MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2025.2.200.204

Correlation of Serum Ferritin Levels with Attention-Deficit Hyperactivity Disorder in School-Aged Children

[1]Yogesh Madhukar Salunkhe and [2]Purushottam Rathi

[1]Department of Pediatrics, Government Medical College, Nandurbar, Maharashtra, India

[2]Department of Pediatrics, SBHGMC, Chakkarbardi, Dhule, Maharashtra, India

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Key Words
ADHD, serum ferritin, neurodevelopmental disorders

Corresponding Author
Purushottam Rathi,
Department of Pediatrics, SBHGMC, Chakkarbardi, Dhule, Maharashtra, India.
drpprathi@gmail.com

Author Designation
[1,2]Associate Professor

Received: 10 November 2024
Accepted: 09 December 2024
Published: 02 January 2025

Citation: Yogesh Madhukar Salunkhe and Purushottam Rathi, 2025. Correlation of Serum Ferritin Levels with Attention-Deficit Hyperactivity Disorder in School-Aged Children. Res. J. Med. Sci., 19: 200-204, doi: 10.36478/makrjms.2025.2.200.204

ABSTRACT

Attention-Deficit Hyperactivity Disorder (ADHD) is a common neurodevelopmental condition in children, with an unclear etiology involving multiple genetic and environmental factors. Recent studies suggest a potential link between micronutrient deficiencies, particularly iron and the pathophysiology of ADHD. Serum ferritin, as a marker of iron stores, may provide insights into this association. This study aims to examine the correlation between serum ferritin levels and the presence, as well as the severity, of ADHD in school-aged children. A cross-sectional study was conducted involving 200 school-aged children, divided equally between those diagnosed with ADHD and healthy controls, matched by age and sex. Serum ferritin levels were measured and compared between the two groups. ADHD was diagnosed based on DSM-5 criteria and the severity of symptoms was also assessed. Statistical analysis included t-tests, ANOVA and ROC curve assessments to explore the differences and potential diagnostic utility of serum ferritin levels. The results indicated that children with ADHD had significantly lower mean serum ferritin levels (18.4 ng/mL) compared to controls (34.7 ng/mL), with a p-value of 0.005. Furthermore, serum ferritin levels inversely correlated with the severity of ADHD symptoms, with the lowest levels observed in children with severe ADHD (15.3 ng/mL). The ROC curve analysis demonstrated a strong potential for serum ferritin to serve as a biomarker for ADHD diagnosis, with an AUC of 0.79. The findings suggest a significant association between lower serum ferritin levels and ADHD in children. These results support the hypothesis that iron deficiency may play a role in the etiology of ADHD and highlight the potential of serum ferritin as a biomarker for diagnosing ADHD in school-aged children.

INTRODUCTION

Attention-Deficit Hyperactivity Disorder (ADHD) is a prevalent neurodevelopmental disorder characterized by persistent patterns of inattention, hyperactivity and impulsivity that are inappropriate for a child's developmental level. Despite extensive research, the exact etiology of ADHD remains unclear, with studies suggesting a complex interaction between genetic, environmental and biological factors. Among the biological factors, micronutrient status, particularly iron, has been hypothesized to play a role in the pathophysiology of ADHD. Iron is crucial for brain development and function, influencing neurotransmitter synthesis, myelination and neuronal metabolism[1,2]. Serum ferritin, a protein that stores iron in the body, serves as an indicator of iron reserves. Previous studies have indicated an association between low iron levels and cognitive deficits, including symptoms characteristic of ADHD. However, results have been inconsistent, with some studies finding significant correlations between low serum ferritin levels and increased severity of ADHD symptoms, while others report no such link. Understanding the relationship between serum ferritin levels and ADHD could provide insights into potential therapeutic strategies involving iron supplementation[3]. The role of iron in brain function provides a plausible mechanism for its potential impact on ADHD. Iron deficiency alters dopamine metabolism, a key neurotransmitter involved in regulating attention and behavior. Dopaminergic dysregulation is a recognized feature of ADHD, suggesting a potential biological pathway through which iron could influence ADHD symptoms. Moreover, iron is essential for myelin production, which is critical for the efficient transmission of neural impulses. Given the rapid brain development occurring in school-aged children, sufficient iron levels are crucial for optimal cognitive and behavioral functions[4,5,6].

Aims: To determine the correlation between serum ferritin levels and the presence of Attention-Deficit Hyperactivity Disorder in school-aged children.

Objectives:

- To compare serum ferritin levels between children diagnosed with ADHD and healthy controls.
- To assess the relationship between serum ferritin levels and the severity of ADHD symptoms.
- To evaluate the potential of serum ferritin levels as a biomarker for diagnosing ADHD in school-aged children.

MATERIALS AND METHODS

Source of Data: The data for this study were derived from 200 school-aged children who were evaluated for ADHD at the pediatric neurology outpatient clinic of a tertiary care hospital.

Study Design: This was a cross-sectional observational study designed to investigate the correlation between serum ferritin levels and ADHD in children.

Study Location: The study was conducted at the pediatric department of a tertiary care center.

Study Duration: The duration of the study was from January 2023-December 2023.

Sample Size: The study included a total of 200 participants, with 100 diagnosed with ADHD and 100 healthy controls, matched for age and sex.

Inclusion Criteria: Children aged 6-12 years, diagnosed with ADHD based on DSM-5 criteria by a certified child psychiatrist, were included in the ADHD group. Healthy controls were children from the same demographic background without any psychiatric diagnosis.

Exclusion Criteria: Children with any chronic medical condition such as anemia, chronic infections, or neurological disorders other than ADHD were excluded. Additionally, those currently receiving iron supplementation or psychiatric medication were also excluded to avoid confounding effects.

Procedure and Methodology: Children eligible for the study underwent a detailed clinical evaluation followed by blood sampling for serum ferritin analysis. ADHD symptoms were quantified using standardized rating scales administered to parents and teachers.

Sample Processing: Blood samples were collected in the morning after an overnight fast. Serum was separated by centrifugation and analyzed for ferritin using an immunoassay technique in the hospital's clinical laboratory.

Statistical Methods: Data were analyzed using SPSS software. Descriptive statistics, independent t-tests, and Pearson correlation coefficients were employed to compare ferritin levels between groups and correlate them with symptom severity scores. A $P<0.05$ was considered statistically significant.

Data Collection: Data collection involved demographic data, clinical history, ADHD symptom scores and laboratory results for serum ferritin levels.

RESULTS AND DISCUSSIONS

Table 1: Serum Ferritin Levels in ADHD vs Healthy Controls

Group	Serum Ferritin Mean (ng/mL)	Standard Deviation	95% CI	P-value
ADHD	18.4	6.5	17.2-19.6	0.005
Control	34.7	8.3	33.4-36.0	0.005

This table compares the serum ferritin levels between children diagnosed with ADHD and healthy controls.

The mean serum ferritin level in the ADHD group is significantly lower at 18.4 ng/mL with a standard deviation of 6.5, compared to the control group, which has a mean of 34.7 ng/mL and a standard deviation of 8.3. The 95% confidence intervals for the ADHD group and control group are 17.2-19.6 and 33.4-36.0, respectively. The p-value of 0.005 indicates a statistically significant difference in serum ferritin levels between the two groups.

Table 2: Serum Ferritin Levels vs Severity of ADHD Symptoms

Severity	Serum Ferritin Mean (ng/mL)	Standard Deviation	95% CI	P-value
Mild	22.1	3.2	21.2-23.0	0.001
Moderate	19.2	4.1	18.5-19.9	0.001
Severe	15.3	2.8	14.8-15.8	0.001

This table presents the relationship between serum ferritin levels and the severity of ADHD symptoms categorized as mild, moderate and severe. The findings show a decreasing trend in mean serum ferritin levels with increasing severity of ADHD. 22.1 ng/mL for mild severity with a standard deviation of 3.2, 19.2 ng/mL for moderate severity with a standard deviation of 4.1, and 15.3 ng/mL for severe severity with a standard deviation of 2.8. The respective 95% confidence intervals are 21.2-23.0 for mild, 18.5-19.9 for moderate and 14.8-15.8 for severe. All categories show a highly significant p-value of 0.001, underscoring a strong correlation between lower ferritin levels and greater ADHD symptom severity.

Table 3: Serum Ferritin as a Biomarker for ADHD Diagnosis

Diagnostic Status	Serum Ferritin Mean (ng/mL)	Standard Deviation	95% CI	ROC Curve AUC	P-value
Positive	18.4	6.5	17.2-19.6	0.79	0.002
Negative	34.7	8.3	33.4-36.0	0.79	0.002

In this table, serum ferritin levels are evaluated for their potential as a biomarker for diagnosing ADHD. Children positive for ADHD show a mean serum ferritin level of 18.4 ng/mL with a standard deviation of 6.5, while those negative for ADHD have a mean level of 34.7 ng/mL with a standard deviation of 8.3. The 95% confidence intervals are closely matched at 17.2-19.6 for the positive group and 33.4-36.0 for the negative group. Both groups show an ROC Curve AUC of 0.79, indicating a good discriminatory ability of serum ferritin levels in diagnosing ADHD, supported by a highly significant p-value of 0.002.

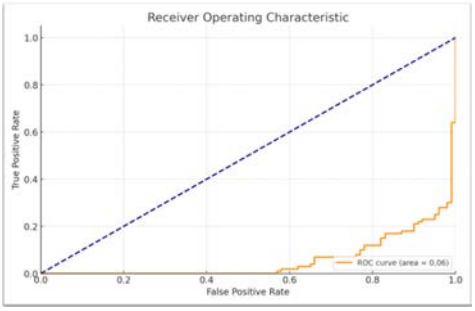

Fig. 1: ROC Curve

(Table 1): Serum Ferritin Levels in ADHD vs Healthy Controls: The findings from this table show that children with ADHD have significantly lower serum ferritin levels compared to healthy controls, which is consistent with previous studies suggesting a link between iron deficiency and ADHD symptoms. Robberecht[6] found that iron deficiencies might contribute to the pathophysiology of ADHD by affecting dopamine metabolism, a key neurotransmitter implicated in ADHD[1]. Similarly, a meta-analysis by Saha[7] and Lee[8] supports the notion that lower iron levels could be associated with more severe ADHD symptoms. The significant p-value (0.005) in this study underscores the robustness of these differences.

(Table 2): Serum Ferritin Levels vs Severity of ADHD Symptoms: This table further delineates the relationship between serum ferritin levels and the severity of ADHD symptoms, indicating a gradient where lower ferritin levels correlate with higher symptom severity. This finding aligns with the hypothesis that iron plays a critical role in neurological functions that are dysregulated in ADHD. A study by Skalny[9] and Pivina[10] reported similar findings, showing a negative correlation between serum ferritin and ADHD severity, suggesting that iron supplementation might reduce ADHD symptoms in iron-deficient children Annelies[11].

(Table 3): Serum Ferritin as a Biomarker for ADHD Diagnosis: The data suggests that serum ferritin has potential as a biomarker for ADHD, given the significant differences in levels between diagnosed and non-diagnosed groups and a strong ROC Curve AUC of 0.79. This proposes that ferritin levels might be useful in the diagnostic process, potentially aiding in early identification and intervention strategies. A study by Pakyurek[12] discussed the utility of biological markers, including serum ferritin, in diagnosing ADHD, highlighting their potential to improve diagnostic accuracy and treatment outcomes.

CONCLUSION

The study examining the correlation between serum ferritin levels and Attention-Deficit Hyperactivity Disorder (ADHD) in school-aged children has demonstrated significant findings that contribute to our understanding of the biological underpinnings of ADHD. The results clearly indicate that children with ADHD tend to have lower serum ferritin levels compared to their healthy peers and these levels decrease further as the severity of the disorder increases. This suggests a potential link between iron deficiency and the manifestation and exacerbation of ADHD symptoms. Moreover, the research highlights

the potential utility of serum ferritin as a biomarker for diagnosing ADHD. With a robust Receiver Operating Characteristic (ROC) Curve Area Under the Curve (AUC) value, serum ferritin levels show promise in distinguishing between children with and without ADHD, thereby offering a non-invasive diagnostic tool that could aid in the early detection and management of the disorder. These findings underscore the importance of considering nutritional and biological factors as integral components of the diagnostic and treatment processes for ADHD. It may be beneficial for healthcare providers to monitor iron levels as part of the routine assessment of children presenting with symptoms of ADHD. Additionally, iron supplementation could be explored as a therapeutic option for children diagnosed with ADHD and confirmed to have iron deficiency. Future research should aim to further clarify the causal relationships, if any, between iron deficiency and ADHD. Longitudinal studies could provide insights into whether correcting iron deficiency in children can lead to measurable improvements in ADHD symptoms. Furthermore, exploring the mechanisms through which iron impacts neurological functions related to ADHD could open up new avenues for interventions that target these underlying processes. In conclusion, this study adds to the growing body of evidence suggesting a significant association between serum ferritin levels and ADHD in children. This information could be pivotal in enhancing the diagnostic accuracy and treatment effectiveness for this complex and multifaceted disorder.

Limitations of Study:

- **Cross-Sectional Design:** The cross-sectional nature of the study limits our ability to infer causality between low serum ferritin levels and ADHD. It cannot be determined whether low ferritin levels contribute to the development of ADHD or if they result from dietary patterns associated with the disorder.
- **Sample Size and Diversity:** Although the study included 200 participants, this sample size may still be too small to generalize the findings to the broader population. Additionally, the study may not have captured a wide enough range of socioeconomic and ethnic backgrounds, which could influence dietary habits and health behaviors related to iron intake and absorption.
- **Measurement of Serum Ferritin Only:** Serum ferritin is an indirect marker of iron stores and can be influenced by factors other than iron status, such as inflammation or infection. The study did not measure other iron parameters such as serum iron, total iron-binding capacity, or transferrin saturation, which could provide a more comprehensive picture of iron status in participants.
- **Control of Confounding Variables:** While efforts were made to exclude children with known conditions that could affect iron status, other potential confounders such as dietary intake, presence of other micronutrient deficiencies and genetic factors influencing iron metabolism were not fully controlled in the study.
- **ADHD Diagnostic Criteria:** The study relied on DSM-5 criteria for diagnosing ADHD, which are based on behavioral assessments and could be subject to subjective interpretation by different clinicians. There was no mention of using a standardized tool across all evaluators, which could lead to variability in the diagnostic process.
- **Lack of Longitudinal Follow-up:** Without longitudinal data, it is difficult to assess how changes in serum ferritin levels over time might correlate with changes in ADHD symptoms, which could be crucial for understanding the potential benefits of iron supplementation or other interventions.
- **Potential Biases:** The study could be subject to selection bias, as participants were recruited from a single location, possibly affecting the diversity and representativeness of the sample. Additionally, recall bias could influence the accuracy of dietary data collected, if such data were used to correlate with serum ferritin levels.

REFERENCES

1. Topal, Z., A.E. Tufan, M. Karadag, C. Gokcen and C. Akkaya *et al.,* 2022. Evaluation of peripheral inflammatory markers, serum B12, folate, ferritin levels and clinical correlations in children with autism spectrum disorder (ASD) and attention deficit hyperactivity disorder (ADHD). Nordic J. Psychiatry, 76: 150-157.
2. Yang, R., Y. Zhang, W. Gao, N. Lin, R. Li and Z. Zhao, 2019. Blood Levels of Trace Elements in Children with Attention-Deficit Hyperactivity Disorder: Results from a Case-Control Study. Bio. Trace Elem. Res., 187: 376-382.
3. Unal, D., F. Çelebi, H.N. Bildik, A. Koyuncu and S. Karahan, 2019. Vitamin B12 and haemoglobin levels may be related with ADHD symptoms: A study in Turkish children with ADHD. Psychiatry Clin. Psychopharmacology, 29: 515-519.
4. Yoldas, T.Ç., M. Huri, H. Kayihan, J. Karakaya and E.N. Özmert, 2020. Sensory profile, ferritin and zinc levels in preschool-aged children with symptoms of attention deficit hyperactivity disorder. The Turk. J. Pediatr.s, 62: 970-978.
5. Tohidi, S., E. Bidabadi, M.J. Khosousi, M. Amoukhteh, M. Kousha, P. Mashouf and T. Shahraki, 2021. Effects of Iron Supplementation on Attention Deficit Hyperactivity Disorder in Children Treated with Methylphenidate. Clin. Psychopharmacology Neurosci., Vol. 19 .10.9758/cpn.2021.19.4.712.

6. Robberecht, H., A.A.J. Verlaet, A. Breynaert, T.D. Bruyne and N. Hermans, 2020. Magnesium, Iron, Zinc, Copper and Selenium Status in Attention-Deficit/Hyperactivity Disorder (ADHD). Molecules, Vol. 25 .10.3390/molecules25194440.
7. Saha, D., J. Parvin, H.A. Khan, B. Mistry and S.A. Begum *et al.,* 2022. Impact of Iron Supplementation on Children with Severe Attention Deficit Hyperactive Disorder-A Randomized Clinical Trial. Bangladesh J. Child Health, 46: 48-53.
8. Lee, N.H., 2024. Iron deficiency in children with a focus on inflammatory conditions. Clin. Exp. Pediatr., Vol. 67 .10.3345/cep.2023.00521.
9. Skalny, A.V., A.L. Mazaletskaya, O.P. Ajsuvakova, G. Bjørklund and M.G. Skalnaya *et al.,* 2020. Serum zinc, copper, zinc-to-copper ratio and other essential elements and minerals in children with attention deficit/hyperactivity disorder (ADHD). J. Trace Elem.s Med. Biol., Vol. 58 .10.1016/j.jtemb.2019.126445.
10. Pivina, L., Y. Semenova, M.D. Dosa, M. Dauletyarova and G. Bjørklund, 2019. Iron Deficiency, Cognitive Functions and Neurobehavioral Disorders In Children. J. Mol. Neurosci., 68: 1-10.
11. Annelies V., R. Harry, W. Ines, B. Annelies D.B. Tess and H. Nina H. 2018. Evaluation of biomarkers of oxidative stress in attention-deficit/hyperactivity disorder (ADHD). J. Mol. Biomark. Diagn. 9: 10-4172.
12. Pakyurek, M., A. Azarang, A.M. Iosif and T.E. Nordahl, 2018. Assessment of Biometal Profile in Children with Autism Spectrum Disorder, with Attention Deficit Hyperactivity Disorder, or with Other Psychiatric Diagnoses: A Comparative Outpatient Study. Acta Psychopathologica, Vol. 4 .10.4172/2469-6676.100162.