

## Original Research Article

# Serum magnesium levels in attention deficit hyperactive disorder in 6-17 years age group: a study in tertiary care center

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## ABSTRACT

**Background:** Attention-deficit/hyperactivity disorder (ADHD) is the most common neurobehavioral disorder of childhood and one of among the most prevalent chronic health conditions affecting school-age children. Magnesium is a crucial mineral and appropriate levels in the body are essential for normal cognitive function and mental health. Seventy-two to 96% of those diagnosed with ADHD have been found to be significantly deficient in magnesium. Studies have shown that in these patients, supplementation with magnesium improves attention and working memory and decreases anxiety, depression and emotional dysregulation. Objective of the study was to measure the serum levels of magnesium in children with attention deficit hyperactive disorder and to assess the relation between serum Magnesium levels and Attention deficit hyperactive disorder (ADHD).

**Methods:** The study was conducted at Niloufer Institute of Child Health, which is tertiary care referral hospital and a teaching institute, affiliated under the esteemed Osmania Medical College, Hyderabad. Ethical committee clearance was taken before conducting the study, 50 cases of ADHD are selected from the outpatient department of the Psychiatry clinic for children and adolescents. And 50 controls are also selected for this study. Serum magnesium levels are assessed in both groups.

**Results:** In ADHD group children with serum Magnesium level <1.5 meq/L are 24% whereas in control group it is 6%. When subgroups were analyzed, 25% of hyperactive ADHD group, 18.75% of inattentive ADHD group and 27.27% of combined ADHD group had serum magnesium levels of less than 1.5 meq/l.

**Conclusions:** The study suggest that there is deficiency of magnesium in ADHD children when compared to healthy controls. Further, the study also recommends that further research is needed to help to identify the etiology, impact, and possible therapeutic implications of magnesium status in ADHD.

**Keywords:** Attention deficit hyperactive disorder, Children, Cognitive functions, Mental health, Serum magnesium levels

## INTRODUCTION

Attention deficit hyperactivity disorder is the most common psychiatric disorder in clinical samples of children and adolescents referring to child psychiatric clinics.<sup>1</sup> Attention-deficit/hyperactivity disorder (ADHD) is a common, early-onset and enduring neuropsychiatric disorder characterized by developmentally inappropriate deficits in attention, hyperactivity, increased impulsivity

and emotional deregulation, resulting in impairments in multiple domains of personal and professional life. Studies of the prevalence of ADHD across the globe have generally reported that 9% of school-age children are affected, although rates vary considerably by country, perhaps partly as a result of differing sampling and testing techniques. Rates may be higher if symptoms (inattention, impulsivity, hyperactivity) are considered in the absence of functional impairment. The prevalence

rate in adolescent samples is 2-6%. Approximately 2% of adults have ADHD. ADHD is often under diagnosed in children and adolescents. The incidence of ADHD appears increased in children with neurologic disorders such as epilepsies, neurofibromatosis, and tuberous sclerosis.

Although empirical evidence supports pharmacological and behavioral treatments, side effects and concerns regarding safety and fears about their long-term use contribute to families searching for alternative methods for treating the symptoms of ADHD.<sup>2</sup> About 10% - 30% of patients are not satisfied with stimulants and they do not tolerate stimulants which are widely used for treating ADHD.<sup>3</sup> Moreover, some patients are unresponsive to medications.<sup>3</sup> Therefore, providing better and safer alternative treatments for managing ADHD is highly needed. Evidence for dietary/nutritional treatments of attention-deficit/hyperactivity disorder (ADHD) varies widely; however recommended daily allowance of minerals and essential fatty acids is an ADHD-specific intervention.<sup>4</sup> In the recent years, there are new researches about the etiology of ADHD and diet, their results have shown a healthy dietary pattern, vitamins, and minerals play a role in this disorder. Dietary patterns are very necessary for providing the new idea about different unknown components in metabolic diseases and behavior disorders. Some studies have evaluated the relation between zinc, iron, and magnesium with ADHD.

Magnesium is the fourth most abundant mineral in the body and is essential for good health.<sup>4</sup> The function of more than 325 enzymes is dependent on magnesium.<sup>6</sup> Magnesium interacts with the serotonergic (5-HT(1A) and 5-HT(2A/2C) receptors), noradrenergic (alpha(1)- and alpha(2)- receptors), and dopaminergic (dopamine D(1) and D(2)receptors) systems.<sup>7</sup> Magnesium deficiency is typified by a number of reductions in cognitive ability and processing, and in particular a reduced attention span along with increased aggression, fatigue and lack of concentration.<sup>8</sup> Other common symptoms of magnesium lack include becoming easily irritated, nervousness, and fatigue and mood swings.<sup>9</sup> Given the nature of these symptoms and the significant amount of overlap that they share with ADHD, this has led many experts involved in the treatment and care of ADHD to hypothesize that children who suffer from the condition also have magnesium deficiency as well.<sup>10</sup> Moreover, magnesium helps in generating ATP and energy, disposing brain ammonia, which is related to inattention and converting essential fatty acids into DHA (docosahexaenoic acid), which is related to proper function and structure of brain cells.<sup>10,11</sup> It has an antioxidant effect, where it can decrease the oxidative stress related to pathophysiology of ADHD.<sup>12</sup> Moreover, magnesium can improve sleep disturbance seen in ADHD which may adversely affect the attention.<sup>13</sup>

Previously many studies conducted to assess the magnesium levels in ADHD children. While many

studies reported that the magnesium levels in ADHD are lower than the controls, others reported that its level in ADHD is higher than the controls.<sup>14-22</sup> In the current study, serum magnesium level in children with attention deficit hyperactivity disorder (ADHD) will be compared to normal children.

Objective of the study was to measure the serum levels of magnesium in children with attention deficit hyperactive disorder and to know how much percentage of Attention-deficit/hyperactivity disorder (ADHD) are deficient in serum magnesium levels.

Aim of the study was to assess the relation between serum Magnesium levels and Attention deficit hyperactive disorder.

## METHODS

Children of age group 6-17 years and children in the above age group who are diagnosed Attention Deficit Hyperactive Disorder according to DSM-V criteria were taken as the cases for the study.

### Exclusion criteria for cases

- Age less than 6 years and more than 17 years.
- Children with co-morbid neurological disorders, with chronic organic diseases.
- Those who did not give consent.

Children of same age group who are healthy without any psychiatric or neurological disorder were taken as control for the study.

### Exclusion criteria for controls

- Known case of ADHD.
- Child with any chronic illness.
- Weight for age or height for age <3rd percentile
- Inability to obtain a blood sample after a maximum of 2 venipuncture attempts

Sample size for the cases were 50 and for controls also 50.

This is a hospital based Observational study at Niloufer Institute for Child Health, Hyderabad, for the duration of one year from September 2016 to September 2017 for collection of samples and October 2017 for final analysis and compilation.

Ethics committee approval was taken from the institutional ethics committee of Osmania Medical College. Totally 50 children (age range 6-17 years) were chosen randomly from our Child and Adolescence Psychiatry outpatient department, Niloufer institute of child health, who had a diagnosis of ADHD. Patients were considered eligible for the study if they fulfilled criteria of ADHD according to DSM-V. Fifty healthy

children gathered from the outpatient clinic were included in the study as controls. These children were visiting the outpatient clinic suffering from minor acute illness (common cold, pharyngitis, Acute GE, Immunization, Headache, Minor Dental problems, Pain abdomen) Psychiatric assessment was done for all control participants to exclude ADHD and other developmental conditions. Informed consent was taken from the parent /guardian. The Xerox copy of the information and consent form was provided to parent /guardian. In case, if the parent/guardian is illiterate, we took the signature of a witness who may be a legally acceptable representative or an impartial witness.

Each patient in this study was subjected to the following:

- Full detailed medical history, including presence of organic or psychological diseases,
- Perinatal and developmental history,
- Family history of similar cases, and the history of previous treatment which was received and
- Clinical Examination including; physical examination and neurological examination. Psychometric evaluation was performed by a trained psychologist for both cases and controls.

A blood sample of 2 ml were withdrawn by venipuncture after wrapping the skin by alcohol 70% and centrifuged for serum separation. A colorimetric method was used for magnesium assay. Data was entered in excel spread sheet and was analyzed with IBM SPSS version 19.00. For categorical variables cross tabs were created and chi square test for association was carried out. For continuous variables descriptive statistics and student t test for significant differences in means in both groups were done, p value of <0.05 was taken as significant.

**RESULTS**

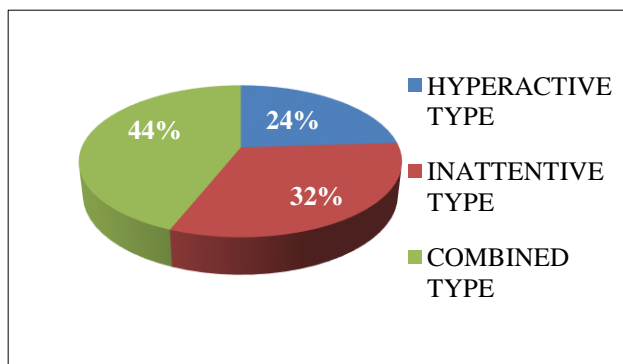
A total of 50 ADHD cases and 50 controls were included in the study. Cases were further classified as Hyperactive, Inattentive and combined type as per the criteria of ADHD according to DSM-V.

**Distribution of cases**

In total 50 cases of ADHD, 12 cases were hyperactive type (24%), 16 cases were inattentive type (32%), and 22 cases were combined type (44%) (Figure 1).

**Table 1: Statistical comparison between cases and controls as regards the personal characteristics.**

Character		Cases No. 50	Controls No. 50	p value	Significance
Age	Range	6-17 yrs	6-17 yrs	0.239	NS
	Mean±SD	8.67±2.62	8.52±2.47		
Sex	Male	34 (68%)	32 (64%)	0.672	NS
	Female	16 (32%)	18 (36%)		
No. of siblings	Mean±SD	1.6±1.3	1.7±0.9	0.7	NS
Order of birth	Mean±SD	2.4±0.8	2.3±0.9	0.4	NS
Residence	Urban	28	36	0.09	NS
	Rural	22	14		
Family history of ADHD	Positive	30	8	0.0006	S
	Negative	20	42		
Consanguinity	Positive	10	12	0.63	NS
	Negative	40	38		



**Figure 1: ADHD cases.**

**Table 2: Distribution of controls.**

URTI	28
Immunization	8
Headache	4
Pain abdomen	3
Acute GE	3
Dental problems	4

**Distribution of controls**

Table 2 shows the distribution of 50 Controls included in the study.

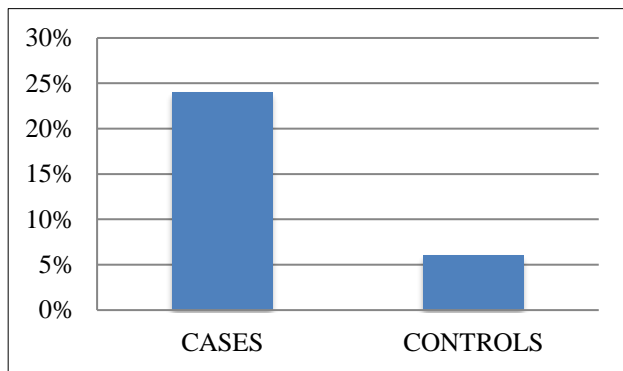
**Table 3: Mean serum magnesium levels in cases and controls.**

Parameter	Cases N=50		Controls N=50		t-test	
	Range	SD	Range	SD	t-value	p value
Serum magnesium	1.69 mEq/L	0.335	1.92mEq/L	0.33	- 3.39	0.001 (S)

**Mean serum magnesium level**

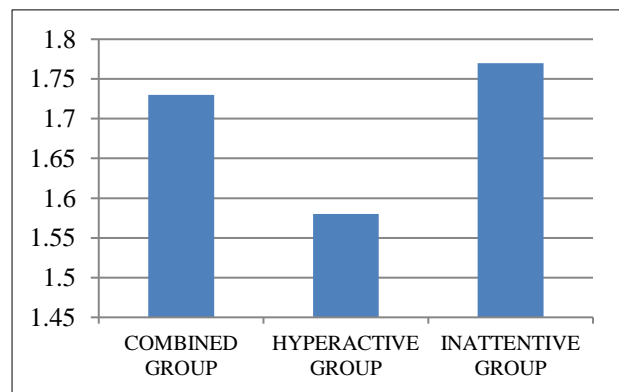
The mean and SD of serum Magnesium levels for cases were 1.69±0.335 (meq/l), whereas for control group were 1.92±0.33 (meq/l) with p value 0.001, which is significant (Table 3).

In ADHD group children with serum Magnesium level <1.5 mEq/L are 24% whereas in control group it is 6% (Figure 4).



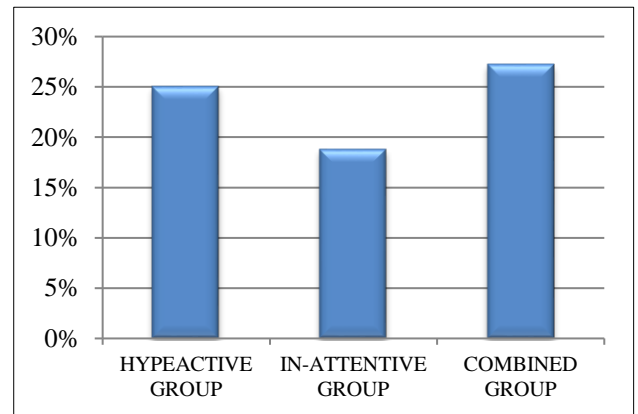
**Figure 4: Serum magnesium levels of <1.5meq/L in subgroups of ADHD.**

Children with ADHD had higher odds (3.89) of being magnesium deficient (cut off point 1.5 meq/l) and the difference was significant (p = 0.0473). Mean values of serum magnesium values in different subgroups of ADHD are as follows Combined group: 1.7±0.33 meq/l, Hyperactive group: 1.58±0.258 meq/l, Inattentive group: 1.77±0.4 meq/l (Figure 5).



**Figure 5: Serum magnesium levels <1.5meq/L in cases and controls.**

In hyperactive group 3 out of 12 children (25%) were having serum magnesium levels <1.5 meq/l. In inattentive group 3 out of 16 children (18.75%) were having serum magnesium levels <1.5 meq/l. In combined group 6 out of 22 children (27.27%) were having serum magnesium levels <1.5 meq/l (Figure 6).



**Figure 6: Serum magnesium levels in subgroups of ADHD.**

**DISCUSSION**

This study aims to measure serum magnesium levels in children with attention deficit hyperactive disorder and comparing it with serum magnesium levels of normal children. This is a hospital based observational study conducted at Niloufer Institute of Child Health. A total of 50 ADHD cases 50 healthy controls were studied in this present study. Cases were diagnosed based on DSM-V criteria and categorized as three subgroups (Hyperactive, Inattentive, combined group).

**Table 4: Comparisons of sample sizes in previous studies.**

Studies	Sample size
Kozielec et al <sup>14</sup>	116 children with ADHD
Mahmoud et al <sup>15</sup>	58 children with ADHD
Farida Elbaz et al <sup>17</sup>	20 children with ADHD
M. Mousain-Bosc et al <sup>20</sup>	40 children with ADHD
Present study	50 children with ADHD

Many other studies were conducted earlier by other authors comparing the levels of serum magnesium in

association with ADHD which are mentioned in (Table 4).

**Age group**

Age group from 6-17 yrs was taken in our study and the mean age was 8.67±2.62 yrs. The mean age of 8.67±2.62 yrs is similar when compared with study done by Mahmoud et al, in which mean age was 8.3±1.8 yrs. In a study conducted by Farida Elbaz the mean age was 7.74±1.48 yrs, which is low when compared to our study.<sup>15,17</sup> In a study conducted by M. Mousain-Bosc et al, the mean age was 6.49 yrs.<sup>20</sup> In the present study healthy children in the age group of 6 - 17 yrs were taken as controls. The mean age of the controls is 8.52±2.47 yrs (Table 5).

**Table 5: Comparisons of age groups between different studies.**

Studies	Age group range	Mean age±SD
Mahmoud et al <sup>15</sup>	5 - 13 yrs	8.3±1.8
Farida Elbaz <sup>17</sup>	6 - 16 yrs	7.74±1.48
M. Mousain-Bosc et al <sup>20</sup>	5 - 12 yrs	6.49
Kozielec et al <sup>14</sup>	9 - 12 yrs	9.89
Present study	6 - 17yrs	8.67±2.62

**Sex**

Out of 50 cases of ADHD in our study, 34 (68%) were male and 16 (32%) were female. In study conducted by Farida Elbaz 80% were male children and 20% were female.<sup>17</sup> In a study conducted by Mahmoud et al, 44.2% were male and 55.8% were female.<sup>15</sup> In a study conducted by Kozielec et al, 81% were male and 19% were female.<sup>14</sup> Male percentage of cases were low when compared to study conducted by Farida Elbaz and Kozielec et al.<sup>14,17</sup> Male percentage of cases were high when compared to study conducted by Mahmoud et al, (Table 6).<sup>15</sup>

**Table 6: Sex distribution in different studies.**

Studies	Males	Females
Kozielec et al <sup>14</sup>	81%	19%
Mahmoud et al <sup>15</sup>	80%	20%
Farida Elbaz et al <sup>17</sup>	68%	32%
M. Mousain-Bosc et al <sup>20</sup>	67.5%	32.5%
Present study	68%	32%

**ADHD subgroups**

Family history of ADHD is seen in 60% of ADHD cases in our study. In a study conducted by Mahmoud et al, family history of ADHD is seen in 65.5% of ADHD cases which is similar to our study.<sup>15</sup>

ADHD cases were categorized in to three subgroups (hyperactive, inattentive, combined type). Out of 50 ADHD cases 12(24%) were hyperactive type, 16 (32%) were inattentive type, 22 (44%) were of combined type. The study conducted by Mahmoud et al, included 32 (55.2%) children with in-attentive type, 10 (17.2 %) children with hyperactive type, 16 (27.6%) children with combined type.<sup>15</sup> In the study proportion of children with in-attentive symptoms is low when compared to study conducted by Mahmoud et al.<sup>15</sup> Proportion of children with combined symptoms (44%) is high when compared to study conducted by Mahmoud et al, (Table 7).<sup>15</sup>

**Table 7: ADHD subgroups.**

ADHD subgroup	Mahmoud et al <sup>15</sup>	Present study
Hyperactive group	27.6%	24%
In-attentive group	55.2%	32%
Combined group	27.6%	44%

**Serum magnesium levels**

In our study mean serum magnesium level in ADHD cases is 1.69 meq/l with a standard deviation of 0.335. In a study conducted by Farida Elbaz the mean serum magnesium level in ADHD cases was 1.62 meq/l with SD 0.48.<sup>17</sup> In the study conducted by Mahmoud et al, the mean serum magnesium level was 1.7 meq/l with SD 0.8.<sup>15</sup> The mean serum magnesium level of ADHD children in our study (1.7±0.335 ) is correlating with the mean serum magnesium level of ADHD children in the study conducted by Mahmoud et al, (1.7±0.8 ).<sup>15</sup> The mean serum magnesium level of ADHD children in the study (1.69±0.335) is high when compared to mean serum magnesium level of ADHD children in the study conducted by Farida Elbaz (Table 8).<sup>17</sup>

**Table 8: Comparisons of mean serum magnesium levels of ADHD children in different studies.**

Studies	Mean serum magnesium levels	SD
Mahmoud et al <sup>15</sup>	1.7 meq/l	0.8
Farida Elbaz <sup>17</sup>	1.62 meq/l	0.48
Present study	1.69 meq/l	0.33

The mean serum magnesium level of controls in our study is 1.92 meq/L with standard deviation 0.33. The mean serum magnesium level of controls in the study conducted by Mahmoud et al, is 2.2±0.9 (Mean±SD).<sup>15</sup> The mean serum magnesium level of controls in the study conducted by Farida Elbaz, is 2.56 meq/l.<sup>17</sup> Mean serum magnesium level of controls (1.92 meq/l) is low when compared to studies conducted by Mahmoud et al, and Farida Elbaz (Table 9).<sup>15,17</sup>

The mean serum magnesium level in ADHD children (1.69±0.335 meq/l) is significantly low when compared



to mean serum magnesium level of controls (1.92±0.33 meq/l) with a “p” value of 0.001 (significant) in our study. Children with ADHD had higher odds (3.89) of being magnesium deficient (cut off point 1.5 meq/l) and the difference was significant (p = 0.0473). Although it is difficult to assume causality in this cross sectional study, it seems more likely that poor body magnesium status was as causal factor that increased ADHD than that ADHD induced low serum magnesium level (Table 10).

**Table 9: Comparisons of mean serum magnesium levels of controls in different studies.**

Studies	Mean serum magnesium levels in controls	SD
Mahmoud et al <sup>15</sup>	2.2 meq/l	0.9
Farida Elbaz et al <sup>17</sup>	2.56 meq/l	0.9
Present study	1.9 meq/l	0.33

**Table 10: Mean magnesium levels in cases and controls in different studies.**

Studies	Cases mean	Controls mean	p value
Mahmoud et al <sup>15</sup>	1.7±0.8	2.2±0.9	0.02
Farida Elbaz et al <sup>17</sup>	1.62±0.48	2.56±0.9	<0.001
Present study	1.69±0.335	1.92±0.33	0.001

In the study 24% of the ADHD children having serum magnesium values less than 1.5 meq/l. In a study conducted by Kozielc et al, serum magnesium deficiency was found in 33.6% of ADHD children.<sup>14</sup> The mean magnesium level in hyperactive subgroup is 1.58±0.258 (meq/l) and in combined group is 1.7±0.316 meq/l, and in in-attentive group is 1.77±0.4 meq/l. The mean serum magnesium level in subgroups is significantly low when compared to control group. In a study conducted by Mahmoud et al, the mean serum magnesium level in hyperactive group was 1.4 meq/l, and that of combined group was 1.3 meq/l, and in in-attentive group was 2.02 meq/l (Table 11).<sup>15</sup>

**Table 11: Mean magnesium levels in ADHD subgroups.**

Mean serum magnesium levels in different subgroups	Mahmoud et al <sup>15</sup>	Present study
Hyperactive	1.4 meq/l	1.58±0.258 meq/l
In-attentive	2.02 meq/l	1.77±0.4 meq/l
Combined	1.3 meq/l	1.7±0.316 meq/l

In agreement with other studies, magnesium levels were significantly lower in both children with hyperactive and combined types than in controls and this may be due to the role of magnesium in protecting cell membranes from excitatory neurotransmitters such as glutamate. Riley et al, reported that preschool children with hyperactive and

combined types of attention deficit hyperactivity disorder demonstrated similar levels of functioning and they suggested that hyperactive type may represent an earlier form of combined type.<sup>23</sup> This supports our results as both children with hyperactive and combined types were lower magnesium levels than controls. In the study conducted by Mahmoud et al, the mean serum magnesium level in inattentive group is 2.02 meq/l which is not significantly low when compared to controls.<sup>15</sup> In our study mean serum magnesium values in inattentive group is also low. Bosc et al, and Mousain et al, reported that magnesium/vit.B6 intake reduces central nervous system hyper-excitability in children with attention deficit hyperactivity disorder and this supports our results as magnesium levels were significantly lower in both hyperactive and combined types.<sup>20,24</sup>

Findings in the study are in agreement with previous studies conducted by Kozielc et al, Farida elbaz et al, Mahmoud et al.<sup>14,15,17</sup> These studies suggest that there is deficiency of magnesium in ADHD children when compared to healthy controls. Further research is needed to help to identify the etiology, impact, and possible therapeutic implications of magnesium status in ADHD.

**CONCLUSION**

The study concludes that the mean serum magnesium level in ADHD children (1.7 ± 0.335 meq/l) is significantly low when compared to mean serum magnesium level of controls (1.92 ± 0.33 meq/l) with a p value of 0.001 which is significant. Children with ADHD had higher odds (3.89) of being magnesium deficient (cut off point 1.5 mg/dl) and the difference was significant (P = 0.0473). Low serum magnesium levels (cut off < 1.5 meq/l) are seen in 24% of ADHD children. However, this study could not establish a cause effect relationship between low serum magnesium levels and ADHD as it is not a prospective study. Hence, there is need for prospective randomized trials in this field to establish cause effect relation between magnesium and ADHD.

One limitation in the study was author could not do hair magnesium levels, which is more indicative of body magnesium levels. Further we recommend that there is also a need for further studies to know the therapeutic role of magnesium in ADHD.

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