Original Article

Effects of haemoglobin and serum ferritin on cognitive function in school children

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The association between iron deficiency anaemia and cognitive function impairment has been widely reported in young children, but whether the impairment is a result of iron deficiency per se or a combination of iron deficiency and anaemia, and how these conditions interact, is still questionable. Four hundred and twenty-seven school children from two schools in socioeconomically deprived communities were selected in southern Thailand. Iron status was determined by haemoglobin and serum ferritin concentrations. Cognitive function in this study was measured by IQ test and school performance, including Thai language and mathematics scores, using *z*-scores based on distributions within the same grade and school. Data on demography and socio-economic status were collected by questionnaire answered by the parents. Linear regression models were used to investigate the effect of anaemia and iron deficiency, reflected by haemoglobin and serum ferritin concentration, on cognitive function and school performance. We found that cognitive function increased with increased haemoglobin concentration in children with iron deficiency, but did not change with haemoglobin concentration in children with normal serum ferritin level. Children with iron deficiency anaemia had consistently the poorest cognitive function (IQ, 74.6 points; Thai language score, 0.3 SD below average; and mathematics score, 0.5 SD below average). Children with non-anaemic iron deficiency but with high haemoglobin levels had significantly high cognitive function (IQ, 86.5 points; Thai language score, 0.8 SD above average; and mathematics score, 1.1 SD above average). This study found a dose–response relationship between haemoglobin and cognitive function in children with iron deficiency, whereas no similar evidence was found in iron sufficient children.

Key words: cognitive function, educational achievement, Hat Yai, IQ, iron deficiency, iron status, school performance, Songkhla, Thailand.

Introduction

Iron deficiency and iron deficiency anaemia (IDA) are common in young children. Cognitive function impairment, the consequence of greatest concern, is well established in school children with late stage iron deficiency once anaemia is recognized,[1–5] but it is still controversial in non-anemic iron deficient children.[2,3,6–8] It has been suggested that tissue iron deficiency may develop early by means of a decrease in iron storage without anaemia that may have non-haematological consequences, for example, cognitive function or physical performance impairment.[6,7] However, previous studies have not demonstrated clearly whether the cognitive function impairment found in children with IDA is due to iron deficiency or a combination of iron deficiency and anaemic status, or how these two conditions interact.

The National Anemia Surveillance Program[9] showed that the prevalence of anaemia has been declining in Thailand. A careful re-evaluation of existing iron supplementation in school children is therefore needed. In this study the baseline data of an intervention study were analysed in order to elucidate the relationships between iron deficiency, reflected by serum ferritin (SF), and anaemia, reflected by haemoglobin (Hb), and their effects on cognitive function in school children. We attempted to separate the effect of iron storage from that of haemoglobin level.

Materials and methods

Study site

From the records of primary schools outside Hat Yai municipality, two primary schools were selected as our study site as they were considered to have a high risk of anaemia, comprised at least 150 students, was accessible by automobile and teachers were willing to co-operate in the study.

These two schools, located approximately 35 km from the research centre, had a mixture of Buddhist and Muslim

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students. Thai-Buddhists speak Thai whereas Thai-Muslims speak both the Thai and Melayu languages. Family incomes were derived mainly from selling plantation products, particularly the rubber latex. The area is free from malaria and no iron supplementation program had been implemented previously at this study site.

Study subjects

An invitation letter providing information about the research project and requesting consent was sent to the parents of children who were in the first to sixth grades. Only children with written informed parental consent were recruited for the study.

Cognitive function assessment

The cognitive function of each subject was measured using the Test of Nonverbal Intelligence (TONI II)[10] and school performance without knowing the child's iron status. TONI II is easy to administer in the field. It is a standardized and culturally fair test for measuring abstract and figural problem solving, a major aspect of intelligence, in 5–80 years-olds.[10,11] Its high test–retest reliability ($R^2 = 0.86$) and its high correlation ($R^2 = 0.7$) with a standard intelligence test (i.e., Wechsler's Intelligence Scale for Children (WISC)) in Thai children was its justification for use in this study.[12]

Each of three trained testers established a rapport with each child and demonstrated how to complete the TONI II (form A). Items are arranged in order of difficulty and each consists of one picture question and four or five available responses, but only one correct response. Each child began with the item indicated in the manual (depending on age) and continued until he/she made three incorrect responses in five consecutive items. Total raw scores were computed and then converted to the corresponding IQ using the table provided within the manual. School performance included the average Thai language and mathematics scores collected from the two latest examinations in the previous academic year.

Determination of iron status

Haemoglobin and SF were used to determine iron status from a single venipuncture. A 2 mL sample of blood was placed into an ethylenediaminetetraacetic acid (EDTA) prepared tube for Hb, and 3 mL was kept in a plastic sealed test tube at ambient temperature (approximately 25°C) for serum ferritin measurement. Within three hours, all blood samples were transferred to the laboratory at Songklanagarind Hospital.

Haemoglobin content was measured using an automated machine (Technicon H*1E™ system; Technicon, Tarrytown, NY, USA) using the cyanmethemoglobin method.[13] Serum ferritin concentration (SF) was assessed by the IMx® assay (Abbott Laboratories, Abbot Park, IL, USA) using the Microparticle Enzyme Immunoassay (MEIA) method.[14]

Collection of other independent variables

Demographic variables, including school, class, sex, age, ethnic group, number of siblings and child ordinal position, and socioeconomic variables, including parents' education in years, father's and mother's occupations (none, casual/farmer/trader, or government officer/private), family monthly income (≤ 5000 baht or > 5000 baht) were collected by a questionnaire answered by parents.

Body weight and height of children wearing school uniforms, without belts or shoes and with empty pockets, were measured using a beam balance Detecto scale and stadiometer (Detecto Scales, Brooklyn, NY, USA) to the nearest 0.1 kg and 0.5 cm, respectively. The weight-to-height ratio of each child was then compared with the weight-to-height data from the Nutrition Division, Ministry of Public Health, in 1996–97.[15] Using cut-off points at the 10th, 90th and 97th percentiles for weight-to-height, the children were classified as underweight (< 10th percentile), normal (10th – 90th percentile), overweight (> 90th – 97th percentile) and obese (> 97th percentile). Physical examination was performed by the first author to detect serious illness or infection.

Ethical consideration

This research was approved by the Ethical Review Committee of the Faculty of Medicine, Prince of Songkla University, Thailand.

Data analysis

Scatter plots were constructed between each cognitive function and Hb, broken down by SF into low SF group (≤ 20 μg/L) and normal SF group (SF > 20 μg/L).[16] On the horizontal axis, the points were grouped into three equal bands. The median values of each band were used to fit a cubic spline smoothing function curve.[17]

For modelling, Hb concentration was classified into three groups at the cut-off points of 11.5 and 12.5 g/dL. Mean IQ, Thai language score and mathematics score converted to *z*-scores, based on the distribution within the same grade and school were compared across each subgroup of Hb and SF, with adjustment for potential confounders. Test for trend was carried out to examine the dose–response relationship between Hb and cognitive function for each group of SF. All analyses were carried out using STATA statistical software version 6 (StataCorp, College Station, TX, USA).[18]

Results

Out of 427 eligible children, the ratio of male to female subjects was 1:1, the average age was 9.6 years and the percentage of underweight and normal weight were 15 and 80%, respectively. Two-thirds of the children were Muslim and slightly more than one half had three siblings or more. Almost all parents were farmers whose formal education averaged 6 years and whose monthly income was less than 5000 baht or US$125.00, compared to the Thai national average of 12 729 baht or $US318.00, reported by the Household Socioeconomic Survey, National Statistical Office. None of the children had overt manifestation of thalassemia disease.

Of the total number of subjects, one-eighth had SF ≤ 20 μg/L and 22% were classified as anaemic (Hb < 11.5 g/dL for 5–11 years old; Hb < 12.0 g/dL for 12–13 years old).[19] The prevalence of IDA in these subjects was 4.2% of all of the children and 19.4% among the anaemic children. A screening test showed that two-thirds were positive for thalassemia traits.

As seen in Table 1, age, height, parents' education and family monthly income were associated significantly with IQ. Sex, parents' education and family monthly income were associated with Thai language scores whereas only sex and parents' education were associated with mathematics scores. The overall average IQ was 78 ± 12 points (mean ± SD); higher IQ scores were found among children who were older and taller and whose parents had higher education levels and whose families had higher monthly incomes. Better school performance was found among children who were female and whose parents had a higher level education.

Figure 1a,c,e shows that IQ, Thai language and mathematics scores increased with increasing Hb in the low SF group with a significant dose–response relationship, while these cognitive function scores barely changed with Hb concentration in the normal SF group (Fig. 1b,d,f). The group with the highest scores were children with high Hb but low SF. This pattern was verified after adjustment for potential confounders (Table 2).

Using a group of exclusively SF > 20 μg/L subjects as the reference, significantly poorer mathematics score were found in children with low Hb and low SF concentrations, whereas significantly higher of IQ, Thai language and mathematics scores were found in children with high Hb but low SF.

Discussion

There was a significant different pattern of association between cognitive function and Hb in the different iron status groups, as reflected by SF level. IQ, Thai language scores and mathematics scores in children with low SF increased with increasing of Hb with a significant dose–response relationship. In contrast, these measures of cognitive function in children with SF above 20 μg/L was not affected by Hb concentration. Unexpectedly, the highest scores for cognitive

Table 1. Characteristics of children in the study

Variables	*n*	IQ (point)	Thai language (Z-score)	Mathematics (Z-score)
Categorical variables†				
Sex	427			
Male	199	79 ± 11	–0.4 ± 1.0	–0.2 ± 1.0
Female	228	78 ± 13	0.4 ± 1.0¶	0.2 ± 1.0¶
Weight for height	427			
Underweight	66	78 ± 12	–0.01 ± 1.0	–0.03 ± 1.1
Normal	341	78 ± 12	0.03 ± 1.0	0.02 ± 1.0
Overweight	11	79 ± 8	0.2 ± 1.2	0.24 ± 1.1
Obese	9	77 ± 11	–0.1 ± 0.8	–0.3 ± 0.8
Ethnic group	427			
Thai-Buddhist	133	78 ± 11	–0.01 ± 1.0	–0.1 ± 0.9
Thai-Muslim	294	79 ± 13	0.04 ± 1.0	0.04 ± 1.0
Child ordinal position	426			
≤3	308	78 ± 11	–0.1 ± 1.0	–0.04 ± 1.0
>3	118	79 ± 14	0.2 ± 1.0	0.2 ± 1.0
Siblings	426			
≤3	203	79 ± 12	0.1 ± 1.0	0.1 ± 1.0
>3	223	78 ± 12	–0.02 ± 1.0	–0.1 ± 1.0
Mother's occupation	424			
None	14	81 ± 13	0.3 ± 1.0	0.6 ± 1.0
Casual/farmer/seller	401	78 ± 12	0.01 ± 1.0	–0.01 ± 1.0
Government/officer/private	9	80 ± 10	0.5 ± 1.0	0.6 ± 1.0
Father's occupation	423			
None	4	72 ± 5	–1.0 ± 1.0	0.2 ± 1.0
Casual/farmer/seller	393	78 ± 12	–0.02 ± 1.0	–0.03 ± 1.0
Government/officer/private	26	84 ± 9	0.6 ± 1.0	1.0 ± 1.0
Family monthly income§	418			
≤5000 baht	338	78 ± 12¶	–0.03 ± 1.0¶	–0.03 ± 1.0
>5000 baht	80	82 ± 12	0.2 ± 1.0	0.2 ± 1.0
Continuous variables‡				
Age (years)	427	0.8 ± 0.3¶	–0.1 ± 0.03	–0.05 ± 0.03
Weight (kg)	427	0.2 ± 0.1	–0.004 ± 0.01	–0.01 ± 0.01
Height (cm)	427	0.2 ± 0.1¶	0.001 ± 0.01	–0.001 ± 0.01
Parents'education (years)	418	0.9 ± 0.2¶	0.1 ± 0.2¶	0.1 ± 0.02¶

†Mean ± SD; ‡Coefficient ± SE; §Family monthly income, 1 baht = US$0.025 at the time of data collection; ¶Statistically significant association ($P < 0.05$).

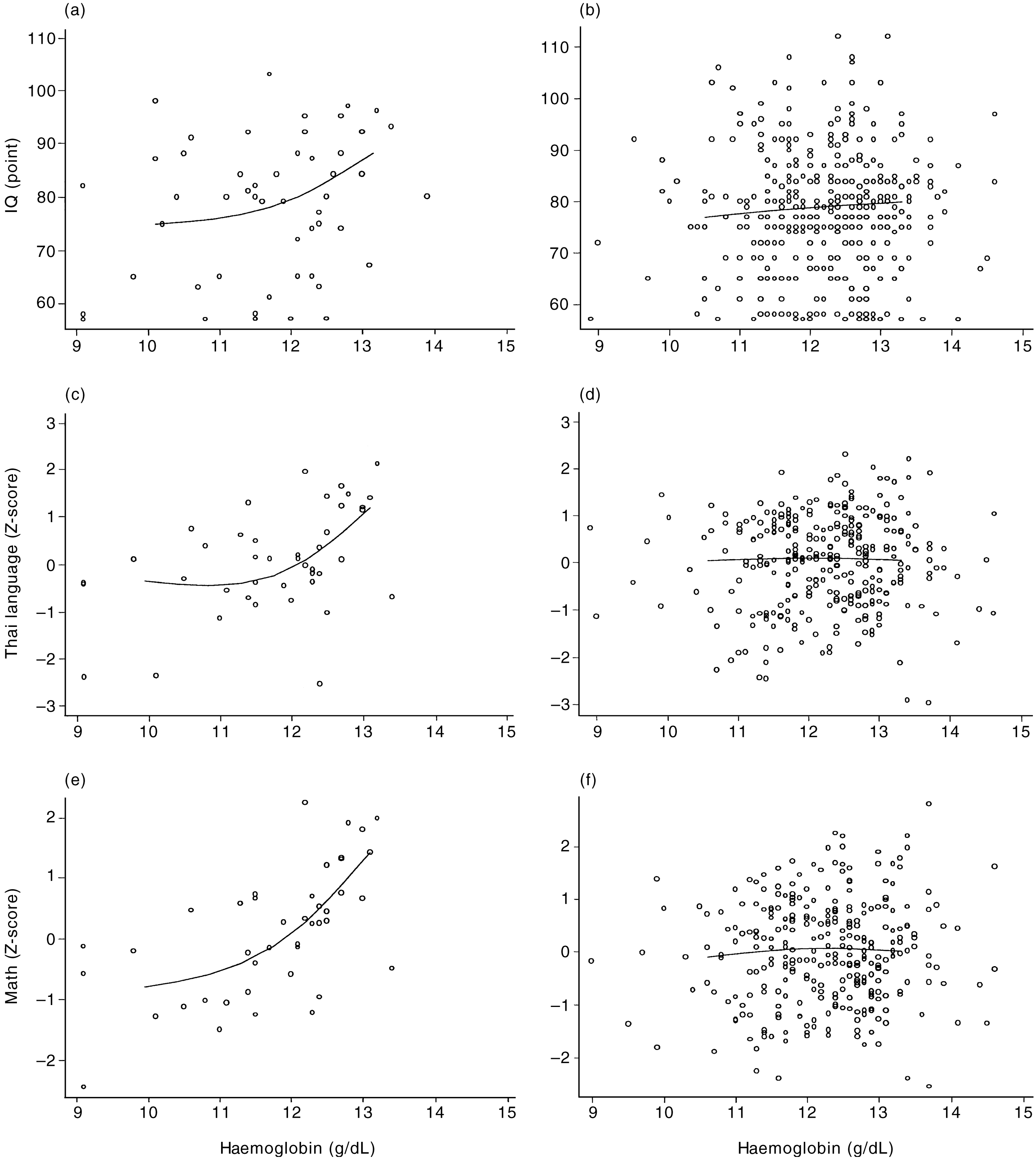

Figure 1. Effect of haemoglobin concentration on IQ, Thai language and mathematics scores in children with (a, c, e) low serum ferritin (≤ 20 μg/L) and (b, d, f) normal serum ferritin (> 20 μg/L) concentrations.

function were in children with high Hb but low SF, whereas the lowest levels were found in those with both low Hb and low SF.

High prevalence of anaemia with relatively low prevalence of iron deficiency (SF ≤ 20 μg/L) suggests that IDA might not be the most common cause of anaemia in this area. Linpisarn *et al.*[20] also found that only 19% of anaemia cases in preschool-age children was IDA, and no IDA was found among anaemic school-age children in Northern Thailand. An SF concentration of ≤ 20 μg/L may not be a gold standard for iron deficiency as it can be elevated with infection or inflammation.[21,22] However, we did not find such infection

Table 2. Mean ± SE of IQ, Thai language and mathematics scores by serum ferritin and haemoglobin categories

Serum ferritin (μg/L)	Hb (g/dL)			P
	<11.5 (n)	11.5–12.5 (n)	>12.5 (n)	
Adjusted mean IQ points†				
≤20	75.0 ± 2.6 (20)	76.2 ± 2.6 (20)	86.5 ± 3.6* (11)	0.03
>20	78.5 ± 1.3 (80)	78.2 ± 1.0 (149)	78.7 ± 1.0 (135)	0.41
Adjusted mean Thai language score (*z*-score)‡				
≤20	–0.3 ± 0.2 (17)	–0.1 ± 0.2 (15)	0.8 ± 0.3* (9)	<0.01
>20	–0.1 ± 0.1 (64)	0.1 ± 0.1 (119)	0.03 ± 0.1 (125)	0.57
Adjusted mean Mathematics score (*z*-score)				
≤20	–0.5 ± 0.2* (17)	0.2 ± 0.2 (15)	1.1 ± 0.3* (9)	<0.01
>20	–0.1 ± 0.1 (64)	0.1 ± 0.1 (119)	–0.01 ± 0.1 (125)	0.67

*Significantly different from serum ferritin concentration > 20 μg/L; †Adjusted for family monthly income and parents' education; ‡Adjusted for sex and parents' education. Statistical significance (test for trend): *P*-values < 0.05 were considered statistically significant.

among our subjects. Nopparatana *et al.* found that 24 and 30% of pregnant women and their spouses who attended the antenatal clinic at the teaching hospital near the study area in 1994–95 had thalassemia traits.[23] In addition, β-thalassemia trait, a local common variant, can protect the carrier from iron deficiency.[24] Thus, the thalassemia trait may be an important contributor to non-iron deficiency anaemia. However, due to budget limitations, Hb typing was not undertaken in this study.

Average IQ on figural problem solving, measured by TONI II in this study (mean, 78; SD, 12 point), was relatively low compared with the average IQ in Southern rural Thai children reported by The National Health Survey (mean, 92; SD, 13 point) using similar measurements.[12] This may be influenced by socioeconomic deprivation in the study area.

Although cognitive function tended to be lower in children with iron deficiency anaemia, only mathematics scores were significantly lower than in the normal SF group. Previous studies reported both significantly and non-significantly different lower IQ scores in children with IDA.[2–4,25,26] The variability may be due to using different measurements, in which different aspects of IQ may be assessed. In contrast to our study, Pollitt *et al.*[2] found that Thai language scores were significantly lower while mathematics scores showed no significant difference in IDA children. This inconsistent finding may be explained by differences in assessment systems at different schools. Owing to the use of different measurements of IQ and assessments of school achievement, we may conclude only that IDA has a significant adverse effect at least in some areas of cognitive function.

The adverse effect of iron deficiency on cognitive function may be explained by diminished synthesis, packaging, uptake and degradation of neurotransmitters.[27] The most prominent feature of iron deficiency on cognitive function is the significant and selective diminution of central dopamine neurotransmission.[28] Electroencephalogram power spectrum also showed a slower activity in children with iron deficiency than in iron replete children, suggesting a developmental lag or central nervous system dysfunction among the former group.[29]

Most studies have reported that children with iron depletion did not differ significantly in cognitive function from their peers,[2,3,8,30] whereas a few studies have reported significantly poorer cognitive function.[6,7] Our study unexpectedly found that children with iron depletion accompanying high Hb had the best cognitive function. When Hb is high enough, increasing iron levels may have some adverse effect on cognitive function. Studies in rats and mice reveal that iron overload may cause oxidative stress and has been related to carcinogenesis of the oesophagus and liver.[31–35] In children, iron supplementation does not always result in improvement of cognition.[2,25] This evidence and the findings of our study suggest a need to carefully review the strategy of the iron supplementation program in Thailand.

Bias, chance and confounders can distort the results of epidemiological studies. Measurement bias in this study was overcome by blinding and a standardized process. The investigation of Hb and SF in this study was performed in a standard laboratory using standardized techniques (coefficient of variation = 0.5–5.3%). Low SF has 95–100% specificity in determining low iron stores.[21,36] This study allowed only a 5% chance of type I error, which is acceptably low, and we also found similar associations in different cognitive function tests. It is therefore unlikely to happen by chance. Potential confounders in this study (including socioeconomic status) were adjusted for.

Although bias was minimised and confounders were adjusted for, these results should be interpreted with caution because of the cross-sectional nature of the study. Further randomised control trials should investigate whether an increase in Hb can increase cognitive function in children with iron depletion.

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References

1. Webb TE, Oski FA, Syracuse NY. Iron deficiency anemia and scholastic achievement in young adolescents. J Pediatr 1973; 82: 827–830.
2. Pollitt E, Hathirat P, Kotchabhakdi NJ, Missell L, Valyasevi A. Iron deficiency and educational achievement in Thailand. Am J Clin Nutr 1989; 50: 687–697.
3. Soewondo S, Hausaini M, Pollitt E. Effect of iron deficiency on attention and learning processes in preschool children: Bandung, Indonesia. Am J Clin Nutr 1989; 50: 667–674.
4. Seshadri S, Golpadas T. Impact of iron supplementation on cognitive functions in preschool and school-aged children: the Indian experience. Am J Clin Nutr 1989; 50: 675–686.
5. Soemantri AG. Preliminary findings on iron supplementation and learning achievement of rural Indonesian children. Am J Clin Nutr 1989; 50: 698–702.
6. Bruner AB, Joffe A, Duggan AK, Casella JF, Brandt J. Randomised study of cognitive effects of iron supplementation in non-anaemic iron-deficient adolescent girls. Lancet 1996; 348: 992–996.
7. Zhu YI, Haas JD. Iron depletion without anemia and physical performance in young women. Am J Clin Nutr 1997; 66: 334–341.
8. Walter T, Kovalskys J, Stekel A. Effect of mild iron deficiency on infant mental development scores. J Pediatr 1983; 102: 519–522.
9. Department of Health. Surveillance of anemia in Thailand 1988–97. Bangkok: Ministry of Public Health, 1997; 1–7.
10. Brown L, Sherbenou R, Johnsen S. Test of Nonverbal Intelligence, 2nd edn. Austin, TX: Pro-Ed, 1990; 1–59.
11. Resnick LB, Glaser R. Problem solving and intelligence. In: Resnick LB, ed. The Nature of Intelligence. Hillsdale, NJ: Erlbaum, 1976; 205–230.
12. Chooprapawan J. National Health Survey 1996–97. Bangkok: Health System Research Institute, 1998; 25–57.
13. Technicon. Hemoglobin method. Reference manual Technicon H*1/H*1E system. New York: Miles, 1991; 5,1-11–5,1-13.
14. Abbott Laboratories. IMX System Operation Manual. Abbott Park, IL: Abbott Laboratories, 1996; 1–8.
15. Department of Health. National Reference Value for Weight, Height, and Nutritional Indices for Thai Population Aged 1 day–19 years. Bangkok: Ministry of Public Health, 1999.
16. Winichagoon P, Chongsuvivatwong V. Iron deficiency and iron deficiency anemia. Thailand: Ministry of Public Health, 1991; 1–11.
17. Stata Corporation. Connect–connect points. Stata Graphics Manual Release 6. Texas: Stata Press, 1999; 44–55.
18. Stata Coporation. Stata Statistical Software: Release 6.0. Texas: Stata Press, 1999.
19. Stoltzfus R, Dreyfuss M. Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anemia. Washington DC: ILSI Press, 1998.
20. Linpisarn S, Tienboon P, Promtet N, Putsyainunt P, Santawanpat S, Fuchs GJ. Iron deficiency and anaemia in children with a high prevalence of haemoglobinopathies: implications for screening. Int J Epidemiol 1996; 25: 1262–1266.
21. Mazza J, Barr R, McDonald JWD, Valberg LS. Usefulness of the serum ferritin concentration in the detection of iron deficiency in a general hospital. Can Med Assoc J 1978; 119: 884–886.
22. De-ji T, Ya-min L, Yi L. Serum ferritin in normal subjects and in some diseases. Chinese Med 1987; 100: 631–635.
23. Nopparatana C, Fukumaki Y, Pornpatkul M. Thalassemia in the South of Thailand: Prenatal and Postnatal Diagnosis. Songkhla, Thailand: Department of Pathology, Faculty of Medicine, Prince of Songkla University, 1996; 13–14.
24. Mehta BC. Iron deficiency: prevalence and problems, Part II. J Assoc Physicians India 1990; 38: 491–494.
25. Soemantri AG, Pollitt E, Kim I. Iron deficiency anemia and educational achievement. Am J Clin Nutr 1985; 42: 1221–1228.
26. Pollitt E. Iron deficiency and educational deficiency. Nutr Rev 1997; 55: 133–141.
27. Beard J, Connor JR, Jones BC. Iron in the brain. Nutr Rev 1993; 51: 157–170.
28. Youdim MBH, Schachar DB, Yehuda S. Putative biological mechanisms of the effect of iron deficiency on brain biochemistry and behavior. Am J Clin Nutr 1989; 50: 607–617.
29. Otero GA, Aguirre DM, Porcayo R, Fernandez T. Psychological and electroencephalographic study in school children with iron deficiency. Int J Neurosci 1999; 99: 113–121.
30. Oski FA, Honig AS, Helu B, Howanit ZP. Effects of iron therapy on behavior performance in nonanemic, iron-deficient infants. Pediatrics 1983; 71: 877–880.
31. Chen X, Ding YW, Yang G, Bondoc F, Lee MJ, Yang CS. Oxidative damage in an esophageal adenocarcinoma model with rats. Carcinogenesis 2000; 21: 257–263.
32. Chen X, Yang G, Ding WY, Bondoc F, Curtis SK, Yang CS. An esophagogastroduodenal anastomosis model for esophageal adenocarcinogenesis in rats and enhancement by iron overload. Carcinogenesis 1999; 20: 1801–1808.
33. Pigeon C, Turlin B, Lancu TC, Leroyer P, Le Lan J, Dengnier Y, Brissot P, Loreal O. Carbonyl-iron supplementation induces hepatocyte nuclear changes in BALB/CJ male mice. J Hepatol 1999; 30: 926–934.
34. Abalea V, Cillard J, Dubos MP, Anger JP, Cillard P, Morel I. Iron-induced oxidative DNA damage and its repair in primary rat hepatocyte culture. Carcinogenesis 1998; 19: 1053–1059.
35. Plummer JL, MacKinnon M, Cmielewski PL, Williams P, Ahern MJ, Ilsley AH, de la M Hall P. Dose-related effects of dietary iron supplementation in producing hepatic iron overload in rats. J Gastroenterol Hepatol 1997; 12: 839–842.
36. Kim SK, Cheong WS, Jun YH, Choi JW, Son BK. Red blood cell indices and iron status according to feeding practices in infants and young children. Acta Paediatr 1996; 85: 139–144.