

# The role of iron deficiency in children with attention deficit/hyperactivity disorder

## Dikkat eksikliği hiperaktivite bozukluğu olan çocuklarda demir eksikliğinin rolü

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### ABSTRACT

**Objective:** Attention Deficit-Hyperactivity Disorder is a common neurobiological syndrome of the childhood. Iron deficiency is suggested to be an etiologic factor of Attention Deficit-Hyperactivity Disorder because of its role in the dopamine metabolism. The objective of this study is to evaluate iron deficiency in patients with Attention Deficit-Hyperactivity Disorder in comparison with healthy children and to predict the severity of the symptoms on admission with reference to serum ferritin levels.

**Methods:** Fifty children with Attention Deficit-Hyperactivity Disorder and fifty age and sex-matched control subjects were evaluated. Ferritin levels in both groups and their relationship with DSM-4 score were investigated.

**Results:** The mean serum ferritin level in the patient group was  $27 \pm 13.2$  ng/ml which was significantly lower than the control group with a mean value of  $41 \pm 26$  ng/ml. In Attention Deficit-Hyperactivity Disorder group, serum ferritin levels did not correlate with the score of the disease described in DSM-4 ( $r=0.09$ ;  $p>0.05$ ).

**Conclusion:** In conclusion, iron deficiency is an etiologic factor in Attention Deficit-Hyperactivity Disorder but the severity of the symptoms on admission did not correlate with serum ferritin levels.

**Key words:** Attention deficit, hyperactivity disorder, children, ferritin

### ÖZET

**Amaç:** Dikkat eksikliği hiperaktivite bozukluğu, çocukluk çağında sık görülen bir nörobiyolojik sendromdur. Demir eksikliğinin, demirin dopamin metabolizmasındaki rolü nedeniyle dikkat eksikliği hiperaktivite bozukluğunda etyolojik faktör olduğu düşünülmektedir. Bu çalışmanın amacı, dikkat eksikliği hiperaktivite bozukluğu olan çocuklarda demir eksikliğinin etyolojide rolünü araştırmak ve serum ferritin düzeylerinin başvuru semptomlarının ağırlığını belirlemede değeri olup olmadığını saptamaktır.

**Yöntemler:** Dikkat eksikliği hiperaktivite bozukluğu olan 50 çocuk çalışma grubu, yaş ve cinsiyet uyumlu 50 çocuk da kontrol grubu olarak alındı. Her iki grupta ölçülen serum ferritin düzeylerinin DSM-4 skoru ile ilişkisi değerlendirildi.

**Bulgular:** Hasta grubunun ortalama ferritin düzeyi  $27 \pm 13.2$  ng/ml ile kontrol grubunun  $41 \pm 26$  ng/ml ortalama ferritin düzeyinden belirgin olarak düşük saptandı. Dikkat eksikliği hiperaktivite bozukluğu grubunda serum ferritin düzeyleri, DSM-4'te tanımlanan hastalık skoru ile korele bulunmadı ( $r=0.09$ ;  $p>0.05$ ).

**Sonuç:** Sonuç olarak demir eksikliği, dikkat eksikliği hiperaktivite bozukluğunda etyolojik bir faktör olarak saptandı ancak semptomların ciddiyetinin ferritin düzeyinin düşüklüğü ile korele olmadığı düşünüldü.

**Anahtar kelimeler:** Dikkat eksikliği, hiperaktivite bozukluğu, çocuklar, ferritin

**Alındığı tarih:** 05.08.2012

**Kabul tarihi:** 29.08.2012

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## INTRODUCTION

Attention Deficit-Hyperactivity Disorder (ADHD) is a neurobiological syndrome affecting an estimated 5%-10% of school-aged children <sup>(1)</sup>. The disorder is characterized by overactivity, inattention, impulsivity and altered executive functions <sup>(2)</sup>. As the patients with ADHD have increased potential of dopamine transporter protein <sup>(3)</sup> and genetic polymorphisms in dopamine receptor <sup>(4)</sup>, dopamine is supposed to be the main neurotransmitter involving in the etiopathogenesis of ADHD. Iron is a cofactor of dopamine synthesis so iron deficiency may be one of the factors in the etiology of the disorder <sup>(5)</sup>. The aim of this study is to investigate the role of iron deficiency as an etiological factor in ADHD and predict the impact of iron deficiency in children diagnosed with ADHD.

## PATIENTS and METHODS

Children admitted to our child and adolescent psychiatry policlinics with symptoms of ADHD between April 2009 and September 2009 were evaluated for this study. The children and their families were interviewed by the same child and adolescent psychiatrist and totally 41 questions defined in DSM-4 criteria were asked which inquired inattention, hyperactivity and impulsivity, oppositional disorder and behavioral disorders. The families' answers were classified as 'there is no problem: 0; a little problem: 1; some problems: 2; much problem :3'. Each criterion was considered positive if there was at least some associated problems (class 2 and 3).

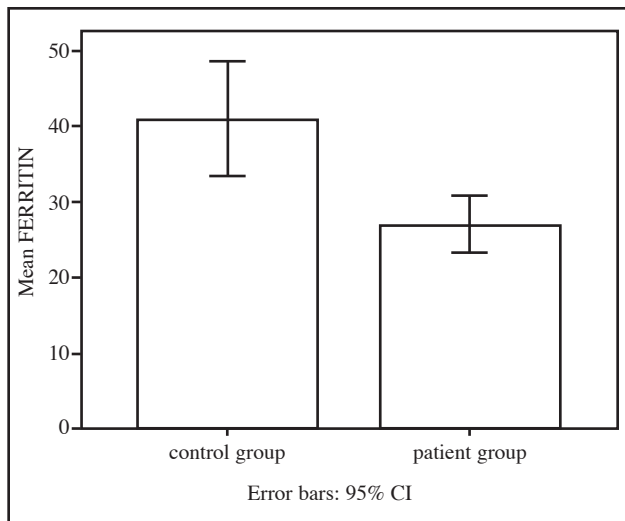
Children meeting 6 criteria of 9 in inattention, 6 criteria of 9 in hyperactivity and impulsivity were diagnosed as compound type ADHD according to DSM-4 criteria <sup>(2)</sup>.

Children diagnosed with compound type ADHD were evaluated as the study group. The children with mental retardation, additional mood and anxiety disorders, acute and chronic illnesses and those using iron supplements for last three months were exclu-

ded. Age and sex matched healthy children were evaluated as the control group following obtaining local ethics committee approval and consent of the families. Whole blood cell counts, serum iron and ferritin levels were assessed in venous blood samples drawn between 09.00 am and 11.00 am. Hemogram and serum iron levels were measured by Symex XT 2000, and Beckman Coulter Synchron LX autoanalyzers, respectively. Serum ferritin levels were measured with electrochemiluminescence method by Roche Elecys E170 modular analytic immunoanalyser. Reference ranges were 22-184 µg/dl for serum iron and 7-140 ng/ml for ferritin levels, respectively. Reference ranges for hemoglobin, hematocrit, erythrocyte, leucocyte, platelet counts, iron and ferritin levels were based on the reference tables of 18th edition of Nelson's textbook of pediatrics <sup>(6)</sup>. Children with anemia, polycythemia, leucocytosis, leucopenia, thrombocytopenia, thrombocytosis and other hematological problems were excluded based on laboratory test results. Finally, 50 children with compound type ADHD and 50 age and sex matched children were evaluated for statistical analysis. Statistical analysis were performed by SPSS 16.0 for Windows using t test, Pearson  $\chi^2$  test and Mann Whitney test;  $p < 0.05$  was considered statistically significant.

## RESULTS

In the ADHD group, patients' mean score described in DSM-4 was  $17 \pm 3$  and  $16 \pm 3$  for cases with inattention and hyperactivity-impulsivity, respectively. The mean values of hemoglobin, hematocrit, and also erythrocyte and leukocyte counts were similar in both groups. Serum iron levels were in normal ranges in both groups, so there was no significant difference ( $p > 0.05$ ). Serum ferritin levels were under normal ranges in 9 patients (18%) of ADHD group, while only 1 child's (2%) ferritin level in control group was lower than 7 ng/ml. The mean serum ferritin level of ADHD group was  $27 \pm 13,2$  ng/ml which was significantly lower than the control group with a



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mean value of  $41 \pm 26$  ng/ml (Figure 1). In the ADHD group, serum ferritin levels were not correlated with the score of the disease described in DSM-4 ( $r=0.09$ ;  $p>0.05$ ).

## DISCUSSION

The results of this study supports the previous studies indicating the effect of iron deficiency in the etiology of ADHD. But this is the first study to describe the relationship between serum ferritin levels and the score of DSM-4 criteria.

It was shown that iron is a coenzyme of tyrosine hydroxylase so it is associated with dopamine metabolism (5,7,8). Among numerous experimental studies demonstrating behavioral alterations in iron deficient rats (9,10), Konofal et al (11) was the first to report a clinical study demonstrating low serum ferritin levels in children with ADHD. They also reported that serum ferritin levels were inversely correlated with the severity of the symptoms when evaluated with CPRS (Conners Parent Rating Scale). Recent studies showed that ferritin levels affect both CPRS and CTRS (Conners Teacher Rating Scale) and comorbidity of ADHD (12,13). Juneja et al showed significant negative correlation between serum ferritin levels and oppositional subscore on Conners Rating Scale

(14). We aimed to predict the severity of the disease on admission according to serum ferritin levels without using any other rating scale during the follow-up period. We hypothesized that ferritin levels were inversely correlated with the score of DSM-4 criteria. But the results of our study did not support the presence of any correlation between ferritin levels and the severity of the symptoms on admission.

In conclusion, iron deficiency is an etiologic factor in ADHD and so, children presenting with symptoms of attention deficit, hyperactivity disorder may be firstly evaluated for iron deficiency before administering psychostimulant drugs. But serum ferritin levels can not be used as a laboratory marker to predict the severity of the symptoms on admission.

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