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Original article

Association between circulating zinc/ferritin levels and parent Conner's scores in children with attention deficit hyperactivity disorder

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ABSTRACT

ADHD is one of the most common neurobehavioral disorders among children and adolescents. In this prospective study, we aimed to measure circulating zinc and ferritin levels in children with ADHD, pick up the deficient ones to give zinc and iron supplements then compare before and after treatment according to their Conner's scores and Wecsler IQ test. Current study included fifty children diagnosed as having ADHD by DSMV criteria, their zinc and ferritin levels were measured by Colorimetric method and enzyme-linked immunosorbent assay (ELISA) respectively. They were divided into: group I (zinc only deficient),group II (zinc and ferritin deficient),group III (non-deficient), cases with mineral deficiency received zinc (55 mg/day) and/or iron (6 mg/kg/day) for 6 months then reassessed by parent Conner's rating scale. In group 1, there was no significant difference between the Wecsler verbal and non-verbal IQ scores and oppositional and cognitive problems in Conner's scores before and after zinc supplements, although there was significant improvement in attention, hyperactivity, emotional liability and impulsivity. In group II, there was significant improvement in verbal and total IQ but not in performance IQ, also there was significant improvement in hyperactivity, emotional liability and impulsivity with no significant difference in oppositional, cognitive problems and inattention before and after zinc/ iron supplements. In Conclusion, Zinc supplements in adjuvant to the main treatment significantly improved symptoms of ADHD children. However, a combined zinc and iron supplements was superior to zinc alone in alleviating ADHD symptoms as well as IQ improvement.

1. Introduction

Attention-deficit/hyperactivity disorder (ADHD) is one of the most common neurobehavioral disorders among children and adolescents, estimated to affect 3–6% of children. The three core features of ADHD include hyperactivity, impulsivity and/or inattention. The core features should persist over time and impair functioning across multiple settings, and be more prominent than expected given the child's age [1].

The pathophysiology of ADHD remains elusive. The findings of various neurobiological investigations suggest that a dysfunction of dopaminergic and noradrenergic neurotransmission within frontostriatal brain regions is a neurobiological correlate of ADHD. Stimulant medications such as methylphenidate are frequently administered in individuals with ADHD, but they are not always effective. Concerns about adverse effects of pharmacotherapy have prompted research on alternative treatment strategies including the use of nutritional supplements. Nutritional supplementation proposed for the treatment of ADHD mainly includes PUFAs and minerals as zinc, iron and magnesium [9].

Zinc (Zn) affects the metabolism of dopamine indirectly as it serves as a co factor to prostaglandins and neuro transmitters and melatonin. Furthermore, the enzyme desaturase requires Zn as a co factor. This enzyme acts on the essential fatty acids linoleic and linolenic acid which are an integral part of the neuronal membranes. About 15% of Zn is found present in the synaptic vesicles, thereby making it crucial for brain development and modulation of synaptic transmission [11].

Iron, cofactor in monoaminergic neurotransmitter metabolism, has a crucial role in the treatments of neuro developmental disorders. Sleep disturbances in ADHD children accelerates iron stores depletion, so a replenishment of iron is mandatory. Iron deficiency in childhood has many drawbacks on the development of the central nervous system, which may lead to behavioral disorders and mental retardation [12]. Furthermore, Tyrosine hydroxylase is a crucial enzyme in the synthesis of dopamine

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which also requires iron as a cofactor. Therefore, both cognition as well as behavioral outcomes could be related to the iron levels in the body [12].

2. Patients and methods

2.1. Patients

The present prospective study was conducted on 50 children at school age diagnosed as having ADHD according to DSM-V criteria (American Psychiatric Association, 2013). Serum zinc and ferritin level were measured for all groups before and after 6 months, the severity of ADHD symptoms was assessed by Conner's Rating Scale. All children were recruited from the Pediatric Department-Psychiatry Clinic, between March 2016 and March 2017. Patients enrolled in this study aged from 6 to 16 years. Only children with decreased circulating level of zinc and/or iron were compensated with deficient supplements for 6 months (55 mg /kg and 6 mg /kg for zinc and iron respectively) then reassessed again. Children with concurrent neurological disorders, chronic organic diseases as blindness or deafness, history of significant head trauma or history of perinatal asphyxia were excluded from the study. An informed consent was obtained from each participant in the study or his guardians in accordance with the guidelines of institutional review board of the Faculty of Medicine ethical committee, Ain Shams University, Cairo, Egypt. The local ethical committee approved the current study. The clinical data were collected from the patients' files retrospectively. The laboratory work was performed in the Medical Biochemistry Department, Faculty of Medicine, Ain Shams University.

Assessment of severity of ADHD symptoms was done using Parents Conners' Rating Scale before and after supplements for 6 months [14]. Assessment of IQ using Wecsler scale and measurement of serum levels of zinc and ferritin before and after treatment for 6 months [15].

The patients were subdivided into three groups: Group I (zinc only deficient) included 28 children with ADHD. Group II (zinc and iron deficient) included 12 children with ADHD and group III (non deficient group on Atomoxetine only) included 10 children (Tables 1–5)

2.2. Blood samples

Two ml venous blood sample was drawn from each participant, poured into sterile gel containing tube and allowed to clot at room temperature. Then, sera were collected after centrifugation for 15 min at 1000 xg. All samples were stored at −80 °C until use.

Table 1
Descriptive data of the ADHD cases.

		number	%
Sex	**Male**	43	86.0%
	Female	7	14.0%
Consanguinity	**Negative**	40	80.0%
	Positive	10	20.0%
Mode of delivery	**Vaginal delivery**	31	62%
	Caesarian section	19	38%
NICU admission	**Negative**	44	88.0%
	Positive	6	12.0%
Feeding type	**Breast Feeding**	42	84.0%
	Artificial feeding	8	16.0%
Family history	**Negative**	37	74.0%
	Positive	13	26.0%
Type	**Inattentive**	3	6.0%
	Hyperactive	14	28.0%
	Mixed	33	66.0%

2.3. Quantitative measurement of ferritin by ELISA

The concentration of feritin in serum samples was determined by enzyme-linked immunosorbent assay (ELISA) kits according to manufacturer's instructions (NOVA TEC IMMUNODIAGNOSTICA GmbH, Germany, catalog no. DNOV100). The intensity of the color in each well was measured within 5 min, using a microplate reader at 450 nm (with the reference absorbance at 540 nm).

2.4. Quantitative colorimetric measurement of Zinc

The concentration of Zinc in serum samples was determined by Colorimetric Test according to manufacturer's instructions (Greiner Diagnostic GmbH, Germany, catalog no. 184 000). Increase of absorbance was proportional to the concentration of total zinc in the sample. The absorbance was measured at 560 nm using spectrophotometer (UNICO Instruments C., Model 1200 USA).

2.5. Statistical analysis

The statistical package for social science version 20 (SPSS Software, SPSS Inc., Chicago, IL, USA) was used to analyze the data, and the results were expressed as mean, standard deviation. Paired *t*-test was used to compare the results before and after supplements. Anova was used as parametric test to show the significance of investigated biomarkers between different groups. The level of statistical significance was set at $p < 0.05$.

3. Results

Current study included 43 male and 7 females, age range was 6–16 years. The mean age of the studied group was 9 ± 2.2 years, their mean weight was 30.4 ± 8.4 kg, mean height was 129.8 ± 10.8 cm and their mean BMI was 17.8 ± 3.4.

Eighty six percent of patients were males while 14% were females with 20% of cases were of consanguineous parents. The mode of delivery was normal vaginal in 62% while 38.8% were born by Caesarian Section.

Twelve percent of cases were admitted in NICU (neonatal intensive care unit) after delivery. The percentage of the breast-fed cases and the artificial feeding were 84% and 16% respectively with 26% of cases had positive family history of ADHD.

The inattentive, hyperactive and mixed types of ADHD cases was 6%, 28%, and 66% respectively. There was statistically significant difference between them as regards their mode of delivery; 56.2% of mixed type cases were delivered by C.S. ($p < 0.05$) while there was no statistically significant difference between them in other parameters as sex, consanguinity, maternal illness during pregnancy, NICU admission and their feeding type.

There was statistically significant difference between them as regards their weight ($p < 0.05$) while there was no statistically significant difference as regards height and BMI ($p > 0.05$).

In group I, there was no statistically significant difference in the Wecsler IQ test before and after zinc supplement ($p > 0.05$), while there was significant improvement in inattention after zinc supplement ($P > 0.05$), and highly significant improvement in their hyperactivity, impulsivity and emotional-liablity scales ($P > 0.001$), but not in oppositional and cognitive problems ($p > 0.05$).

In group II, there was significant improvement in their verbal and total I.Q test after zinc and iron supplementation ($P > 0.05$), but there was no statistically significant improvement in their performance IQ ($P > 0.05$). Also, there was a significant improvement in their hyperactivity, impulsivity and emotion liability after iron and zinc supplementation ($P > 0.05$), but not in oppositional, cognitive problems and inattention subscales ($p > 0.05$).

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Table 2
Comparison between types of ADHD as regards their anthropometric measures.

		N	Mean	Std. Deviation	95% CI for Mean		Min	Max	F	P
					Lower Bound	Upper Bound				
Weight	**Inattentive**	**3**	**24.00**	**8.660**	**2.49**	**45.51**	**19**	**34**	**3.393**	**.042***
	Hyperactive	**14**	**26.93**	**6.765**	**23.02**	**30.83**	**18**	**38**		
	Combined	**33**	**32.48**	**8.419**	**29.50**	**35.47**	**16**	**58**		
Height	**Inattentive**	**3**	**123.00**	**12.166**	**92.78**	**153.22**	**115**	**137**	**1.210**	**.307**
	Hyperactive	**14**	**127.64**	**12.150**	**120.63**	**134.66**	**106**	**153**		
	Combined	**33**	**131.33**	**10.077**	**127.76**	**134.91**	**113**	**162**		
BMI	**Inattentive**	**3**	**15.33**	**2.309**	**9.60**	**21.07**	**14**	**18**	**2.860**	**.067**
	Hyperactive	**14**	**16.43**	**2.954**	**14.72**	**18.13**	**12**	**23**		
	Combined	**33**	**18.55**	**3.501**	**17.30**	**19.79**	**12**	**26**		

F = ANOVA test (*) result is significant.

Table 3
Wecsler IQ Test before and after zinc supplementation in group I.

Group I		N	Mean	Std. Deviation	Paired t test	P
Verbal IQ	Before	28	94.92	13.206	−1.889	.071
	After	28	97.92	13.038		
Performance IQ	Before	28	93.04	9.374	−.598	.555
	After	28	93.62	11.100		
Total IQ	Before	28	94.92	9.933	−1.400	.174
	After	28	96.68	10.812		

Table 4
Group one Conner's parent rating score before and after zinc supplementation.

		N	Mean	Std. Deviation	Paired t test	P
Oppositional	Before	28	72.96	10.623	1.847	.077
	After	28	70.46	9.778		
Cognitive problems	Before	28	68.54	11.455	2.026	.054
	After	28	65.42	8.571		
Inattention	Before	28	70.73	13.947	2.254	.033*
	After	28	67.27	11.446		
Hyperactivity	Before	28	79.88	7.596	4.154	.000*
	After	28	75.23	6.755		
Emotional liability	Before	28	82.00	7.849	5.076	.000*
	After	28	77.04	7.639		
Impulsivity	Before	28	80.46	8.026	5.515	.000*
	After	28	74.96	8.017		

Table 5
Group 2 Conner's parent rating scores before and after supplementation by iron and zinc Group 2.

Group II		N	Mean	Std. Deviation	Paired t test	P
Oppositional	Before	14	73.14	10.862	−.484	.637
	After	14	74.57	13.949		
Cognitive problems	Before	14	72.36	8.335	−.752	.465
	After	14	75.00	15.221		
Inattention	Before	14	73.57	11.514	−.492	.631
	After	14	75.79	15.423		
Hyperactivity	Before	14	82.21	11.477	2.804	.015*
	After	14	75.64	12.220		
Emotional liability	Before	14	77.07	11.658	3.706	.003*
	After	14	73.36	10.846		
Impulsivity	Before	14	82.50	9.420	4.112	.001*
	After	14	74.71	9.025		

4. Discussion

This study was conducted on 50 ADHD children, their ages ranged from 6 to 15 years with a mean value of 9 ± 2.2 years, 86% of ADHD children were males and 14% were females, with a male/female ratio of 6.1:1, it is commonly reported in literature to have higher incidence in males than females. Similar to our results ElBaz et al. [16] & Martin et al. [17] revealed that male gender was predominant, at a male-female ratio of 7:1 and Mueller et al. [18] found that ADHD is more common in boys as compared to girls.

In the present study, the inattentive type was 6% of cases while hyperactive type was 28% and mixed type was 66%, this was in agreement with the study done by Hergüner and Hergüner [19] who reported that the frequency of ADHD inattentive, hyperactive and combined type was 36.1%, 3%. was 60.9% respectively.

Twenty percent of the studied ADHD patients had positive history of consanguineous parents, by comparing the 3 subtypes studied ADHD patients: there was no statistically significant differences between them as regards the previously mentioned factor ($p > 0.05$). In agreement with our results, Elbaz et al. [16] stated that there was no statistically significant difference between patients as regards consanguinity, three of the patients were the result of consanguineous marriage and 17 were not. In contrast to our result, Khoushabi et al. [20] found that positive consanguinity was significantly higher in the ADHD cases and Bener [21] also reported that there were statistically significant differences between ADHD and healthy children control subjects as regards consanguineous marriage of parents ($p = 0.019$). Moreover, Hasan et al. [22] revealed that consanguinity increases the risk of having ADHD in the next generation.

The current study showed that 26% of the studied ADHD patients had positive family history of similar disease without statistical significance among the different types of ADHD cases; ($p > 0.05$).Similar to our results, Elbaz et al. [16] found that there was no statistically significant difference between cases and control as regards the family history of similar disease as 35% only had positive family history while 65% had negative family history.

There was statistically significant difference between ADHD subtypes as regards their mode of delivery 56.2% of mixed type cases were delivered by C.S. ($p < 0.05$). In agreement with our results, Amiri et al. [23] suggested that participants born via C-section reported a significantly higher degree of internal restlessness than those born vaginally, which is considered an indicator of ADHD. In contrast to the present study Curran et al. [24] found that no association was found between mode of delivery and ADHD.

There was no statistically significant difference between the 3 subtypes as regards their type of feeding, 78.8% of mixed type were breast fed while 21.2% were formula fed and 92.9% of hyperactive type were breast fed and 7.1% were artificially fed while all inattentive type were breast fed. Against our results, Adesman et al. [25] reported that compared with breastfed infants, ADHD was more common among formula-fed infants. Mimouni-Bloch et al. [26] found that children with ADHD were less likely to be breastfeed at 3 months and 6 months of age than children in the control group. They speculated that breastfeeding may act as a protective factor against developing ADHD later in childhood.

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On comparing between the three types of ADHD cases as regards their anthropometric measures, there was statistically significant difference as regards their weight ($p < 0.05$) as combined type was more obese than other types, while there was no statistically significant difference between them in other parameters as height and body mass index ($p > 0.05$).

Elkins et al. [27] in his study provided meta-analytic evidence for a significant association between ADHD and obesity/overweight. Cortese et al. [12] found that a significant association between obesity and ADHD was found for both children and adults. The pooled prevalence of obesity was increased by about 70% in adults with ADHD compared with those without ADHD and by about 40% in children with ADHD compared with those without ADHD.

There was no statistically significant difference between 3 subtypes of ADHD as regards their maternal illness during pregnancy, NICU admission; ($p > 0.05$). Amor et al. [28] suggested that medical conditions that were more frequent in ADHD included several events occurring during the first 2 months of life: neonatal admission to hospital, having been in an incubator, oxygen therapy, general anesthesia and surgery being the most frequent. Arpino et al. [29] found that an increased risk of this disorder among children born to women experiencing a viral rash during pregnancy in their case-control study conducted to evaluate risk factors for ADHD.

In current study, levels of zinc and ferritin were measured and the deficient patients were supplemented by zinc (55 mg /day) and iron (6 mg/kg/day) for 6 months with assessment of degree of improvement according to their parents Conner's Rating Scores and their Wecsler IQ test before and after treatment.

There was no statistically significant difference in the Wecsler IQ test before and after zinc supplementation. Similar findings were reported by many authors as Pongcharoen et al. [30] showed that Supplementation with iron or zinc or both during infancy does not lead to long-term cognitive improvement in 9-y-old children. Rico et al. [31] also showed that daily supplementation with iron and/or zinc may be of limited usefulness for improving cognition in lead-exposed schoolchildren and there were no consistent or lasting differences in cognitive performance among treatment groups.On the other hand, De Moura et al. [32] found that zinc supplementation significantly increased the VIQ and PIQ scales which indicated that the schoolchildren increased their abilities in long-term memory, and recall, as well as alertness to detail, visual discrimination, planning, logical thinking, social knowledge, spatial analysis, abstract visual problem solving, visual analysis, and construction of objects. Moreover, zinc was more efficient in improving PIQ scores than in improving VIQ scores.

In the zinc deficient group in our study (group1), there was statistically significant improvement in oppositional disorder after zinc supplementation ($P < 0.05$) as regard mild cases became 5 cases instead of 3 before zinc supplementation and moderate cases become 10 instead of 6 and severe cases decreased to 11 instead of 17. In agreement with our result, Üçkardeş et al. [33] found that there was clinically significant improvement in the oppositional behavior in the study group ($p < 0.05$) after supplementation with zinc in dose 15 mg/day for 10 weeks.In contrast, Kordas et al. [34] found that the regimen of supplementation did not result in consistent improvements in ratings of oppositional behavior in lead-exposed children for 6 months with zinc oxide at a dose 30 mg. Their study group was exposed to lead. The toxic substance exposed may also affect the response to zinc supplementation.

We also found that there was statistically significant difference in cognitive problems after zinc supplementation ($P < 0.05$) as regard mild cases become 8 cases instead of 5 before zinc supplementation and moderate cases become 13 instead of 12 and severe cases decreased to 5 instead of 9. Kordas et al. [34] in his double-blind, randomized trial in mixco, 602 first-grade children received 30 mg zinc oxide daily for 6 months, found that at follow-up, parent ratings of cognitive problems decreased.

On comparing between group 1 cases with zinc deficiency in our study as regards inattention subscale, there was highly statistically significant difference after zinc supplementation ($P>0.001$) as regards mild cases became 10 cases instead of 9 before zinc supplementation and moderate cases became 6 instead of 5 and severe cases decreased to 10 instead of 12. Üçkardeş et al [33] study supported these findings, it was done in a low-income district primary school in Turkey, children in each class were randomized either to the study group to receive 15 mg/day elemental zinc syrup or to placebo group to receive the syrup without zinc for 10 weeks. They found that the mean Conner's Rating Scale for Parents scores on attention decreased significantly in the study group after supplementation. Also, Kordas et al. [34] found that at follow-up, parent ratings of inattention decreased. In contrast to our findings, Bilici et al. [35] suggested that zinc sulfate was statistically superior to placebo in reducing both hyperactive, impulsive and impaired socialization symptoms, but not in reducing attention deficiency symptoms.

In our present study, there was statistically significant improvement in hyperactivity after zinc supplementation ($P>0.05$) as regard moderate cases became 6 cases instead of 3 before zinc supplementation and severe cases decreased to 19 instead of 22.In agreement with our results, Biliciet al. [35] in his large randomized clinical trial, 400 children with a primary DSM-IV diagnosis of ADHD (328 boys and 72 girls, mean age 9.6 years) were randomly assigned to a 12-week double-blind treatment with zinc sulfate (150 mg/day, $n = 202$) or placebo ($n = 198$). The children treated with zinc sulfate showed marked improvements in hyperactivity and impulsivity but not inattention, as assessed with the ADHD Scale, Conners' Teacher Questionnaire, and DuPaul Parent Ratings of ADHD.

On the other hand, Kordas et al. [34] reported that zinc seemed to be related to behavior problems and among children with zinc deficiency; those who were supplemented with zinc, the mean oppositional behaviour ratings by parents declined significantly but not hyperactivity.

Also there was statistically significant improvement in emotional liability after zinc supplementation ($P < 0.05$) as regard moderate cases become 7 cases instead of 3 before zinc supplementation and severe cases decreased to 18 instead of 23. Brown et al. [36] reported that a number of zinc-related behavioral abnormalities have also been included as changes in mood, loss of affect and emotional liability, anorexia, dysfunction of smell and taste, irritability, and depression.

We also found that there was statistically significant improvement in impulsivity subscale after zinc supplementation ($P < 0.05$) as regards moderate cases became 1 case instead of 9 before zinc supplementation and severe cases decreased to 16 instead of 21. Similarly, Bilici et al. [35] stated that the children treated with zinc sulfate at dose 150 mg/day for 12 weeks showed marked improvements in hyperactivity and impulsivity. Akhondzadeh et al. [37] also found that zinc either alone or in combination with drug treatment, also seems to improve parent and teacher ratings of ADHD, hyperactivity, or impulsivity.

In our study, in group2 (zinc and ferritin deficient), there was statistically significant improvement in the verbal and total I.Q test before and after zinc (55 mg/day) and iron (6 mg/kg/day) supplementation for 6 months ($P < 0.05$), but there was no statistically significant improvement in performance IQ ($P > 0.05$).

In line with our results, a randomized controlled trial of iron and zinc supplementation in infants was conducted by Pongcharoen et al. [21] in Thailand, 675 infants aged 4–6 months were recruited, of whom 609 completed the study. Infants were randomly assigned

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to 4 groups: 10 mg Fe in the form of ferrous sulfate, 10 mg Zn in the form of zinc sulfate, 10 mg Fe plus 10 mg Zn, or a placebo. Infants received supplements on a daily basis for 6 months, Cognitive performance was assessed by using the Wechsler Intelligence Scale for Children–third edition and found that no significant differences in performance IQ scores were observed between groups, there was also no significant differences in verbal and total IQ scores, also Hermosoet al. [38] found that there was no statistically significant improvement in IQ in an Indonesian study in children who received 2 mg/kg/day iron for 3 months compared to the control group.

In group 2, there was statistically significant improvement in all Conner's rating scale including oppositional, cognitive problems, hyperactivity, impulsivity, emotion liability and inattention subscales after iron and zinc supplementation for 6 months ($P < 0.05$). In Consistent with our findings, Kordas et al. [34] reported that there was also an iron by zinc interaction. Children with Zn deficiency receiving either placebo or the combined treatment had greater declines in mean hyperactive score than the other 2 groups (iron alone and zinc alone). In terms of teacher ratings, children who received iron had a significantly greater decline in mean oppositional scores than children who did not receive iron. On the other hand, children with depleted iron stores at baseline who received iron supplements had greater increase in mean cognitive problem ratings than children who did not get iron.

In Group 3 (zinc and ferritin non deficient) who were on Atomoxetine only, there was no statistically significant difference in their verbal, performance and total I.Q test ($p > 0.05$). In contrast to our study, Yang et al. [39] reported that after 6 months of Atomoxetine treatment, children with ADHD showed significant improvement in FIQ ($p = 0.002$) and PIQ ($p = 0.011$), and in agreement with our results there is a non-significant improvement trend in VIQ.

Also, in group 3 there was statistically significant improvement in their cognitive problems, hyperactivity and impulsivity ($P < 0.05$). Weiss et al. [40], found that Conner's rating total scores were significantly lower for children treated with Atomoxetine compared with those treated with placebo ($p = .001$). Similar results were observed for the inattentive ($p = .016$) and hyperactive/impulsive subscales ($p < .001$). Also Kilincaslan et al. [41] in his study out of 37 participants, 32 completed the 12-week period on ATX. On the ADHD- parent Rating Scale, there were significant reductions between baseline and 4th week, and between baseline and 12th week in total, hyperactivity, and inattention scores. Besides, the difference between baseline and 12th week was also significant in impulsivity. Twenty-one (56.8%) of the patients showed improvement in ADHD total score. The percentage of patients showing improvement in inattention, hyperactivity, and impulsivity scores was 48.6%, 45.9%, and 45.9%, respectively. Moreover, Fujioka et al. [42] reported a significant improvement in ADHD scores during the follow-up period with methylphenidate or Atomoxetine medication for inattentive symptom score, hyperactivity/impulsivity symptom.

There is some evidence that using zinc in combination with stimulant medications will help to improve ADHD symptoms and possibly lead to lower dose requirements, with as much as a 37% reduction in the dose of medication [9].

In our present study we found that dose of Atomoxetine had been decreased in 30 ADHD children after zinc and iron supplementation. While in zinc only deficient group, 21 children (52.5%), Atomoxetine dose had been decreased after zinc supplementation.

Supporting our results, Akhondzadeh et al. [37] in his 6-week randomized, double-blind, placebo-controlled trial, the effects of zinc sulfate (55 mg/day) plus methylphenidate (1 mg/kg/day) were assessed in 44 children with ADHD (26 boys and 18 girls, mean age 7.9 years). Add-on treatment with zinc sulfate resulted in a greater improvement in ADHD symptoms (Teacher and Parent ADHD Rating Scale) than the sole administration of methylphenidate.

5. Conclusion

Based on findings in current study, there is a relevant association between low circulating zinc/ ferritin levels and ADHD in childhood, which suggests the need for regularly monitoring of serum zinc and ferritin levels and treatment of deficient cases with zinc and iron supplements. In addition, life style and diet should be modified and directed towards eliminating the nutritional deficiencies in the society.

Declaration of Competing Interest

The authors declare that they have no competing interests.

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