

Impact of iron deficiency on attention among school-aged adolescents in Hong Kong

YT Cheung, Dorothy FY Chan, CK Lee, WC Tsoi, CW Lau, Jennifer NS Leung, Jason CC So, Stella TY Tsang, Chris LP Wong, Yvonne YL Chu, CK Li *

ABSTRACT

Introduction: Adolescence is a critical period for higher-order cognitive function development. The adverse effects of low iron reserves on attention are particularly relevant to school-aged students. Based on our previous study identifying a 11.1% prevalence of iron deficiency (ID) among Chinese school-aged adolescents aged 16 to 19 years in Hong Kong, the present study examined the association between iron status and attention outcomes in these adolescents.

Methods: This cross-sectional study recruited 523 adolescents (65.0% female; mean age=17.5 years) from 16 local schools. Serum ferritin levels and complete blood counts were measured. Iron deficiency was defined as serum ferritin concentration <15 µg/L. The Conners Continuous Performance Test Third Edition was administered to assess impairments in three attention domains, namely, sustained attention, inattention, and impulsivity. Multivariable analyses, conducted both for the overall cohort and stratified by sex, were used to evaluate the associations between serum ferritin levels and attention outcomes, adjusting for fatigue and dietary patterns.

Results: In the overall cohort, a lower serum ferritin concentration was significantly associated with sustained attention impairment (risk ratio [RR]=0.825, 95% confidence interval [95% CI]=0.732-0.946; P=0.040). Among female participants, those with sustained attention impairment had significantly lower serum ferritin concentrations than those with intact attention function (median=40.0 µg/L; interquartile range [IQR]=18.8-52.1 vs median=48.5 µg/L; IQR=21.8-73.8; P=0.038). Multivariable analysis showed a similar trend, though

the association was not statistically significant (RR=0.954, 95% CI=0.904-1.005; P=0.073). Among male adolescents, iron reserves were not significantly associated with attention outcomes.

Conclusion: These findings highlight the importance of timely ID screening and correction in school-aged adolescents, particularly among female adolescents.

Hong Kong Med J 2025;31:Epub

<https://doi.org/10.12809/hkmj2310950>

¹ YT Cheung, PhD

² DFY Chan, MB, ChB

³ CK Lee, MB, BS, MD

³ WC Tsoi, MB, ChB

³ CW Lau, MB, ChB

³ JNS Leung, MB, BS

⁴ JCC So, MB, BS

⁵ STY Tsang, PhD

⁶ CLP Wong, PhD

⁷ YYL Chu, MB

⁷ CK Li *, MB, BS, MD

¹ School of Pharmacy, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

² Department of Paediatrics, Prince of Wales Hospital, Hong Kong SAR, China

³ Hong Kong Red Cross Blood Transfusion Service, Hospital Authority, Hong Kong SAR, China

⁴ Department of Pathology, Hong Kong Children's Hospital, Hong Kong SAR, China

⁵ Department of Pathology, Hong Kong Molecular Pathology Diagnostic Centre, Hong Kong SAR, China

⁶ Amber Medical Group Limited, Hong Kong SAR, China

⁷ Department of Paediatrics, Faculty of Medicine, The Chinese University of Hong Kong, Hong Kong SAR, China

* Corresponding author: ckli@cuhk.edu.hk

This article was published on 9 Apr 2025 at www.hkmj.org.

This version may differ from the print version.

New knowledge added by this study

- The prevalence of iron deficiency among Chinese school-aged adolescents aged 16 to 19 years in Hong Kong is 11.1%.
- Lower serum ferritin reserves were associated with sustained attention impairment in the overall cohort.

Implications for clinical practice or policy

- The consequences of low iron reserves on health and functional outcomes should be emphasised among school-aged adolescents.
- Adolescents with low ferritin concentrations should receive counselling on the consumption of iron-rich foods and iron supplementation.
- Future research should evaluate the effects of iron supplementation on functional outcomes.

缺鐵對香港學齡青少年專注力的影響

張彥婷、陳鳳英、李卓廣、蔡偉超、劉靜華、梁雅詩、
蘇志釗、曾瑋瑩、黃利寶、朱婉玲、李志光

引言：青少年是高階認知功能發展的關鍵時期。低鐵儲備對專注力的負面影響與學生尤為相關。我們早前的研究估計香港16至19歲的華裔學齡青少年缺鐵流行率為11.1%，我們現以該研究為基礎，檢視這些青少年的鐵狀態與專注力結果之間的關聯。

方法：這項橫斷面研究招募了來自16所本地學校的523名青少年（65.0%女性；平均年齡=17.5歲）接受血清鐵蛋白水平測量和全血細胞計數。缺鐵定義為血清鐵蛋白濃度 $<15\text{ }\mu\text{g/L}$ 。我們採用Conners持續專注力測試第三版來評估持續專注力、專注力不集中和衝動這三個專注力領域的受損情況，然後在整體隊列及按性別分層進行多變量分析以評估血清鐵蛋白水平與專注力結果之間的關聯，並調整疲勞和飲食模式的影響。

結果：在整體隊列中，較低血清鐵蛋白濃度與持續專注力受損顯著相關（風險比=0.825，95%置信區間=0.732-0.946； $P=0.040$ ）。在女孩中，持續專注力受損者的血清鐵蛋白濃度顯著低於專注力功能正常者（中位數=40.0 $\mu\text{g/L}$ ，四分位間距=18.8-52.1與中位數=48.5 $\mu\text{g/L}$ ，四分位間距=21.8-73.8； $P=0.038$ ）。多變量分析顯示類似趨勢，儘管該關聯在統計上並不顯著（風險比=0.954，95%置信區間=0.904-1.005； $P=0.073$ ）。在男孩中，鐵儲備與專注力結果之間並無顯著關聯。

結論：這些發現突顯了為學齡青少年（特別是女孩）及時進行缺鐵篩查和糾正的重要性。

Introduction

Adolescence marks a critical stage of physical growth, lean body mass development, and pubertal maturation. These biological and physiological changes increase the demand for micronutrients. In particular, iron deficiency (ID) remains a global public health concern.¹ Iron deficiency is the most common nutritional deficiency and the leading cause of iron deficiency anaemia (IDA). Because dietary intake is the primary source of iron for most individuals, inadequate dietary iron intake is the main cause of IDA, particularly in adolescents, who are more likely to have poor dietary patterns.² The Global Burden of Disease 2020 report estimated that approximately 60% of the total global burden of anaemia in 2019 arose from inadequate dietary iron intake.³ Consequently, ID was identified as the most important cause of anaemia-related disability.^{3,4}

In addition to its essential role in haemoglobin synthesis, iron is a key element in brain metabolism and is vital for multiple cellular processes, including neurotransmitter synthesis, neuron myelination, and mitochondrial function.⁵ Studies in young children have demonstrated that ID during early life adversely affects psychomotor development, concentration, memory, and learning ability.^{6,7} Notably, the attention domain has received

considerable research interest because iron plays a crucial role in the regulation of dopaminergic activity, which is implicated in the pathogenesis and symptoms of attention-deficit hyperactivity disorder (ADHD). Some studies have detected lower ferritin concentrations in children diagnosed with ADHD than in non-ADHD controls.^{8,9} However, many cognitive studies regarding ID have involved children aged ≤ 15 years.^{8,10} Few population-based studies have examined the effect of iron status on cognitive outcomes in adolescents and young adults, and no such studies have been conducted in Chinese populations.

Our previous study¹¹ reported a prevalence of 11.1% for ID among Chinese school-aged adolescents aged 16 to 19 years in Hong Kong, with ID and IDA affecting 17.1% and 10.9% of girls, respectively, while no male participants were affected. More than one-third of these adolescents reported regularly skipping at least one meal per day.¹¹ Notably, lower serum ferritin concentrations were observed in adolescents who skipped meals, reported infrequent intake of iron-rich foods, or had heavy menstrual bleeding.¹¹ Consistent with findings from other studies, poor iron reserves were associated with greater self-reported fatigue, reduced physical functioning, and worse school performance.¹¹ Adolescence represents the second most critical period for the development of higher-order cognitive functions, including attention, self-control, and executive function. The adverse effects of low iron reserves on attention span and attentiveness are particularly relevant to upper secondary students in Hong Kong, who are expected to excel academically and prepare for the Hong Kong Diploma of Secondary Education Examination, the city's university entrance examination. This study aimed to examine the association between iron status and attention outcomes among school-aged adolescents in Hong Kong.

Methods

This cross-sectional study recruited healthy adolescent students through the Hong Kong Red Cross Blood Transfusion Service blood donation campaigns at 16 secondary schools between October 2020 and December 2021. The detailed methodology was described in our previous report,¹¹ which aimed to identify the risk factors of ID and IDA in this cohort to facilitate future association studies on health and functional outcomes. In the present study, the dataset was used to delineate the impact of iron reserves on performance-based attention functioning, which is distinct from the self-reported daily functioning outcomes presented in the previous report.¹¹

Study population

Students eligible for this study were aged ≥ 16 years

and had agreed to participate in blood donation screening. Students were excluded if they exhibited signs or symptoms of an active infection, reported a history of anaemia, or were receiving treatment for anaemia. Students who did not pass the blood donation screening were still permitted to participate in the study.

Prevalences of iron deficiency and iron deficiency anaemia

A serum ferritin concentration $<15 \mu\text{g/L}$ was considered indicative of ID in both male and female participants, based on the World Health Organization definition.¹² Iron deficiency anaemia was defined as the presence of both ID and anaemia. In accordance with the recommendations of the World Health Organization, anaemia was defined as a haemoglobin concentration $<12 \text{ g/dL}$ in female participants and $<13 \text{ g/dL}$ in male participants.¹³ All assays were conducted on the same day in the Department of Pathology Laboratory at Hong Kong Children's Hospital. The specifications of the instruments and tests have been reported in our prior study.¹¹

Attention outcomes

Before blood donation, participants completed the Conners Continuous Performance Test Third Edition (CPT-III), a validated assessment commonly used in clinical and research settings to evaluate attention.¹⁴ The CPT-III requires 14 minutes to complete and generates specific CPT attention measures (online supplementary Tables 1 to 3). Raw scores for each CPT measure were converted into *T*-scores based on normative samples (mean=50, standard deviation [SD]=10). Each CPT measure was classified as indicating no/mild (*T*-score within $<1 \text{ SD}$), moderate (*T*-score within 1-2 SDs), or severe (*T*-score within $>2 \text{ SDs}$) impairment.

Based on the CPT-III manual and the clinical discretion of a developmental specialist (the second author), attention measures were categorised into three clinically relevant attention domains of interest,¹⁴ namely, sustained attention impairment (inability to maintain attention), inattention (inability to focus or concentrate), and impulsivity (difficulty with response inhibition).

Covariates

Fatigue, a recognised risk factor for diminished neurocognitive function, is associated with ID.^{11,15} Participants completed the PedsQL Multidimensional Fatigue Scale, which has been validated in young adults up to 25 years of age.¹⁶ Each item was scored on a 100-point reverse scale, where lower scores indicated more severe fatigue. The Traditional Chinese version of the PedsQL

Multidimensional Fatigue Scale has demonstrated good internal consistency, reliability, and content validity in the Chinese population.^{17,18}

We previously reported that dietary patterns are associated with iron reserves in Hong Kong adolescents.¹¹ All participants self-reported their dietary patterns, including meal-skipping habits (breakfast, lunch, or dinner) and the frequency of consuming common iron-rich foods, namely, seafood, meat, iron-fortified cereal, leafy vegetables, beans, nuts, dried fruits, and eggs.¹¹

Statistical analyses

The demographic and haematological characteristics of the cohort, along with their attention outcomes, were summarised using descriptive analysis.

The primary outcome was attention impairment. Serum ferritin concentration was used as the predictor of interest, rather than a comparison of attention outcomes between participants with and without ID or IDA, considering that clinical thresholds for diagnosing ID and IDA may not be applicable when evaluating the effect of iron on functional outcomes. Even if an adolescent is not clinically diagnosed with ID or IDA, a low-to-normal ferritin concentration may affect functional outcomes; previous studies have shown that the impact of ID on neurodevelopment may occur before ID manifests as clinical anaemia.^{19,20} The Mann-Whitney *U* test was utilised to compare serum ferritin concentrations between participants with normal attention function (ie, those who did not exhibit impairment in any of the three attention domains) and those with moderate or severe impairment in sustained attention, inattention, or impulsivity.

Multivariable analysis using a log-binomial regression model was conducted, with serum ferritin concentration, fatigue, dietary pattern, and dietary iron intake as predictors. Models were adjusted for age and sex. Risk ratios (RRs) and 95% confidence intervals (95% CIs) were calculated.

Given that previous studies have shown a positive association between iron reserves and functional outcomes regardless of sex,^{8,15,20,21} we first conducted all analyses in the overall cohort. Subsequently, analyses were performed separately for male and female participants.

The significance threshold was set at $P < 0.05$. All statistical analyses were performed using SAS 9.4 (SAS Institute, Cary [NC], US) and were two-tailed.

Results

As reported in our previous study,¹¹ a total of 523 students were recruited (participation rate: 70%). Twenty-nine students were deferred from blood donation due to low haemoglobin concentrations

but still completed the study procedures. Two-thirds of participants were female (n=340, 65.0%). The demographics of the study cohort, stratified by sex, are presented in Table 1.

The median ferritin concentration in male participants was 136.17 µg/L (interquartile range [IQR]=89.89-219.83; Fig a); no male participants were diagnosed with ID. Among female participants diagnosed with ID (n=58/340, 17.1%), the median haemoglobin concentration was 11.6 g/dL (IQR=11.1-12.2; Fig b). Among female participants with normal serum ferritin concentrations (n=282/340, 82.9%), the median serum ferritin concentration was 56.07 µg/L (IQR=33.82-84.11; Fig c).

Attention outcomes

Overall, 249 participants (47.6%) exhibited normal function in all three attention domains. Approximately one-quarter of the participants demonstrated moderate-to-severe impairment in sustained attention (n=131/523, 25.0%), inattention (n=145/523, 27.7%), and impulsivity (n=157/523, 30.0%).

Among female participants with ID, the rates of moderate-to-severe impairment in sustained attention, inattention, and impulsivity were 36.2% (n=21/58), 27.6% (n=16/58), and 37.9% (n=22/58), respectively. The rates of moderate-to-severe impairment in inattention and impulsivity among female participants with IDA were numerically higher at 43.5% (n=10/23 for both domains). Among male participants, the rates of moderate-to-severe impairment in sustained attention, inattention, and impulsivity were 18.0% (n=33/183), 23.5% (n=43/183), and 22.4% (n=41/183), respectively (Table 2).

Association between iron reserves and attention outcomes in the overall cohort

In the overall cohort, participants with sustained attention impairment had significantly lower serum ferritin concentrations relative to those with intact attention function (median=51.2 µg/L, IQR=27.1-106.8 vs median=73.9 µg/L, IQR=37.8-138.0; P=0.020). Although the associations were not statistically significant, trends of lower serum ferritin concentrations were also observed in participants with impulsivity impairment (median=68.1 µg/L, IQR=29.0-114.8 vs median=73.9 µg/L, IQR=37.8-138.0; P=0.067) and inattention impairment (median=69.9 µg/L, IQR=32.0-110.8 vs median=73.9 µg/L, IQR=37.8-138.0; P=0.142) relative to those with intact attention function.

Pooled analysis of the overall cohort, adjusted for age and sex, showed a significant association between lower serum ferritin concentration and sustained attention impairment (RR=0.825, 95% CI=0.732-0.946; P=0.040), suggesting that each 10 µg/L increase in serum ferritin concentration was associated with a 17.6% decrease in the risk of sustained attention impairment. A higher level of fatigue was associated with impairment in sustained attention (RR=0.772, 95% CI=0.652-0.926; P=0.004), inattention (RR=0.824, 95% CI=0.733-0.942; P=0.016), and impulsivity (RR=0.792, 95% CI=0.683-0.922; P=0.004). Serum ferritin concentration was not significantly associated with risks of impairment in inattention or impulsivity (Table 3).

Association between iron reserves and attention outcomes stratified by sex

Female participants with sustained attention impairment had marginally lower serum ferritin

TABLE 1. Demographics and dietary characteristics of participants (n=523)*

	Female (n=340)		Male (n=183)
	Iron deficiency (n=58)	Normal serum ferritin levels (n=282)	
Age, y	17.77±1.19	17.57±1.03	17.47±1.02
16-16.9	17 (29.3%)	97 (34.4%)	69 (37.7%)
17-17.9	17 (29.3%)	102 (36.2%)	64 (35.0%)
18-18.9	13 (22.4%)	46 (16.3%)	27 (14.8%)
19-19.9	11 (19.0%)	37 (13.1%)	23 (12.6%)
Regular habit of skipping ≥1 meal	27 (46.6%)	111 (39.4%)	51 (27.9%)
Skip breakfast	21 (36.2%)	83 (29.4%)	45 (24.6%)
Skip lunch	6 (10.3%)	16 (5.7%)	7 (3.8%)
Skip dinner	6 (10.3%)	29 (10.3%)	6 (3.3%)
Dietary iron score†	94.67±16.58	97.64±15.73	99.00±16.44

* Data are shown as mean±standard deviation or No. (%)

† A composite measure based on the self-reported types and frequency of food intake. Each food type is ranked according to its general iron content per serving, as determined by the Department of Health. A higher score indicates greater dietary iron content

concentrations relative to those with intact attention function (median=40.0 $\mu\text{g/L}$, IQR=18.8-52.1 vs median=48.5 $\mu\text{g/L}$, IQR=21.8-73.8; $P=0.038$). Although the associations were not statistically significant, trends for lower serum ferritin concentrations were also observed in participants with impulsivity impairment (median=43.0 $\mu\text{g/L}$, 95% CI=19.5-63.2 vs median=48.5 $\mu\text{g/L}$, IQR=21.8-73.8; $P=0.071$) relative to those with intact attention function. No significant difference was observed for inattention impairment. Additionally, no significant association was detected between iron reserves and attention impairment in male participants.

Multivariable analysis revealed that the association between iron reserves and sustained attention impairment in female participants was attenuated and not statistically significant (RR=0.954, 95% CI=0.904-1.005; $P=0.073$). A higher level of fatigue was associated with an increased risk of sustained attention impairment (RR=0.793, 95% CI=0.652-0.964; $P=0.021$). Among male participants, iron reserves did not affect attention outcomes, but fatigue was associated with impulsivity impairment (RR=0.712, 95% CI=0.548-0.942; $P=0.018$). Dietary patterns were not significantly associated with attention outcomes in either male or female participants (Table 3).

Discussion

In the overall cohort, a lower serum ferritin concentration was associated with a higher risk of sustained attention impairment, consistent with previous reports that iron reserves play an essential role in functional performance in adolescents.^{6-8,21} When the analysis was stratified by sex, a similar but modest association between low iron reserves and sustained attention impairment was observed in female school-aged adolescents. This finding is supported by studies regarding the neurobiology of attention-related developmental disorders associated with ID.^{6,7,9,10} A meta-analysis of 10 studies, comprising 2191 healthy children and 1196 children with ADHD, showed that serum ferritin concentrations were 0.4-fold lower in children with ADHD than in those without developmental disorders.⁸ Iron deficiency may be associated with disruptions in monoamine synthesis and monoamine signal transduction, which manifest as attention deficits.^{10,22} Adequate iron intake and iron stores may, therefore, be important factors influencing the onset of attention problems in the developing brain. This finding should be prospectively validated in larger cohorts with a comprehensive assessment of cognitive domains beyond attention. However, from a developmental perspective, sustained attention is closely related to performance on targeted assessments, such as mathematical fluency and reading comprehension,

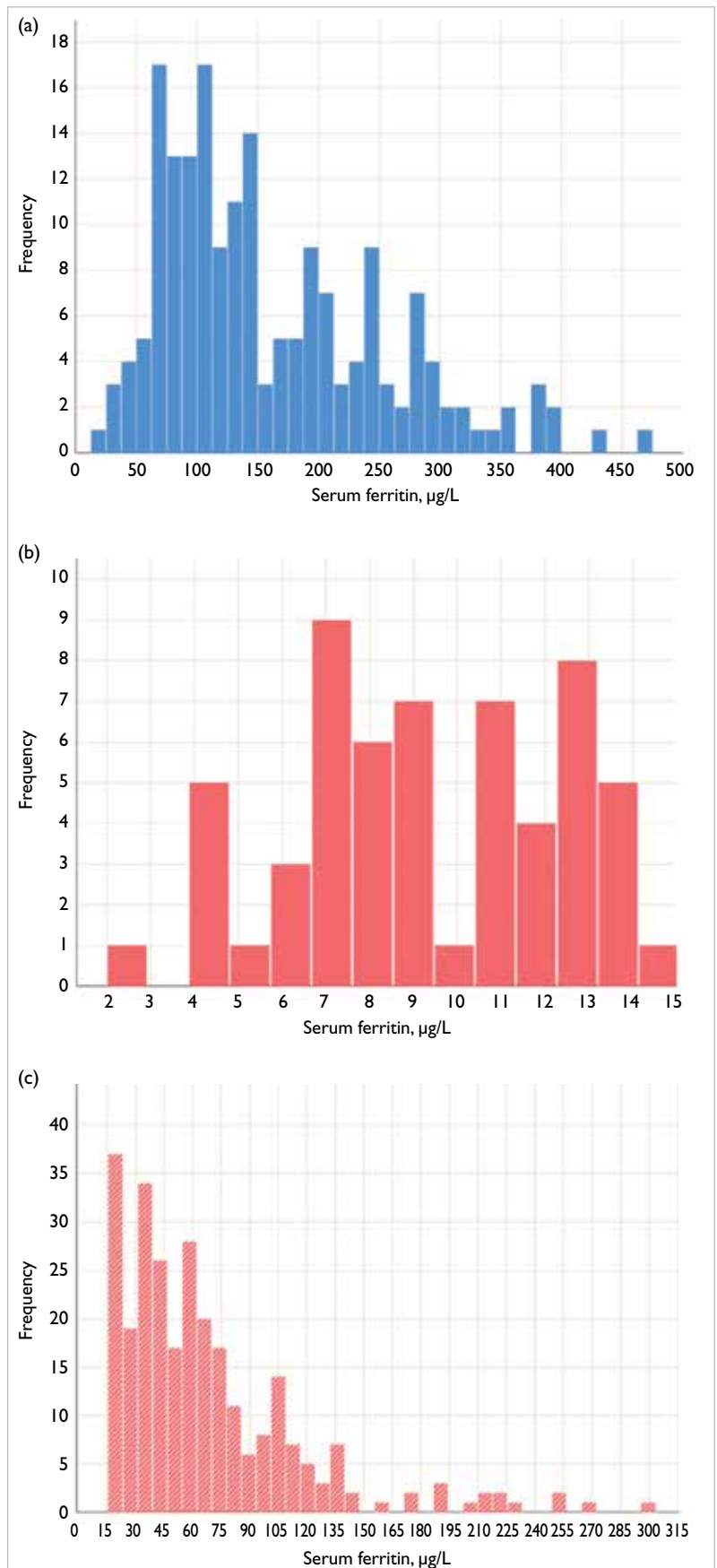


FIG. Distribution of serum ferritin level among participants stratified by sex. (a) Male participants. (b) Female participants diagnosed with iron deficiency. (c) Female participants with normal serum ferritin concentrations

TABLE 2. Attention outcomes stratified by sex and iron deficiency status*

	Female				Male All (n=183)
	All (n=340)	Normal serum ferritin levels (n=282)	Iron deficiency (n=58)	Iron deficiency anaemia (n=23)	
Normal	142 (41.8%)	122 (43.3%)	20 (34.5%)	8 (34.8%)	107 (58.5%)
Impairment					
Sustained attention					
Normal/mild	242 (71.2%)	205 (72.7%)	37 (63.8%)	17 (73.9%)	150 (82.0%)
Moderate	54 (15.9%)	40 (14.2%)	14 (24.1%)	5 (21.7%)	18 (9.8%)
Severe	44 (12.9%)	37 (13.1%)	7 (12.1%)	1 (4.3%)	15 (8.2%)
Inattention					
Normal/mild	238 (70.0%)	196 (69.5%)	42 (72.4%)	13 (56.5%)	140 (76.5%)
Moderate	79 (23.2%)	68 (24.1%)	11 (19.0%)	6 (26.1%)	30 (16.4%)
Severe	23 (6.8%)	18 (6.4%)	5 (8.6%)	4 (17.4%)	13 (7.1%)
Impulsivity					
Normal/mild	224 (65.9%)	188 (66.7%)	36 (62.1%)	13 (56.5%)	142 (77.6%)
Moderate	92 (27.1%)	74 (26.2%)	18 (31.0%)	9 (39.1%)	28 (15.3%)
Severe	24 (7.1%)	20 (7.1%)	4 (6.9%)	1 (4.3%)	13 (7.1%)

* Data are shown as No. (%)

TABLE 3. Factors associated with attention impairment stratified by sex and overall cohort

All participants* (n=523)	Sustained attention		Inattention		Impulsivity	
	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Serum ferritin (per 10 µg/L)	0.825 (0.732-0.946)	0.040	0.982 (0.946-1.010)	0.122	0.969 (0.948-1.010)	0.060
Fatigue†	0.772 (0.652-0.926)	0.004	0.824 (0.733-0.942)	0.016	0.792 (0.683-0.922)	0.004
Habit of skipping meals						
Yes	1.325 (0.851-2.069)	0.214	0.979 (0.620-1.539)	0.937	1.212 (0.788-1.872)	0.365
No	Ref		Ref		Ref	
Dietary iron score (per 10 points)‡	0.929 (0.804-1.057)	0.272	0.863 (0.773-1.012)	0.057	0.886 (0.791-1.010)	0.091
Female participants§ (n=340)	Sustained attention		Inattention		Impulsivity	
	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Serum ferritin (per 10 µg/L)	0.954 (0.904-1.005)	0.073	0.985 (0.944-1.032)	0.521	0.981 (0.942-1.033)	0.490
Fatigue†	0.793 (0.652-0.964)	0.021	0.839 (0.703-1.028)	0.110	0.864 (0.714-1.034)	0.103
Habit of skipping meals						
Yes	1.344 (0.792-2.293)	0.271	1.021 (0.579-1.772)	0.938	1.233 (0.728-2.082)	0.419
No	Ref		Ref		Ref	
Dietary iron score (per 10 points)‡	0.897 (0.751-1.067)	0.179	0.908 (0.773-1.058)	0.279	0.908 (0.774-1.066)	0.248
Male participants§ (n=183)	Sustained attention		Inattention		Impulsivity	
	RR (95% CI)	P value	RR (95% CI)	P value	RR (95% CI)	P value
Serum ferritin (per 10 µg/L)	0.991 (0.952-1.052)	0.969	1.001 (0.963-1.050)	0.828	1.010 (0.969-1.052)	0.623
Fatigue†	0.849 (0.608-1.214)	0.380	0.805 (0.612-1.052)	0.101	0.712 (0.548-0.942)	0.018
Habit of skipping meals						
Yes	1.00 (0.412-2.402)	0.991	0.808 (0.349-1.849)	0.622	0.916 (0.403-2.101)	0.846
No	Ref		Ref		Ref	
Dietary iron score (per 10 points)‡	1.072 (0.826-1.386)	0.642	0.854 (0.665-1.072)	0.173	0.892 (0.713-1.104)	0.279

Abbreviations: 95% CI = 95% confidence interval; RR = risk ratio

* Pooled analysis was adjusted for age and sex

† A lower score indicates more severe fatigue

‡ A lower score indicates lower dietary iron intake

§ Stratified analysis was adjusted for age

as well as broader academic measures in national standardised examinations.^{23,24} This relationship is particularly relevant because the Hong Kong educational system is well known for its examination-dominated culture. Most examinations range from 2 to 3 hours, requiring students to maintain a high level of sustained attention. Therefore, these findings may have long-term implications for students' academic success. Future research should investigate the effects of ID and IDA on subsequent academic achievement in Hong Kong adolescents.

Evidence regarding the effectiveness of iron supplementation in terms of improving neurocognitive function in children and adolescents has been inconclusive. Furthermore, iron supplements are associated with gastrointestinal symptoms and constipation, which contribute to non-adherence, particularly in adolescents.²⁵ A systematic review of 14 randomised controlled trials indicated that iron supplementation improved attention and intelligence quotient in anaemic older children and adults.²⁶ However, these effects were inconsistent across studies; they were influenced by socio-economic factors, participant age, and the clinical thresholds used to define ID and IDA.^{20,25,26} The benefits for cognitive development in older adolescents remain uncertain and warrant further investigation.²⁶

In this study, we found that students who reported higher levels of fatigue were more likely to have worse attention outcomes. We also previously reported that lower serum ferritin concentrations are associated with self-reported fatigue in adolescents.¹¹ Evidence supporting the role of iron supplementation in fatigue reduction is more consistent than its effects on cognitive function in young adults, particularly among non-anaemic menstruating women with low ferritin concentrations.^{21,27} Notably, iron supplementation has been associated with reductions in subjective measures of fatigue among non-anaemic iron-deficient adults.²¹ The present findings suggest that ID correction in adolescents could reduce fatigue levels, which may indirectly improve attention outcomes. Using a serum ferritin concentration threshold of 15 µg/L to diagnose clinical ID, some researchers have demonstrated that iron supplementation can improve fatigue and physical performance among individuals with serum ferritin concentrations at the lower end of the normal range (30–50 µg/L).²¹ Collectively, the known health risks of ID, including impaired physical growth, fatigue, and reduced fitness in adolescents, underscore the need to educate students about maintaining a balanced diet with adequate iron intake. Adolescents with low ferritin concentrations should receive counselling focused on the consumption of iron-rich foods and iron supplementation to alleviate fatigue, even in the

absence of documented anaemia.

Dietary patterns and self-reported intake of iron-rich foods were not directly associated with attention outcomes in the multivariate analysis, likely because neurocognitive function is a multifactorial and complex phenotype influenced by both nutritional and non-nutritional factors. Additionally, we did not use a comprehensive measure of dietary iron intake. However, we previously showed that skipping at least one meal per day or exhibiting low dietary iron intake was associated with lower iron reserves.¹¹ Iron deficiency prevention in adolescents requires effective management of knowledge gaps related to food nutrition, dieting, and body image. Collectively, these findings highlight the importance of developing nutrition education programmes to encourage proactive adoption of dietary and other nutrition-related behaviours that promote health and well-being.

Limitations

Despite the relatively large cohort of school-aged adolescents and the well-characterised haematological assessments, this study had several important limitations. First, the participation rate in the blood donation programme was affected by the coronavirus disease 2019 pandemic and school closures. This change in participation rate may have introduced sampling bias because students with worse health statuses may have been more likely to decline blood donation. Second, we only assessed attention measures in this study. It was not feasible to administer a full neurocognitive test battery, which typically requires >1 hour, in a school-based environment with limited time, space, and supervisory personnel. Future studies should include a more comprehensive evaluation of neurocognitive function. Finally, we did not evaluate factors potentially associated with the causes of anaemia and cognitive function, such as markers of socio-economic status, family functioning, living environment, and physical activity.^{28,29} Nevertheless, our findings regarding the association between iron status and attention outcomes provide valuable local population data and guidance for future iron supplementation initiatives.

Conclusion

Lower serum ferritin concentrations and self-reported fatigue were associated with an increased risk of sustained attention impairment among school-aged adolescents in Hong Kong. The potential health consequences of ID without anaemia, particularly its effects on physical well-being and school performance, should be effectively communicated to the Hong Kong population, especially to female adolescents. Dietary interventions should target

groups with risk factors for nutritional deficiencies. Future research should investigate the effects of iron reserves on neurocognitive function and academic outcomes in adolescents. There is also a need to evaluate the benefits of iron supplementation for individuals with low ferritin concentrations.

Author contributions

Concept or design: All authors.

Acquisition of data: CK Lee, WC Tsoi, CW Lau, JNS Leung, STY Tsang, CLP Wong, YYL Chu, CK Li.

Analysis of data: YT Cheung, DFY Chan.

Interpretation of data: All authors.

Drafting of the manuscript: YT Cheung.

Critical revision of the manuscript for important intellectual content: All authors.

All authors had full access to the data, contributed to the study, approved the final version for publication, and take responsibility for its accuracy and integrity.

Conflicts of interest

All authors have disclosed no conflicts of interest.

Acknowledgement

The authors thank the principals and staff of the participating schools, as well as Mr Calvin Lam from Department of Paediatrics of The Chinese University of Hong Kong for assistance with data collection.

Declaration

Part of the results was presented at the Joint Annual Scientific Meeting 2022 (hybrid meeting) of The Hong Kong Paediatric Society, Hong Kong College of Paediatricians, Hong Kong Paediatric Nurses Association, and Hong Kong College of Paediatric Nursing in Hong Kong on 26 September 2022.

Funding/support

This research was funded by the Health and Medical Research Fund, the former Food and Health Bureau, Hong Kong SAR Government (Ref No.: 17180441). The funder had no role in study design, data collection, analysis, interpretation, or manuscript preparation.

Ethics approval

This research was approved by the Joint Chinese University of Hong Kong—New Territories East Cluster Clinical Research Ethics Committee, Hong Kong (Ref No.: 2019.107). Participants aged ≥ 18 years provided written informed consent, whereas those aged < 18 years provided written assent along with informed consent from a parent or legal guardian.

Supplementary material

The supplementary material was provided by the authors and some information may not have been peer reviewed. Accepted supplementary material will be published as submitted by the authors, without any editing or formatting. Any opinions or recommendations discussed are solely those of the author(s) and are not endorsed by the Hong Kong Academy of Medicine and the Hong Kong Medical Association. The Hong Kong Academy of Medicine and the Hong Kong

Medical Association disclaim all liability and responsibility arising from any reliance placed on the content. To view the file, please visit the journal online (<https://doi.org/10.12809/hkmj2310950>).

References

1. Powers JM, O'Brien S, Berlan ED, Hoppin AG, editors. Iron requirements and iron deficiency in adolescents. UpToDate. Available from: <https://www.uptodate.com/contents/iron-requirements-and-iron-deficiency-in-adolescents>. Accessed 1 Apr 2025.
2. Camaschella C, Girelli D. The changing landscape of iron deficiency. *Mol Aspects Med* 2020;75:100861.
3. Safiri S, Kolahi AA, Noori M, et al. Burden of anemia and its underlying causes in 204 countries and territories, 1990-2019: results from the Global Burden of Disease Study 2019. *J Hematol Oncol* 2021;14:185.
4. Institute for Health Metrics and Evaluation, University of Washington. GBD results. 2020. Available from: <https://vizhub.healthdata.org/gbd-results/>. Accessed 6 May 2023.
5. Hare D, Ayton S, Bush A, Lei P. A delicate balance: iron metabolism and diseases of the brain. *Front Aging Neurosci* 2013;5:34.
6. Jáuregui-Lobera I. Iron deficiency and cognitive functions. *Neuropsychiatr Dis Treat* 2014;10:2087-95.
7. Pivina L, Semenova Y, Doşa MD, Dauletyarova M, Bjørklund G. Iron deficiency, cognitive functions, and neurobehavioral disorders in children. *J Mol Neurosci* 2019;68:1-10.
8. Wang Y, Huang L, Zhang L, Qu Y, Mu D. Iron status in attention-deficit/hyperactivity disorder: a systematic review and meta-analysis. *PLoS One* 2017;12:e0169145.
9. Bener A, Kamal M, Bener H, Bhugra D. Higher prevalence of iron deficiency as strong predictor of attention deficit hyperactivity disorder in children. *Ann Med Health Sci Res* 2014;4(Suppl 3):S291-7.
10. Tseng PT, Cheng YS, Yen CF, et al. Peripheral iron levels in children with attention-deficit hyperactivity disorder: a systematic review and meta-analysis. *Sci Rep* 2018;8:788.
11. Cheung YT, Chan DF, Lee CK, et al. Iron deficiency among school-aged adolescents in Hong Kong: prevalence, predictors, and effects on health-related quality of life. *Int J Environ Res Public Health* 2023;20:2578.
12. World Health Organization. WHO guideline on use of ferritin concentrations to assess iron status in individuals and populations. 2020. Available from: <https://apps.who.int/iris/handle/10665/331505>. Accessed 6 Oct 2023.
13. World Health Organization. Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. 2011 May 31. Available from: <https://www.who.int/publications/i/item/WHO-NMH-NHD-MNM-11.1>. Accessed 6 Oct 2023.
14. Conners CK, Sitarenios G. Conners' Continuous Performance Test (CPT). In: Kreutzer JS, DeLuca J, Caplan B, editors. *Encyclopedia of Clinical Neuropsychology*. New York: Springer; 2011: 681-3.
15. Sulheim D, Fagermoen E, Sivertsen ØS, Winger A, Wyller VB, Øie MG. Cognitive dysfunction in adolescents with chronic fatigue: a cross-sectional study. *Arch Dis Child* 2015;100:838-44.
16. Varni JW, Limbers CA. The PedsQL Multidimensional Fatigue Scale in young adults: feasibility, reliability and validity in a university student population. *Qual Life Res*

- 2008;17:105-14.
17. Yeung NC, Lau JT, Yu X, et al. Psychometric properties of the Chinese version of the Pediatric Quality of Life Inventory 4.0 Generic Core Scales among pediatric cancer patients. *Cancer Nurs* 2013;36:463-73.
18. Hao Y, Tian Q, Lu Y, Chai Y, Rao S. Psychometric properties of the Chinese version of the Pediatric Quality of Life Inventory 4.0 Generic Core Scales. *Qual Life Res* 2010;19:1229-33.
19. Camaschella C. Iron deficiency. *Blood* 2019;133:30-9.
20. Hermoso M, Vucic V, Vollhardt C, et al. The effect of iron on cognitive development and function in infants, children and adolescents: a systematic review. *Ann Nutr Metab* 2011;59:154-65.
21. Houston BL, Hurrie D, Graham J, et al. Efficacy of iron supplementation on fatigue and physical capacity in non-anaemic iron-deficient adults: a systematic review of randomised controlled trials. *BMJ Open* 2018;8:e019240.
22. Kim J, Wessling-Resnick M. Iron and mechanisms of emotional behavior. *J Nutr Biochem* 2014;25:1101-7.
23. Gallen CL, Schaerlaeken S, Younger JW; Project iLEAD Consortium; Anguera JA, Gazzaley A. Contribution of sustained attention abilities to real-world academic skills in children. *Sci Rep* 2023;13:2673.
24. Schmengler H, Peeters M, Stevens GW, et al. Educational level, attention problems, and externalizing behaviour in adolescence and early adulthood: the role of social causation and health-related selection—the TRAILS study. *Eur Child Adolesc Psychiatry* 2023;32:809-24.
25. Finkelstein JL, Herman HS, Guetterman HM, Peña-Rosas JP, Mehta S. Daily iron supplementation for prevention or treatment of iron deficiency anaemia in infants, children, and adolescents. *Cochrane Database Syst Rev* 2018;2018:CD013227.
26. Falkingham M, Abdelhamid A, Curtis P, Fairweather-Tait S, Dye L, Hooper L. The effects of oral iron supplementation on cognition in older children and adults: a systematic review and meta-analysis. *Nutr J* 2010;9:4.
27. Vaucher P, Druais PL, Waldvogel S, Favrat B. Effect of iron supplementation on fatigue in nonanemic menstruating women with low ferritin: a randomized controlled trial. *CMAJ* 2012;184:1247-54.
28. Hess SY, Owais A, Jefferds ME, Young ME, Cahill A, Rogers LM. Accelerating action to reduce anemia: review of causes and risk factors and related data needs. *Ann N Y Acad Sci* 2023;1523:11-23.
29. Meredith WJ, Cardenas-Iniguez C, Berman MG, Rosenberg MD. Effects of the physical and social environment on youth cognitive performance. *Dev Psychobiol* 2022;64:e22258.