and well-being are measured simultaneously, and followed over time through iron restoration, is in progress. The results should shed more light on the intriguing relationship between iron deficiency, tiredness and general well-being.

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