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ORIGINAL ARTICLE

Trends in ferritin measurements in children and adolescents: A Finnish 9-year observational study

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Abstract

Aim: A lack of stored iron, indicated by low serum ferritin, has been associated with various clinical symptoms. There are no longitudinal data on the frequency of ferritin measurements in children and adolescents.

Methods: A total of 2834 children aged <18 years with serum ferritin and other anaemia-related blood parameters taken during an outpatient visit between 2012 and 2019 were investigated. Patients with acute infections were excluded. Nationwide temporal and regional variations and correlations with public information searches through Google were analysed.

Results: A significant increase in the frequency of ferritin measurements was seen starting in 2018, with a 47-fold rise in 2019 compared to 2012. A simultaneous escalation in Google Search activity was seen. Deficiency of stored iron was relatively common: 21.6% of children with normal haemoglobin and 14.9% of non-anaemic children with normal red cell indices exhibited ferritin levels below 15 μg/L.

Conclusion: Ferritin measurement has increased greatly among children and adolescents. Our results suggest that public interest and popular trends can significantly influence health care practices. This calls for further investigation into the causes and consequences of such a phenomenon. Prospective randomised intervention studies are needed to evaluate the utility of iron supplementation in patients with low iron storage levels.

KEYWORDS
anaemia, health seeking, iron deficiency, public health, serum ferritin, social media, trends

1 | INTRODUCTION

Ferritin is an iron-binding protein that plays a central role in iron homeostasis.[1] The primary role of ferritin is to convert Fe(II) to Fe(III) and to sequester it into the ferritin core.[2] Ferritin protects the body from iron-related free radicals by capturing and buffering the intracellular iron pool. Expression of ferritin is regulated by iron-responsive elements such that higher intracellular iron concentrations increase, while iron deficiency (ID) decreases, its expression.[3] The measurable ferritin in the serum is largely derived from macrophages, and low

Abbreviations: CBC, Complete blood count; CI, confidence interval; CRP, C-reactive protein; Hb, haemoglobin; HER, electronic health records; ID, iron deficiency; IDA, iron-deficiency anaemia; MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; ROC, receiver operating characteristics; SF, Serum ferritin.

serum ferritin (SF) concentrations reflect to some extent the degree of iron depletion in the body.[4,5] In mild forms, ID can be inconspicuous, but as the body becomes more deficient in iron, the signs of anaemia escalate, with significant clinical consequences.[6] Ferritin is also an acute-phase protein, and serum concentrations are increased in inflammatory processes.[7] In addition, cellular damage from various causes will result in ferritin leaking into blood plasma.

Over the past few years, there has been increasing interest among laypeople in the association between low ferritin levels and various clinical symptoms. This has been supported by recent studies in adults and children that have found an association between low ferritin levels and symptoms such as fatigue, restlessness, behavioural issues and cognitive disorders, and symptoms have been, to some extent, alleviated by iron supplementation.[8–15] This has gained notable public interest and has increased the demand for measuring ferritin. It has also spurred the initiation of iron supplementation. Our aim was to investigate temporal trends and regional variations in ferritin measurements and to evaluate correlations between the ferritin, haemoglobin and red cell indices.

Key Notes

- Public interest in ferritin as a biological indicator or mediator of various symptoms has increased recently; however, its accuracy for detecting iron deficiency is still not well established.
- A 47-fold increase in the ferritin measurement coincided with an increase in Google search activity, suggesting that public interest and popular trends can significantly influence health care practices.
- 21.6% of children with normal haemoglobin exhibited ferritin levels below 15 μg/L.

2 | METHODS

This is a nationwide retrospective study based on electronic health records (EHR) in a private outpatient clinical setting. Finland provides comprehensive, high-quality health services for children, including child health clinics and school health care. The primary health care includes municipal (public) health care centres where children are mostly treated by general practitioners. Approximately, 47% of children are covered by private insurance policies. For primary care, parents can also choose from a range of private health care services such as Terveystalo Healthcare. Terveystalo offers primary and secondary health care services to corporate and private customers, as well as the public sector. The network includes more than 300 clinics across Finland that serve approximately 1.2 million individuals, with 3.7 million annual visits to physicians. This constitutes 15% of outpatient visits in Finland. All diagnoses, clinical information, laboratory results and drug prescription data were recorded online in a centralised EHR system.

All children below 18 years of age who underwent ferritin measurements during a doctor's appointment between 2012 and 2019 were identified using the EHR. Red cell parameters (haemoglobin, mean corpuscular volume MCV and mean corpuscular haemoglobin MCH), C-reactive protein (CRP), age, sex and place of residence were also recorded. Patients with an acute infection (CRP ≥10 mg/L) were excluded from the analysis. Ferritin values were analysed separately by age group, sex and region of the outpatient clinic. If several test results for ferritin were recorded for an individual patient, only the first value was included, as it was presumed to represent the situation before the interventions.

Ferritin and complete blood count (CBC) were analysed in Synlab's core clinical laboratory using standard protocols. Ferritin levels were measured using an immunoassay instrument (ADVIA Centaur® XP, Siemens Healthcare Diagnostics), while CBC analysis was performed using the Sysmex XE-2100 automated blood cell counter instrument (Sysmex). For clinical interpretation, Synlab's age-adjusted reference values were used for Hb, MCH and MCV (Table S1). Cut-offs of 10 and 15 μg/L for ferritin were chosen based on previously published literature.[16–18]

2.1 | Statistical analysis

Standard descriptive statistics were used to characterise the study cohort. The Mann–Whitney U-test was used to test for differences regarding time period. Openly available Google Trends data for the search terms 'Ferritiini (protein)' in Finnish and 'Ferritin (protein)' in English (downloaded on 7 Jan 2021) were used to explore regional public interest in ferritin (Google, 2021). Line plots were used to visualise differences in ferritin measurements by age group, sex and region, and they were adjusted for the total number of visits. Scatter plots with Pearson's correlation coefficients between ferritin and Hb, MCV and MCH were plotted. Receiver operating characteristic (ROC) curves were plotted for Hb, MCV and MCH to test for optimal points of sensitivity and specificity for low ferritin. Linear regression models were fitted for log10-transformed ferritin using Hb, MCV, MCH, CRP, age groups and sex as explanatory variables. Both univariate and multivariate models were reported considering multicollinearity. Statistical analyses were carried out using R (version 4.0.2). All tests were two-tailed, and *p*-values below 0.05 were considered statistically significant.

2.2 | Ethical considerations

This study was carried out in accordance with national regulations and was approved by the chief medical officer of Terveystalo. According to Finnish law, approval from the ethics committee was not required. All data were de-identified, and patients were not contacted. Hence, according to Finnish law, informed consent was not needed from the subjects and/or their legal guardians.

3 | RESULTS

3.1 | Significant increase in ferritin measurements over time

A total of 2834 children and adolescents had at least one available ferritin measurement during a visit to a physician at Terveystalo Healthcare between 2012 and 2019 (Figure 1). The overall frequency of ferritin measurements was low from 2012 to 2018 but increased dramatically towards the end of the follow-up period; the visit-adjusted frequency was 47-fold higher in 2019 compared to 2012 and sixfold higher compared to 2017 (Figure 2A). Measurements increased over time in all age groups, including infants, and were slightly more frequent in females (Figure 2B,C). Marked regional differences were noted: South Ostrobothnia had an approximately two-fold higher measurement frequency compared with the Pirkanmaa region (Figure 2D and Figure S1). We also investigated whether the public interest in ferritin changed over time by analysing the use of the search term 'ferritiini' or 'ferritin (protein)' in the Google Trends database. As shown in Figure 2A, the Google Trends plot faithfully followed the actual ferritin measurements and showed a steep increase from 2018 onwards (Figure 3). An increasing Google trend can be observed in many other countries (Figure S3).

3.2 | Levels of ferritin in children and adolescents

The median ferritin concentration was 24.4 (IQR 15.3–38.1), with males having higher median levels compared with females (27.9 vs. 22.5, $p < 0.001$) (Table 1). Children 1–5 years old had a lower median ferritin level compared with older age groups ($p < 0.001$) (Table 1, Table 2 and Figure S2). The median ferritin value increased slightly from the period before 2018 to the period after 2018 (23.4 vs. 24.7, $p = 0.04$), and the rise was more notable in females (20.8 vs. 22.9, $p = 0.004$). Out of all ferritin measurements, 24% were below 15 μg/L and 12% were below 10 μg/L. The multivariate model reached a moderate r^2 of 32% (Table 2).

The proportion of anaemia decreased by two-thirds between the two time periods: 12.2% (66/539) of patients with ferritin measurement were anaemic from 2012 to 2017, while only 4.2% (66/1570) had low Hb during 2018 and 2019 ($p < 0.001$). On the contrary, 21.6% of subjects with normal Hb ($n = 1978$) had ferritin levels below 15 μg/L, and 14.9% of subjects with normal Hb and other parameters of anaemia (MCV and MCH) ($n = 1734$) had low ferritin levels (Figure 4).

3.3 | Correlation of ferritin values to parameters of anaemia

We evaluated the correlation of ferritin levels with the parameters of anaemia; only weak-to-moderate correlations with age-adjusted Hb, MCV and MCH values were noted (see Figure 5 and Table S1 for reference values). Likewise, the ROC curves for ferritin values below 15 μg/L showed modest performance: AUC for Hb was 72.7% (95% CI 70.2%–75.3%); for MCV, it was 66.9% (95% CI 64.1%–69.8%); and for MCH, it was 72.6% (95% CI 69.9%–75.3%) (Figure 5).

4 | DISCUSSION

Public interest in ferritin as a biological indicator or mediator of various symptoms has increased recently. We utilised nationwide outpatient clinic data to evaluate trends in ferritin measurements in children and adolescents and found a 47-fold increase in the ferritin measurement rate during the study period, coinciding with an increase in Google Search activity. Marked regional differences in ferritin measurements were observed. In addition, 21.6% of children with normal Hb and 14.9% of non-anaemic children with normal red cell indices had ferritin levels below 15 μg/L.

The level of SF in a steady-state condition correlates with stores of iron; thus, ferritin measurement can be a convenient laboratory test for estimating iron stores in the body.[2,19] When anaemia is suspected, SF is often evaluated along with red cell parameters, such as haemoglobin, MCV and MCH. Bone marrow sampling, the gold standard for measuring stored iron, is generally not attainable for practical and ethical reasons. Hence, the lower reference limit for SF is typically based on the diagnosis of anaemia rather than verified iron deficiency and varies considerably, from 5 to 30 μg/L.[16–18,20–22] The commonly reported threshold of 15 μg/L is likely to be specific,

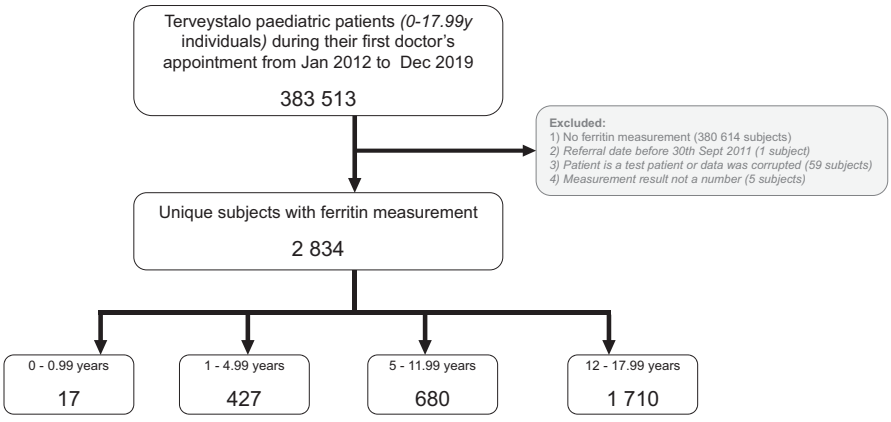

FIGURE 1 Flow chart of the exclusions and the final study cohort. The depicted cohort was used primarily when analysing trends (Figure 2) and represents the upper limit of the sample size in our study. In the ROC curves, scatter plots and regression analyses, the subjects were required to have studied all laboratory measurements available (Hb, MCV, MCH and CRP) as well, resulting in slightly (<10%) smaller sample sizes

but may miss non-anaemic cases with iron deficiency. In our data set, 14.9% of the non-anaemic patients with normal red cell indices had ferritin levels below that threshold. These represent cases

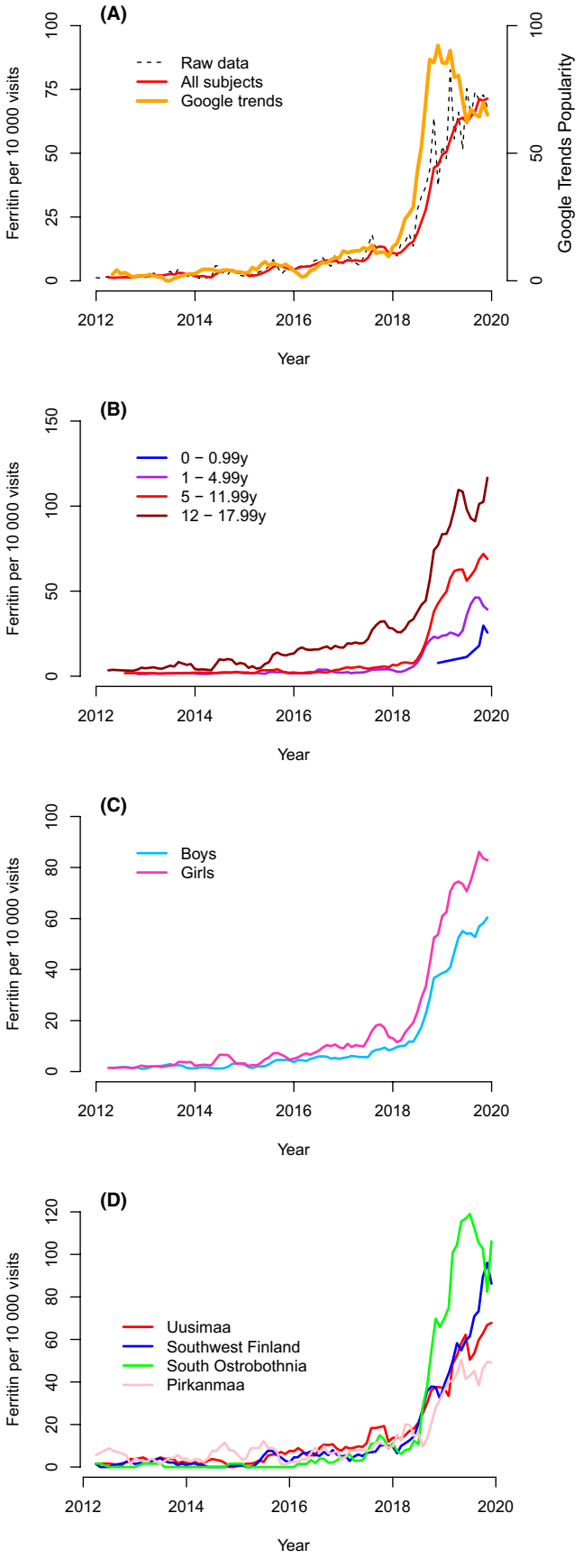

FIGURE 2 Visit-adjusted line plots of serum ferritin measurements in Finland. (A) Smoothed (moving average, 3 mo) numbers of serum ferritin measurements for the full cohort (red) with overlaid smoothed (moving average, 3 mo) Google Trends interest (yellow). The crude number of measurements with higher variance is shown with a black dashed line. (B) Smoothed (moving average, 3 mo) number of serum ferritin measurements for different age groups. (C) Smoothed (moving average, 3 mo) number of serum ferritin measurements for both sexes. (D) Smoothed (moving average, 3 mo) number of serum ferritin measurements for three large Finnish regions (Uusimaa, Southwest Finland, Pirkanmaa) and one smaller region with a higher measurement rate (South Ostrobothnia)

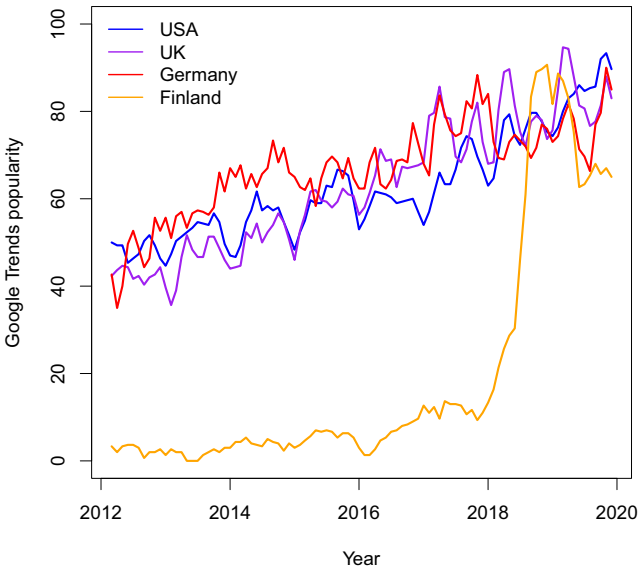

FIGURE 3 Google Trends popularity for the term 'ferritin' and 'ferritiini' in the USA, UK, Germany and Finland. The line plots were smoothed using a 3-month moving average

that have decreased stored iron reserves, yet have sufficient erythropoiesis, but are at increased risk for developing iron-deficiency anaemia (IDA) without interventions. The critical questions here are whether a low ferritin level independently associates with the patients' symptoms and whether it could be relieved by iron supplementation. We did not have the data available regarding the reasons for seeking a doctor's appointment, which would have been relevant to understanding the potential association between low ferritin levels and their symptoms. In the future, non-anaemic children with low ferritin and various symptoms should be further investigated in a randomised study that incorporates interventions with oral iron supplementation.

The major finding was a dramatic increase in the frequency of ferritin measurements towards the end of the study period. This coincided with a decrease in the proportion of low age-adjusted Hb values, suggesting that the increase was due to increased public interest and awareness through, for example, social media. This notion was supported by the simultaneous activity in Google searches. Our study setting did not allow for the evaluation of the necessity and utility of ferritin measurements in the study population, but the proportional decrease in anaemia findings suggests that the reasons

TABLE 1 Median ferritin concentration by age group and sex

	TOTAL		1/2012–12/2017		1/2018–12/2019		
	Median (IQR)	N	Median (IQR)	N	Median (IQR)	N	p-Value
Total	24.4 (15.3, 38.1)	2834	23.4 (13.0, 39.3)	692	24.7 (15.7, 37.8)	2142	0.04*
Age groups (years)							
0 - <1	32.9 (20.2, 46.4)	17	37.8 (33.4, 42.1)	2	32.9 (19.0, 46.4)	15	0.72
1 - <5	18.6 (12.3, 28.3)	427	15.0 (9.2, 25.8)	72	19.3 (12.7, 28.4)	355	0.006*
5 - <12	25.4 (17.7, 36.0)	680	24.0 (14.2, 37.0)	89	25.4 (17.9, 35.9)	591	0.481
12 - <18	26.1 (15.3, 42.4)	1710	24.6 (13.6, 42.0)	529	26.7 (15.7, 42.4)	1181	0.04*
Sex							
Male	27.9 (17.7, 43.3)	1183	29.4 (16.2, 45.5)	275	27.8 (17.8, 42.3)	908	0.69
Female	22.5 (13.4, 34.2)	1651	20.8 (11.0, 32.1)	417	22.9 (14.2, 34.6)	1234	0.004*

Note: *p*-values for the difference in ferritin levels between the two different time intervals were calculated using Mann–Whitney U-test. Statistically significant values ($p < 0.05$) were marked with an asterisk (*). No correction for multiple testing was used.

Abbreviation: IQR, interquartile range.

TABLE 2 Multivariate and univariate log-linear regression modelling of the serum ferritin (log_{10}) concentration

	Multivariate			Univariate		
	Coeff	95% CI	p	Coeff	95% CI	p
Hb (g/l)	0.008	0.006 0.011	<0.001	0.012	0.011, 0.013	<0.001
MCV (fl)				0.021	0.019, 0.024	<0.001
MCH (pg)	0.048	0.034 0.061	<0.001	0.065	0.059, 0.070	<0.001
CRP (mg/l)	0.010	0.006 0.013	<0.001	0.005	0.001, 0.010	0.007
Age groups (years)						
0 - <1	0[a]			0[a]		
1 - <5	−0.250	−0.488 -0.013	0.04	−0.341	−0.519, −0.164	<0.001
5 - <12	−0.281	−0.517 -0.045	0.02	−0.204	−0.380, −0.027	0.023
12 - <18	−0.406	−0.639 -0.172	<0.001	−0.215	−0.389, −0.040	0.016
Sex						
Male	0[a]			0[a]		
Female	−0.033	−0.082 0.017	0.20	−0.092	−0.121, −0.064	<0.001

Note: The ferritin concentration was $\log_{10}$-transformed for normality and better fit. Hb, MCV, MCH and CRP were treated as continuous variables. Age groups and sex were treated as categorical variables. MCV was excluded from the multivariate model due to multicollinearity. The multivariate model reached a moderate r^2 of 32%. For the categorical variables, the reference categories were marked with [a].

for sampling were not entirely based on the current official recommendations. Results from adult studies have suggested that various symptoms may be alleviated by supplemental iron,[8,10] but sound data are lacking in the underage population. However, the notion of the possible unfavourable effect of ID and the supposed beneficial effects of iron supplementation may have contributed to the increased interest in measuring ferritin in children. This carries the risk of excessive or inappropriate utilisation of health care resources.

There was also marked regional variation in the rate of SF measurements. The reasons for this are not known but may be related to differences in the proportion of physicians' specialities, doctor's habits, activity of regional lay influencers or general attitudes towards health-related issues. There were more SF measurements in females throughout the study period, although only 47.5% of all physician visits were for females. This may be related to the expected more common occurrence of IDA in teen females.[23]

Our study has several strengths. It comes from an outpatient setting and represents the general population better than the respective hospital data. We excluded cases with acute infections by using CRP as a surrogate marker of infection. The study population came from the whole country, and laboratory tests were carried out in a single centralised laboratory. Our study also has limitations. The data are retrospective and may not be generalisable to the whole population of Finland or to other populations outside of Finland. We

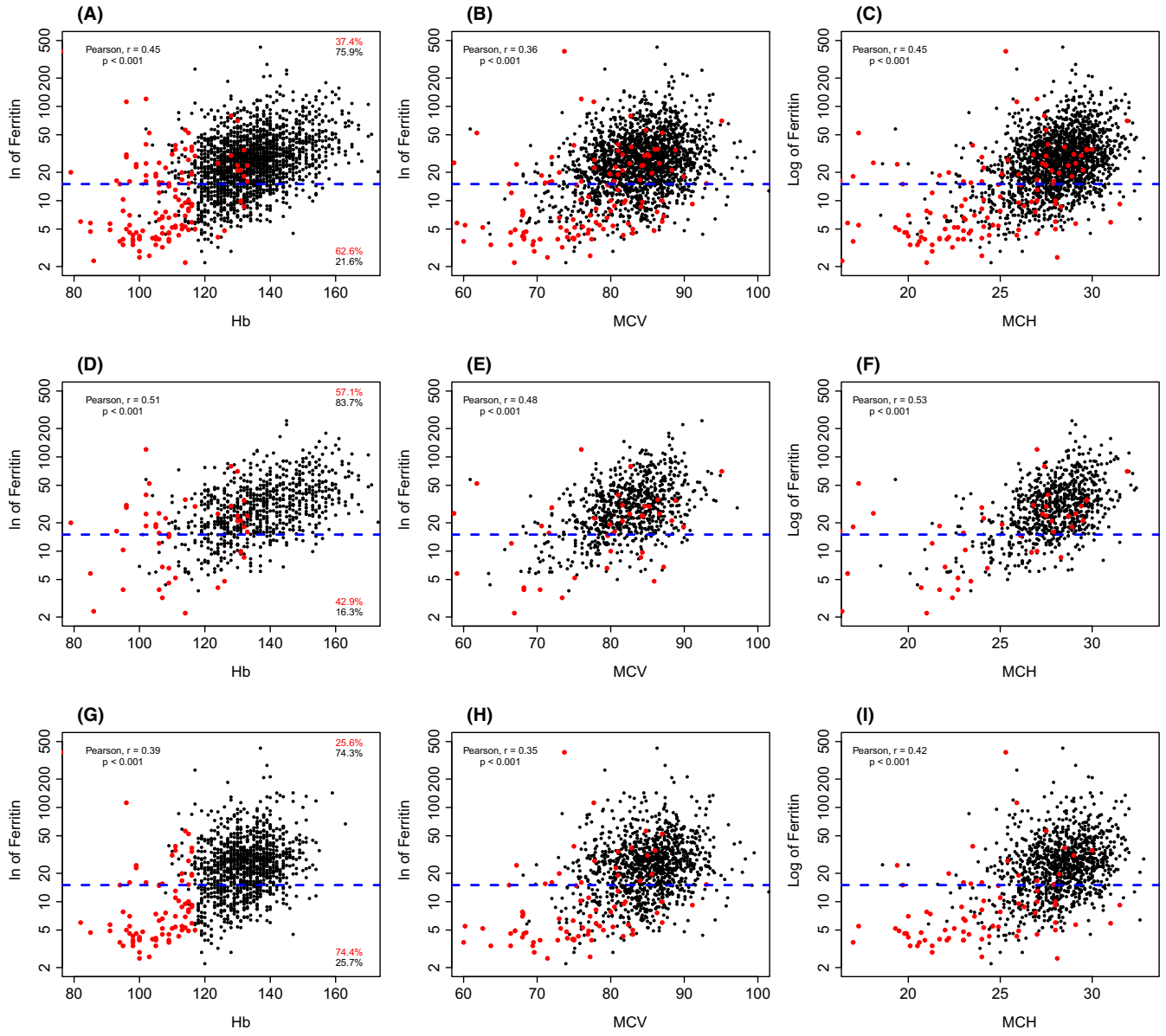

FIGURE 4 Scatter plots of the natural logarithm of serum ferritin against Hb, MCV and MCH for all subjects, males and females. Panels (A–C) are for all subjects; panels (D–F) are for males and G, H and I are for females. The red points show the subjects with anaemia in all panels. The percentages in the upper and lower right-hand corners of the first (Hb) panel represent the distribution of low ferritin (<15 μg/L) among subjects with or without anaemia. The red percentage is for subjects with anaemia, and the black percentage is for those without. The horizontal dashed blue line in all panels represents a serum ferritin value of 15 μg/L. The Pearson correlation coefficients with respective *p*-values are reported in the upper right corners for all panels

did not have data on the symptoms and on whether the patients were already receiving iron supplementation during the first sampling of ferritin. Moreover, the data come from the private sector and may not fully represent the whole population.

To conclude, the popularity of ferritin measurement has recently increased dramatically among children and adolescents. The reasons for this increase are not clear, but may be strongly driven by public interest and social media activity. This calls for further investigation into the causes and consequences of such a phenomenon. Nonetheless, children and adolescents with low ferritin and normal red cell parameters and haemoglobin sought a doctor's appointment due to various symptoms and may represent a poorly recognised group of patients with a medical need that warrants further investigation.

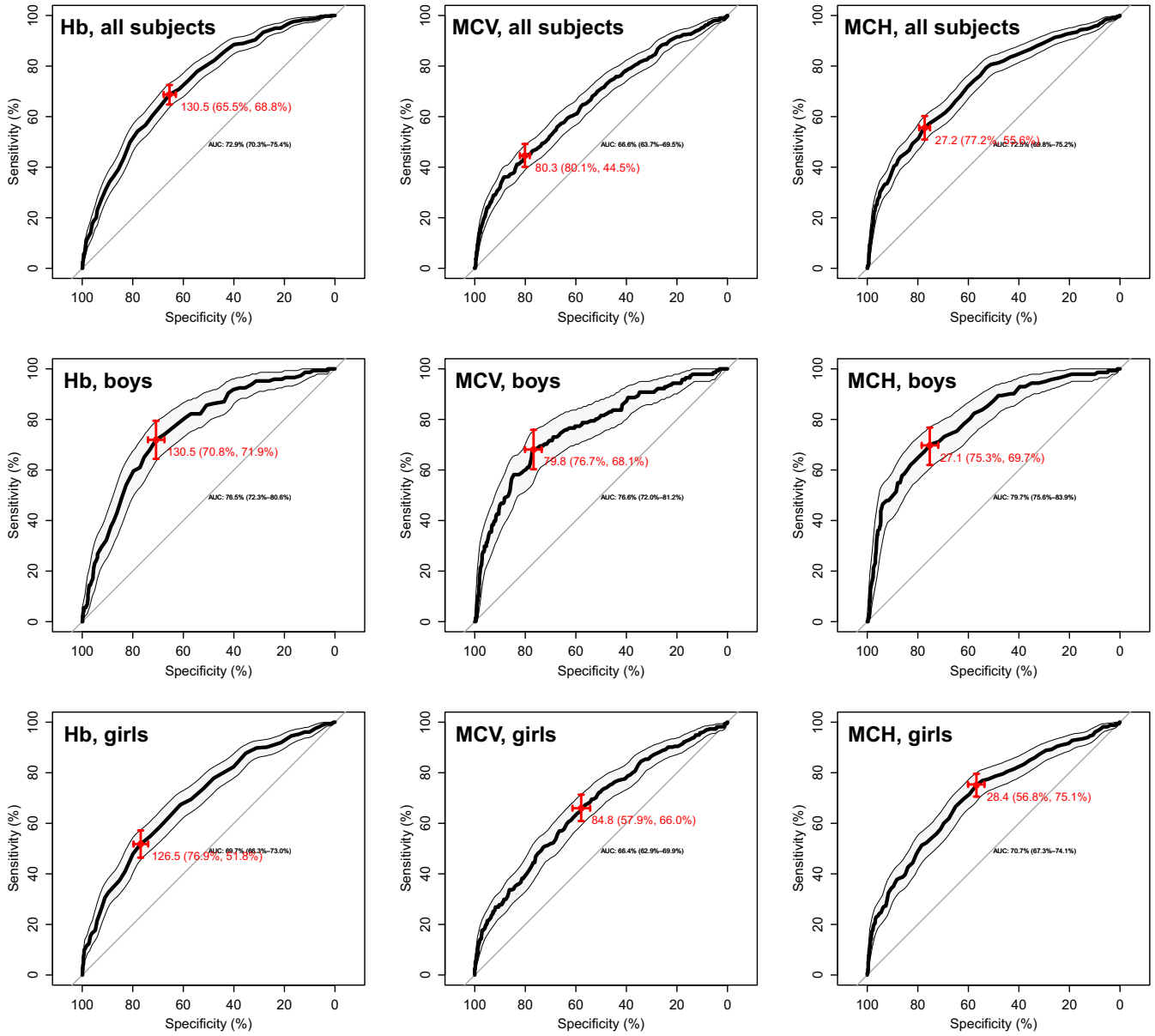

FIGURE 5 ROC curves of low (<15 μg/L) serum ferritin levels for Hb, MCV and MCH for all subjects, males and females. The algorithm-suggested optimal thresholds with respective sensitivities and specificities are reported alongside the AUC value with its 95% confidence intervals. The curves were plotted using the R library pROC

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CONFLICT OF INTEREST

The authors have no conflicts of interest relevant to this article to disclose.

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REFERENCES

1. Torti FM, Torti SV. Regulation of ferritin genes and protein. Blood. 2002;99(10):3505-3516. doi:10.1182/blood.V99.10.3505
2. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood Rev. 2009;23(3):95-104. doi:10.1016/j.blre.2008.08.001
3. Muckenthaler MU, Galy B, Hentze MW. Systemic iron homeostasis and the Iron-Responsive Element/Iron-Regulatory Protein (IRE/IRP) regulatory network. Annu Rev Nutr. 2008;28(1):197-213. doi:10.1146/annurev.nutr.28.061807.155521
4. Cohen LA, Gutierrez L, Weiss A, et al. Serum ferritin is derived primarily from macrophages through a nonclassical secretory pathway. Blood. 2010;116(9):1574-1584. doi:10.1182/blood-2009-11-253815

5. Garcia-Casal MN, Pasricha SR, Martinez RX, Lopez-Perez L, Peña-Rosas JP. Serum or plasma ferritin concentration as an index of iron deficiency and overload. Cochrane Database Syst Rev. 2021;50(5):CD011817. doi:10.1002/14651858.CD011817.pub2
6. Cappellini MD, Musallam KM, Taher AT. Iron deficiency anaemia revisited. J Intern Med. 2020;287(2):153-170. doi:10.1111/joim.13004
7. Elin R, Wolff S, Finch C. Effect of induced fever on serum iron and ferritin concentrations in man. Blood. 1977;49(1):147-153. doi:10.1182/blood.V49.1.147.147
8. 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(4):e019240. doi:10.1136/bmjopen-2017-019240
9. Tilma J, Tilma K, Norregaard O, Ostergaard JR. Early childhood-onset restless legs syndrome: symptoms and effect of oral iron treatment. Acta Paediatr. 2013;102(5):221-226. doi:10.1111/apa.12173
10. 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(11):1247-1254. doi:10.1503/cmaj.110950
11. Grim K, Lee B, Sung AY, Kotagal S. Treatment of childhood-onset restless legs syndrome and periodic limb movement disorder using intravenous iron sucrose. Sleep Med. 2013;14(11):1100-1104. doi:10.1016/j.sleep.2013.06.006
12. Shafir T, Angulo-Barroso R, Jing Y, Angelilli ML, Jacobson SW, Lozoff B. Iron deficiency and infant motor development. Early Hum Dev. 2008;84(7):479-485. doi:10.1016/j.earlhumdev.2007.12.009
13. Dosman C, Witmans M, Zwaigenbaum L. Iron's role in paediatric restless legs syndrome – A review. Paediatr Child Health. 2012;17(4):193-197. doi:10.1093/pch/17.4.193
14. 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):1-10. doi:10.1007/s12031-019-01276-1
15. Lozoff B, Smith JB, Kaciroti N, Clark KM, Guevara S, Jimenez E. Functional significance of early-life iron deficiency: outcomes at 25 years. J Pediatr. 2013;163(5):1260-1266. doi:10.1016/j.jpeds.2013.05.015
16. Centers for Disease Control and Prevention (CDC). Recommendations to prevent and control iron deficiency in the United States. 1998. https://www.cdc.gov/mmwr/preview/mmwrhtml/00051880.htm. Accessed February 10, 2022.
17. Grant CC, Wall CR, Brewster D, et al. Policy statement on iron deficiency in pre-school-aged children. J Paediatr Child Health. 2007;43(7–8):513-521. doi:10.1111/j.1440-1754.2007.01128.x
18. World Health Organization. Serum ferritin concentrations for the assessment of iron status in individuals and populations: technical brief. 2020. https://apps.who.int/iris/handle/10665/331505. Accessed February 10, 2022.
19. Mei Z, Cogswell ME, Parvanta I, et al. Hemoglobin and ferritin are currently the most efficient indicators of population response to iron interventions: an analysis of nine randomized controlled trials. J Nutr. 2005;135(8):1974-1980. doi:10.1093/jn/135.8.1974
20. The Royal College of Pathologists of Australasia. Iron Studies Standardised Reporting Protocol, 2nd Edn. The Royal College of Pathologists of Australasia; 2021. https://www.rcpa.edu.au/Library/Practising-Pathology/NCRPQF/Docs/Iron-Studies-Standardised-Reporting-Protocol.aspx. Accessed February 10, 2022.
21. Mei Z, Addo OY, Jefferds ME, Sharma AJ, Flores-Ayala RC, Brittenham GM. Physiologically based serum ferritin thresholds for iron deficiency in children and non-pregnant women: a US National Health and Nutrition Examination Surveys (NHANES) serial cross-sectional study. Lancet Haematol. 2021;8(8):e572-e582. doi:10.1016/S2352-3026(21)00168-X
22. Daru J, Allotey J, Peña-Rosas JP, Khan KS. Serum ferritin thresholds for the diagnosis of iron deficiency in pregnancy: a systematic review. Transfus Med. 2017;27(3):167-174. doi:10.1111/tme.12408
23. Kassebaum NJ, Jasrasaria R, Naghavi M, et al. A systematic analysis of global anemia burden from 1990 to 2010. Blood. 2014;123(5):615-624. doi:10.1182/blood-2013-06-508325

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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