e-ISSN: 0975-1556, p-ISSN:2820-2643

Available online on www.ijpcr.com

International Journal of Pharmaceutical and Clinical Research 2023; 15(2); 1227-1233

Original Research Article

A Hospital-Based Assessment of the Association between Serum Vitamin D and Serum Ferritin Levels in Children with ADHD

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Received: 01-10-2022 / Revised: 06-11-2022 / Accepted: 11-01-2023
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Conflict of interest: Nil

Abstract

Aim: The aim of the study was to study the association between Serum Vitamin D and Serum Ferritin levels in children with ADHD.

Methods: The study was conducted in the Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India for the period of 1 year. A total of 60 children meeting the inclusion criteria were enrolled in the study. Subjects included all new or follow-up patients with diagnosed or suspected ADHD and healthy children of the comparable sex and age group attending the pediatric outpatient department (OPD) were taken as controls. Informed and written consent was taken from parents and assent from children above 12 years of age to participate in the study.

Results: 25 cases were diagnosed with ADHD and their results were compared to age and sex matched controls. Serum Ferritin and Vitamin D levels were measured in both cases and controls. Since we matched age, similar age distribution was present in controls. The study found a significant difference in the mean value of serum ferritin levels in cases and controls (p−0.035). No significant difference in the mean value of serum Vitamin D in cases and controls (p–0.550) was noted.

Conclusion: ADHD is a common neurobehavioral disorder presenting in pediatric OPD with higher prevalence in males than females. Combined type was found to be the most dominant type of ADHD in the study population. We observed a significant difference in the levels of Serum Ferritin in children with ADHD and controls.

Keywords: Attention Deficit Hyperactivity Disorder, Iron, Vitamin D.

Introduction

Attention deficit hyperactivity disorder (ADHD) is one of the most prevalent mental health disorders that affect about 5.3–7.1 percent of children and adolescents. [1] Attention deficiency, hyperactivity and impulsivity are three main symptoms that help diagnose the disorder before the age of twelve years. [1,2] Besides, other accompanying secondary symptoms such as aggression, social incompetence, conflict with peers and anti-social behavior other clinically important symptoms. [2,3] So far, drug therapy is the main treatment method. However, there are limitations in drug interventions. For instance, 30 percent of ADHD children do not respond to the drug treatment. [4,5] More effective treatment

and strategies are needed to control the disease. [6,7]

Micronutrients have imperative roles in neurologic function, including involvement in neurotransmitter synthesis. Iron deficiency is one of the most common cause of anemia in India A decrease in iron concentration causes changes in the normal brain functioning such as changes in conduction of cortical fibers, changes in serotonergic, and dopaminergic systems, as well as in the formation of myelin. [8,9] Iron deficiency impairs cognitive and behavioral functions and is linked with symptoms such as poor attention and hyperactivity. [10] Iron also is a coenzyme of tyrosine hydroxylase, which is required for dopamine synthesis and its degradation. It has been found that iron deficiency is linked with decreased expression of D2 and D4 receptors and dopamine transporter in the brain. [11] These changes in neurotransmitter changes along with basal ganglia dysfunction are believed to be the etiopathogenesis of ADHD. [12] Vitamin D is a versatile hormone with a major role in calcium and bone metabolism but also plays part in cardiovascular, immune, endocrine, and psychiatric diseases. [13] It is important for cerebral function and thought to have a neurotropic and neuroprotective effects. It is important in cerebral function and its deficiency may have role in the etiopathogenesis of ADHD. Vitamin D alters the neurotrophic factors and monoamine levels, facilitating the oxidative stress responses, and changes in neurotransmitters. Vitamin D deficiency, therefore, results in changing in abnormal dopamine regulation, linking it to have a role in etiopathogenesis of ADHD. [14]

Vitamin D receptors and 1α-hydroxylase enzyme are responsible for the formation of the active form of Vitamin D, and these are found to be widely distributed in the central nervous system, mainly in the neuronal cells of the substantia nigra, hippocampus, hypothalamus, prefrontal cortex, and cingulated gyrus. [14-16] Most of these regions have seen to be associated in the pathogenesis of ADHD. [16,17] Recommended treatment for ADHD is multimodal including medication, parent training, skills training counseling, behavioral therapy, and educational support. Despite treatment only 30–70% of patients respond to currently available ADHD therapies. [18]

The aim of the study was to study the association between Serum Vitamin D and Serum Ferritin levels in children with ADHD.

Materials and Methods

The study was conducted in the Department of Pediatrics, JLNMCH, Bhagalpur, Bihar, India for the period of 1 year. A total of 60 children meeting the inclusion criteria were enrolled in the study. Subjects included all new or follow-up patients with diagnosed or suspected ADHD and healthy children of the comparable sex and age group attending the pediatric outpatient department (OPD) were taken as controls. Informed and written consent was taken from parents and assent from children above 12 years of age to participate in the study.

Diagnosis of ADHD was confirmed. This step was in two-fold- (a) Using child behavior checklist (CBCL) – to rule out other behavior abnormalities. (b) Using INCLEN diagnostic tool for ADHD [INDT-ADHD] for confirmation of ADHD. [19] Blood sample was taken for all the subjects under all aseptic techniques and samples were analyzed for serum ferritin and serum Vitamin D estimation.

Inclusion criteria for cases

The following criteria were included in the study:

1. Any child aged between 6 and 15 years diagnosed with

ADHD

1. Any child attending regular schools

Inclusion criteria for controls:

1. Children aged between 6 and 15 years presenting to OPD.

The following criteria were excluded from the study:

1. Any child with seizures.
2. Any child with acute febrile illness.
3. Any child with intellectual and neurological impairment.
4. Any child with other psychiatric disorder.
5. Any child with a chronic systemic disease.
6. Any child on stimulant medication.
7. Any child treated for rickets.
8. Any child taking iron or Vitamin D supplements.

Study Tools

Case recording form, CBCL - Child Behavior Checklist, INCLEN diagnostic tool for ADHD [INDT-ADHD], Serum Ferritin estimation: Enzyme Linked Fluorescent Assay technique through VIDAS, Serum Vitamin D estimation: Enzyme Linked Fluorescent Assay via VIDAS Study.

Data Management and Statistical Analysis: The data were collected and entered in MS excel 2010. Different statistical analysis was performed by using statistical package for the social sciences software version 22. The one sample Kolmogorov–Simonov test was employed to determine whether the data sets differed from a normal distribution or not. Normally distributed data were analyzed using parametric tests and non-normally distributed data were analyzed using non-parametric tests. Descriptive statistics was calculated for quantitative variables. Frequency along with percentages was calculated for qualitative and categorical variables. Categorical data were analyzed using chi square test/Fisher Exact test. Student's t-test was used for comparison of quantitative data. Value of $p<0.05$ was said to be statistically significant and $p>0.05$ was said to be statistically insignificant.

Results

Table 1: Age and gender-wise distribution of children

Age group (Years)	Gender	Cases n=25	Controls n=25
6–9	Male	10	8
	Female	5	6
10–12	Male	3	5
	Female	4	3
13–15	Male	3	2
	Female	2	1

25 cases were diagnosed with ADHD and their results were compared to age and sex matched controls. Serum Ferritin and Vitamin D levels were measured in both cases and controls. Since we matched age, similar age distribution was present in controls.

Table 2: ADHD result on INCLEN tool

Subtype of ADHD	No.	Percentage
Hyperactivity	7	28
Inattention	8	32
Combined	10	40

40% cases were having combined ADHD as compared to hyperactivity and inattention.

Table 3: Serum Ferritin levels and Vitamin D levels in cases and controls

Serum Ferritin levels	Cases n=25	Controls n=25	P value
High	0	4	0.035
Low	11	6	
Normal	14	15	
Vitamin D levels			
Low	20	21	0.550
Normal	5	4	

The study found a significant difference in the mean value of serum ferritin levels in cases and controls (p−0.035). No significant difference in the mean value of serum Vitamin D in cases and controls (p–0.550) was noted.

Table 3: Mean value of S. Ferritin and S. Vitamin D in different subtypes of ADHD

	Inattentive type (n=8)	Hyperactive type (n=7)	Combined type (n=10)	P value
S. Ferritin (ng/ml)	33.49±31.79	24.98±20.38	37.88±40.50	0.680
S. Vitamin D (nmol/L)	35.45±18.01	37.93±13.67	39.74±17.20	0.820

The mean value of serum ferritin levels in cases was observed to be in inattentive type 33.49±31.97 ng/ml, in hyperactive was 24.98±20.38 ng/ml and in combined 37.88±40.50 ng/ml. The mean value of serum ferritin levels in cases was observed to be in inattentive type 35.45±18.01ng/ml, in hyperactive was 37.93±13.67 ng/ml and in combined 37.88±40.50 ng/ml. The difference was non-significant.

Discussion

Despite being one of the most studied psychiatric disorders, the exact cause of ADHD is still unknown; both genetic and environmental risk factors contribute to the development of ADHD. [20] Iron deficiency is considered a potent cause of poor cognitive impairment, learning disabilities, and psychomotor instability [21], which also supports the hypothesis that iron deficiency may play a role in the pathophysiology of ADHD. [22]

In our study, the prevalence of ADHD in children with age group 6–9 years was more than in adolescent age children. It was 50% in school going children of 6–9 years, 28% in early adolescents (10–12 years) and 22% in middle adolescents (13–15 years of age). This was in agreement with Bener et al. [23] and Hassan et al. [24] who observed prevalence of ADHD to be more in school age children of 6–9 years than adolescents. Ramtekkar et al. [25] also in their study found the mean age of ADHD to be 7–12 year.

Serum ferritin levels are a dependable measure of iron stores in the body tissues and its levels are an early precursor of iron deficiency. Also binding of exogenous ferritin to cell receptors is important pathway for delivery of iron in brain tissue. Low ferritin levels are highly specific for iron deficiency. [26] The range of normal values of ferritin as set by out laboratory was 20–165 ng/ml; therefore, cutoff for low ferritin was set at values <20 ng/ml. We found 44% of cases and 28% of controls to have low ferritin levels.

In our study, 80% of cases and 84% of controls had low levels of Vitamin D. Mean value of vitamin D was 37.77±16.05 nmol/L in cases and 63.87±116.43 nmol/L in controls. We observed slightly lower mean value in cases as compared to controls but the difference was not statistically significant. We found no association between Vitamin D levels and ADHD. On assessing mean Vitamin D values among different subtypes of

ADHD, lowest value was observed in cases with Inattentive type ADHD (33.49±18.01 nmol/L), followed by hyperactive type (37.93±13.67 nmol/L) and combined types (39.74±17.20 nmol/L). The difference observed in the mean values of Vitamin D was not statistically significant. No association was found between Vitamin D and subtypes of ADHD. Deficient levels of Vitamin D in majority of both cases and controls could be explained by higher prevalence of vitamin D deficiency in apparently healthy Indian children as shown in study done by Angurana et al. [27]

Kamal et al. [28] too observed a significantly lower level of Vitamin D in children in ADHD than controls (7.6 vs. 4.6%). Elshorbagy et al. [29] found a greater incidence of Vitamin D deficiency in children with ADHD than controls and proved that supplementation of Vitamin D to children with ADHD can cause an improvement in symptoms of ADHD. Like our results, Gustafsson et al. [30] found no significant difference in cord blood Vitamin D concentration between children with ADHD and controls. There were some limitations to the study. [31] The predetermined sample size could not be taken due to decreased OPD visit of patients during the COVID-19 pandemic. This could lead to underestimation of prevalence of ADHD. Sample size of the study was also not sufficient to establish a causal relationship of S. Ferritin and S. Vitamin D with ADHD. Serum Ferritin levels although being a reliable marker of iron stores in the body its level could be elevated in conditions other than increased iron stores, such as acute inflammatory conditions, cancers, Hemophagocytic lymphohistiocytosis, and hemochrom - atosis. [26]

Conclusion

ADHD is a common neurobehavioral disorder presenting in pediatric OPD with higher prevalence in males than females. Combined type was found to be the most dominant type of ADHD in the study population. We observed a significant difference in the levels of Serum Ferritin in children with ADHD and controls. There was seen an association between low levels of serum ferritin and ADHD. Therefore, levels of S. Ferritin should be measured in children with ADHD.

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