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The prevalence of iron deficiency anemia in children with Attention- Deficit/ Hyperactivity Disorder in Tabriz

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Abstract

Background: Iron deficiency anemia (IDA) is a major public health issue leading to an increased risk of child mortality and has a negative effect on cognition and physical development. It has been suggested as a possible cause of the Attention-deficit/ hyperactivity disorder (ADHD). So we decided to estimate prevalence of iron deficiency anemia in children with this disorder.

Methods: A total of 295 children and adolescents with ADHD aged 3-18 based on DSM-IV diagnostic criteria after parental consent enrolled the study and 5 ml blood was taken to measure hematological parameters.

Results: The mean±SD age of children was 7.6±3.54 years. Forty-five point one percent of boys and 49.1% girls had serum ferritin levels lower than normal and 19.7% had extremely low serum ferritin level.

Conclusion: Low levels of ferritin may be associated with ADHD symptoms and suggest that children with this disorder screening and treatment for anemia.

Keywords: Attention deficit/ hyperactivity disorder, Iron deficiency, Iron deficiency anemia, Iron, Children, Adolescent

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Background

Attention-deficit/hyperactivity disorder(ADHD) is one of the most common psychiatric disorders in children and is characterized by inappropriate impulsivity, hyperactivity, inattention and altered executive functions (1). The worldwide rate of ADHD is 5 to 10 percent of school age children and it is more common in boys (2, 3). ADHD is multifactorial and the exact etiology is unknown, but studies have suggested genetic factors, brain injuries, low birth weight, imbalance of neurotransmitters, heavy metal toxicity, nutritional deficiencies (such as iron) are responsible in the etiology of this disorder (4-6).

Iron deficiency (ID) and Iron deficiency anemia (IDA) is expressed as a major worldwide nutritional concern especially in developing countries (7, 8). Among the numerous biological effects of iron, there is considerable evidence that iron is important for neurological functioning and development in the brain (9, 10), so the ID is raised in the pathogenesis of a number of psychiatric disorders, including ADHD (11-13). Iron has a major role as a coenzyme in the synthesis of neurotransmitters, such as the role of coenzyme in tryptophan hydroxylase (serotonin) and tyrosine hydroxylase (norepinephrine such as dopamine) (14-16). Also, studies have shown that iron deficiency affects dopamine levels in substantia Niagra and putamen, alters dopamine receptor density and activity in animals; noticing that dopamine deficit theory is the most widely accepted in ADHD (16).

Some studies have shown that ferritin (a marker of iron stored) decreased in children with ADHD, and this decrease inversely correlated with the severity of the symptoms (12, 13). The Konofol et al study shows that significantly lower serum ferritin levels have been observed in children with attention deficit hyperactivity disorder, almost 90 percent of attention deficit hyperactivity disorder children had serum ferritin levels of 30 ng/ml, compared with18% of controls, and all children in

their study had normal hemoglobin levels (11) but Millichap et al. found a proportion of children with ADHD with relatively low levels of ferritin suggestive of iron deficiency, but without a specific relationship to the ADHD symptoms (17), and Sever et al., reported that supplementation of 5 mg/kg of iron to 14 ADHD children for 30 days resulted in increased serum ferritin level and reduced scores of ADHD based on Conner's Rating Scale (12).

ID can have a major and long term impact on child health and according to the hypothesis of the pathogenesis and severity of the disorder associated with iron deficiency, we decided to estimate the prevalence of iron deficiency and iron deficiency anemia in children with ADHD in the Tabriz in North West of Iran.

Methods

The sample was enrolled from the child and adolescent Psychiatry Clinics of Tabriz University of Medical Sciences. The inclusion criteria were children aged 3-18 years with a diagnosis of ADHD according to the DSM-IV criteria that do not take iron supplementation during the past year. Children with co-morbid psychiatric and serious medical disorders were excluded. The objectives of the study were explained to the parents and finally 295 children and adolescents with ADHD (236boys and 59 girls) with parental consent were enrolled in the study. Five ml fasting venous blood was taken from each child to measure hemoglobin (Hb), hematocrit (HCT), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentrate (MCHC), serum ferritin (SF), serum iron, total iron binding capacity (TIBC), red blood cells count (RBC), and red cell distribution width (RDW).

Cut-off points were determined based on the WHO recommendations and studies:

Hemoglobin: 3 to 11 years old (< 11.5g/dl), 12 to 14 years old (< 12g/dl), over 15 years old (< 13g/dl); Ferritin: < 30 ng/mL; RDW: > 14.5%; iron serum: <55µg/dL; TIBC: >400µg/dL; MCV< 77 fl and MCHC< 31 g/dl. The results were analyzed by Statistical Package for the Social Sciences Version 16.0 (SPSS). Continuous variables (e.g. hematologic variables) were described through mean and standard deviation (symmetrical distribution) or median and interquartile range (asymmetrical distribution). Continuous data were presented as mean ± standard deviation (SD) or median ±interquartile range. Categorical data (e.g. gender) were described as absolute and relative frequencies.

Results

Mean± standard deviation age of the participants was 7.60±3.54 years. Eighty percent (236) of children and adolescents were boys and 20.0% (59) were girl. Table 1 shows the mean and stand-

Table 1. Hematological and iron indices in ADHD children by sex

Variables	Boy	Girl	Total
Hb (g/dl)*	13.51± 1.07	13.25± 0.95	13.45± 1.05
HCT (%) *	40.84± 3.07	40.59± 3.08	40.79± 3.06
MCV (fl)*	27.95 (27, 29.10)	28.00 (26.8, 29.5)	84.67± 5.45
MCH (pg) **	27.95± 2.16	28.00± 2.51	27.96 (27, 29,20)
MCHC (g/dl)*	33.07± 1.51	32.69± 1.87	33.00 ± 1.57
RBC/µ **	4.84 (4.55, 5.10)	4.75 (4.48, 4.96)	4.82 (4,53, 5.08)
Serum iron (µg/dl)*	87.46± 28.72	80.06± 31.61	81.57± 31.22
Serum ferritin (ng/ml)**	40.41 (19.03, 48.68)	37.26(18.6, 50.92)	39.79 (19.02, 48.72)
TIBC (µg/dl)*	351.51± 60.95	349.78± 54.54	350.46±55.87

Hb: hemoglobin, HCT: hematocrit, MCV: mean corpuscular volume, MCH: mean corpuscular hemoglobin, MCHC: mean corpuscular hemoglobin concentrate, RBC: red blood cells count, TIBC: total iron binding capacity.
* expressed as mean ± SD. ** expressed as median (percentile 25, 75).

Table 2. Laboratory measures and cut-off scores of iron deficiency

Variables	Boys % (n)	Girls % (n)	Total % (n)
Hb	5.5 (13)	10.2 (6)	6.4 (19)
Ferritin	44.3 (104)	49.2 (29)	45.1 (133)
Serum iron	19.1 (45)	10.2 (6)	17.3 (51)
TIBC	12.9 (30)	22(13)	14.8 (43)
MCV	6.4 (15)	6.8 (4)	6.4 (19)
MCHC	8.9 (21)	22 (13)	11.5 (34)
RDW	25.8 (61)	18.6 (11)	24.4 (72)

Hb: hemoglobin, MCV: mean corpuscular volume, MCHC: mean hemoglobin concentrate, TIBC: total iron binding capacity.red Cell Distribution Width (RDW)

ard deviation (for normally distributed data) and mean and percentiles (for not normally distributed data) of examining parameters in ADHD children by sex. Almost mean or median of all the parameters were similar in boys and girls and there was no significant difference between them (not shown in table). In Table 2, the frequency and percentage of children with abnormal blood parameters were shown. Anemia based on hemoglobin levels was seen in 5.5% of boys and 10.2% of girls. Forty-five point one percent of boys and 49.1% girls had serum ferritin levels lower than normal. In total, 45.1% of children had serum ferritin below 30. The minimum and maximum serum ferritin were 1.10 and 228.30. If serum ferritin levels below 15 were considered as extremely low iron stores, 58 subjects (19.7%) had extremely low serum ferritin level (data not shown in Table 2.

Fifty one subject (17.3%) presented serum iron below 55g/dL, 43 (14.8%) >TIBC 400, 19 (6.4%) <mcv 77Fl, 72 (24.4%) > RDW 14.5% and 34 (11.5%) had values of MCHC <31%.

Discussion

In our study, about 7% of children with ADHD were anemic, considering the hemoglobin index as the cutoff point for anemia. Konofol et al's study on 53 ADHD and 27 healthy children revealed that all children had normal hemoglobin and there were no significant differences between the two groups (11). Ferritin has been proposed as an indicator of iron deficiency and was allocated the largest decrease percentage in our study. Almost 50% of children in this study had serum ferritin levels below 30 and 19.7% had extremely low serum ferritin level. In Juneja et al's study that was conducted in 2010, ferritin levels in children with ADHD was lower than healthy children and there was a significant negative correlation between serum ferritin levels and oppositional subscore based on Conner's rating scale(18), In contrast, in the study by Millichap et al, the serum ferritin level in ADHD children was not different from the control children(17). Sever et al found increased serum ferritin levels and decreased ADHD symptom scores in children with ADHD after iron supplementation and suggesting that no anemic children with ADHD may benefit from iron supplementation(12). In a systematic review and meta-analysis review of the iron status of children with ADHD in 2017, it was concluded that serum ferritin levels rather than serum iron may be associated with this disorder(19).

Serum ferritin is a more sensitive marker which can be detected at the early stage of iron deficiency even without anemia and due to the high prevalence of decreased plasma ferritin levels in children with ADHD, the hypothesis can be considered that low ferritin levels might decreased dopaminergic function in the brain.

Conflicts of interest: None declared.

References

1. Willcutt EG. The prevalence of DSM-IV attention-deficit/hyperactivity disorder: a meta-analytic review. Neurotherapeutics. 2012;9(3):490-9.
2. Association AP. Diagnostic and statistical manual of mental disorders (DSM-5®): American Psychiatric Pub; 2013.
3. Farahat T, Alkot M, Rajab A, Anbar R. Attention-deficit hyperactive disorder among primary school children in Menoufia governorate, Egypt. Int J Family Med. 2014;2014.
4. Wolraich ML, Lambert W, Doffing MA, Bickman L, Simmons T, Worley K. Psychometric properties of the Vanderbilt ADHD diagnostic parent rating scale in a referred population. J Ped Psychol. 2003;28(8):559-68.
5. Yousef S, Adem A, Zoubeidi T, Kosanovic M, Mabrouk AA, Eapen V. Attention deficit hyperactivity disorder and environmental toxic metal exposure in the United Arab Emirates. J Trop Ped. 2011;57(6):457-60.
6. Sinn N. Nutritional and dietary influences on attention deficit hyperactivity disorder. Nutrit Rev. 2008;66(10):558-68.
7. Walter T, De Andraca I, Chadud P, Perales CG. Iron deficiency anemia: adverse effects on infant psychomotor development. Pediatrics. 1989;84(1):7-17.
8. Walker SP, Wachs TD, Gardner JM, Lozoff B, Wasserman GA, Pollitt E, et al. Child development: risk factors for adverse outcomes in developing countries. Lancet. 2007;369(9556):145-57.
9. Lozoff B, Georgieff MK, editors. Iron deficiency and brain development. Seminars in pediatric neurology; 2006: Elsevier.
10. Grantham-McGregor S, Ani C. A review of studies on the effect of iron deficiency on cognitive development in children. J Nutrit. 2001;131(2):649S-68S.
11. Konofal E, Lecendreux M, Arnulf I, Mouren MC. Iron deficiency in children with attention-deficit/hyperactivity disorder. Arch Ped Adoles Med. 2004;158(12):1113-5.
12. Sever Y, Ashkenazi A, Tyano S, Weizman A. Iron treatment in children with attention deficit hyperactivity disorder. Neuropsychobiology. 1997;35(4):178-80.
13. Konofal E, Cortese S, Lecendreux M, Arnulf I, Mouren MC. Effectiveness of iron supplementation in a young child with attention-deficit/hyperactivity disorder. Pediatrics. 2005;116(5):e732-e4.

14. Erikson KM, Jones BC, Beard JL. Iron deficiency alters dopamine transporter functioning in rat striatum. J Nutrit. 2000;130(11):2831-7.
15. Sachdev P. The neuropsychiatry of brain iron. The J Neuropsy Clinic Neurosci. 1993.
16. Lozoff B. Early iron deficiency has brain and behavior effects consistent with dopaminergic dysfunction. J Nutrit. 2011;141(4):740S-6S.
17. Millichap JG, Yee MM, Davidson SI. Serum ferritin in children with attention-deficit hyperactivity disorder. Ped Neurol. 2006;34(3):200-3.
18. Juneja M, Jain R, Singh V, Mallika V. Iron deficiency in Indian children with attention deficit hyperactivity disorder. Ind Ped. 2010;47(11):955-8.
19. 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(1):e0169145.