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CORRELATION OF SERUM FERRITIN, CALCIUM AND MAGNESIUM LEVEL IN CHILDREN WITH ADHD

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ABSTRACT

INTRODUCTION

Impaired functions, be it cognitive or motor skills are developed since the early childhood stage of life; wherein other skills like language as well as social skills are assimilated by their surrounding environment and their interactions with the same. Attention Deficit Hyperactivity Disorder is written off as unpredictable sternness in attention deficit levels and hyperactivity, which is associated with neurodevelopmental ailments, which has escalated steeply over the past era.

AIMS & OBJECTIVES

To evaluate & compare levels of Serum Ferritin, Serum Magnesium and Serum Calcium in children presenting with ADHD.

MATERIALS & METHODS

Our study consisted of two groups with 30 patients in each group (study & control), who were evaluated for Serum Ferritin, Serum Magnesium and Serum Calcium levels.

RESULTS

The mean Serum Ferritin levels in the case and study group was found to be 45.68 ± 27.16 & 56.14 ± 30.40 respectively and the mean Serum Calcium levels in the case and study group was found to be 9.04 ± 0.76 & 9.05 ± 0.60 respectively. Further, the mean Serum Magnesium level in the case and study group was found to be 2.01 ± 0.37 & 2.06 ± 0.30 respectively.

CONCLUSION

Therefore, we conclude that serum levels of ferritin, calcium and magnesium are elevated in ADHD patients and can be used as reliable markers to assess the status of the affected individual. These minerals have shown a significant

increase in the group, however there remains a need for additional studies to provide substantial evidence to make them a reliable diagnostic marker.

Keywords

Attention, Hyperactivity, Disorientation, Psychology, Cognitive skills, Anxiety

INTRODUCTION

Attention-deficit hyperactivity disorder (ADHD) is characterized by impaired levels of inattention, hyperactivity, or impulsivity, or a combination that is not congruent with age-appropriate behaviour.¹ About 5% of children aged ≤ 18 years² and 2.5% of adults are affected worldwide.³ DSM V recommends that ADHD should not be diagnosed if another disorder can explain the presenting symptoms in a child, therefore, ADHD continues to be a diagnosis of exclusion.¹

Attention Deficit Hyperactivity Disorder is written off as unpredictable sternness in attention deficit levels and hyperactivity, which is associated with neurodevelopmental ailments, which has escalated steeply over the past era.⁴

The fundamental causative factors responsible for ADHD remain multifaceted, with a single factor alone not clearly established with presently available data.⁵ ADHD is most commonly noted in individuals who have low academic as well as social development associated with learning disabilities. Further at the social level, they have low self-esteem with compromised emotional encumbrance levels.²

Common risk factors attributable to ADHD include low birth weight, preterm delivery, exposure to noxious waste like organophosphates, polychlorinated biphenyls, lead, artificial dye ores and substance abuse can also play a role.⁵

Behavior patterns, if ignored at an early stage or delays in initiation of any treatment can lead to progression of unwanted changes which may not be reversible in nature. Therefore, an early intervention is highly beneficial and recommended in most of the cases to improve overall quality of life.

Several studies have tried to explore the relationship between serum calcium and magnesium values in ADHD with varying results. A study done by Altun vermis et al. found out that the serum values of calcium and magnesium were significantly higher in children with ADHD ⁶. Another study done by Skalny et al, found out that there was no significant difference in serum magnesium levels in children with and without ADHD ⁷. A study by Villagomez et al, also suggest that children with ADHD present with a deficiency of iron, calcium and magnesium ⁴.

Through our study, we aim to evaluate the serum ferritin, serum magnesium and serum calcium levels in children between 3 to 15 years of age in South India who were diagnosed with ADHD and compare the results against controls.

AIMS AND OBJECTIVE(S) OF THE STUDY

1. To determine Serum Magnesium, Serum calcium & Serum Ferritin Levels in children diagnosed with Attention-deficit/Hyperactivity disorder.
2. To compare Serum Magnesium, Serum calcium & Serum Ferritin Levels in children presenting with Attention-deficit/Hyperactivity disorder and normal children

MATERIALS & METHODS

It is a prospective study done at Rajarajeshwari medical college & hospital on in-patients admitted at ward and out-patients presenting to department of paediatrics.

Study Setting: Rajarajeshwari Medical College and Hospital (RRMCH)

1. Outpatients presenting to the Department of Pediatrics, RRMCH
2. Inpatients admitted in the wards of the Department of Pediatrics, RRMCH

Study Population: Children between the ages of 3 to 15 years

Study Period: August 2019 to July 2021

Selection Criteria:

Inclusion Criteria:

1. Children who are diagnosed with ADHD & who are willing to participate in the study
2. Parent or Guardian of those children within the age group: 3 - 15 years consenting to the study.

Exclusion Criteria:

1. Children suffering from Chronic Liver Diseases & Chronic kidney diseases .
2. Children who are currently on Anti-Epileptics medication such as Sodium Valproate and Carbamazepine & who are taking Iron, Calcium, Magnesium and/or Vitamin D supplements.

Methodology

DataCollection:

60 subjects were chosen based on the inclusion and exclusion criteria. Written informed consent was obtained from the parents'/guardians' of the selected subjects, in the language of their understanding, after explaining the nature and purpose of the study.

These 60 patients were further divided into two groups:

1. Study Group: consisting of 30 patients who were diagnosed with ADHD
2. Control Group: 30 patients who do not have ADHD

4 ml of blood was drawn in a plain bulb under aseptic precautions. The blood sample was evaluated for Serum Iron, Magnesium and Calcium levels; which was analyzed by the Beckman Coulter Immunoassay Assay, Rajarajeshwari Hospital Laboratory.

RESULTS

In our study the mean age of the patients in the case and control group was found to be 6.70 ± 2.38 & 6.66 ± 2.42 respectively, with 70% of the patients being predominantly males

Mean levels:

Value Tested	ADHD Group	Control Group
Serum Ferritin levels	45.68 ± 27.16	56.14 ± 30.40
Serum Calcium levels	9.04 ± 0.76	9.05 ± 0.60
Serum Magnesium levels	2.01 ± 0.37	2.06 ± 0.30

Mean levels	Mild Case Group of ADHD	Moderate Case Group of ADHD	Severe Case Group of ADHD
Serum Ferritin	48.02	51.67	21.36
Serum Calcium	8.94	9.24	8.95

Serum Magnesium	2.01	2.04	1.95
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Mean Levels	Combined Presentation of ADHD	Predominantly hyperactive	Predominantly attention deficit
Serum Ferritin	45.13	47.76	61.58
Serum Calcium	9.05	9.56	8.25
Serum Magnesium	2.08	2.16	1.85

On further Correlation analysis, it was observed that Serum Ferritin, Serum Calcium & Serum Magnesium with ADHD Index T Value Score were 0.20 and 0.03 in case and control groups respectively.

DISCUSSION

Iron deficiency is the most predominant nutritional deficit with data suggesting that it is responsible for augmented risk of psychiatric disorders along with attention deficit hyperactivity disorder.⁸

Enormous research has been carried out to find out if anomalies in serum iron levels can cause ADHD, but there is no conclusive evidence. Even though there are reduced serum iron levels in ADHD children, the controversy exists that these reductions are noted after the initiation of the disease process rather than being the causative factor of the disease process. The difference in mean serum ferritin levels between cases and controls in our study were found to be statistically insignificant.

Similar results were noted in the study done by Bener et al, wherein serum ferritin levels in cases were found to be lower in comparison to that assessed against the control group⁹.

During further analysis, we found an increase in the serum ferritin levels at the moderate stage of the disease process, however a significant drop was noted in the serum ferritin levels in the severe stage of the disease process. Even though there is minimal data available to understand the cause of the depletion.

Analysis of serum ferritin levels showed lowest ferritin levels in combined presentation, followed by the patients who were predominantly hyperactive. However, the patients who were predominantly inattentive, there was a significant increase for which the cause remains unknown.

In another study done by Sever et al⁸, wherein the correlation between iron deficiency and ADHD was studied, it was concluded that management with 5 mg/kg of iron amongst 14 ADHD children for 30 days, led to elevated serum ferritin level and reduced levels of ADHD on Conner's Rating Scale using standardized assessment tools.^{10,11,12}

The mean serum calcium levels showed only a miniscule difference amongst the groups but lower in the ADHD study group. On evaluation of the calcium levels in the predominantly hyperactive and predominantly inattentive groups, there was a marked drop in the serum calcium levels in the

inattentive group in comparison to that of the children who were predominantly hyperactive, which can be hypothesized as impaired or reduced activity of the child due to reduced calcium levels, as we all know that calcium plays a vital role in many activities in the body and also in the neurological conduct system of the body.

Similarly in another study done by Bener et al., the calcium levels were found to be reduced in the study group in comparison to the control group.⁹

Magnesium is a mineral; highly nutritive in nature which helps in development of cognitive function, whose impairment may manifest in the form of mood swings, lack of concentration, nervousness and fatigue.¹³

In our study, the mean serum magnesium levels were found to be lower in patients with ADHD when compared to controls. Further, the magnesium levels were found to be lowest in patients with severe forms of ADHD. In the severe stage, the patient shows increased impairment of cognitive function which can be correlated but the exact pathogenesis remains inconclusive.

A meta-analysis conducted by Effatpanah et al., amongst children and adolescents with ADHD found similar results.¹⁴ In another study across France, the results were in accordance with our study wherein the study group showed lower magnesium levels.^{15,16,17}

In a study conducted in Egypt, serum magnesium levels were significantly lower in children with hyperactive and combined type ADHD. However, there were no differences noted in children with ADHD-inattentive type.

However, we hypothesize that the depleted magnesium levels lead to reduced synthesis of fatty acids, decreased reactions in the body and increased storage within the bone leading to reduced levels in the muscles and blood which hamper the muscle activity and brain function of the individual. The higher levels of serum magnesium can be thought of as an attempt to restore the serum magnesium levels back to normal.

On evaluation of the magnesium levels in the predominantly hyperactive and predominantly inattentive groups, there was a marked drop in the serum magnesium levels in the inattentive group in comparison with children who were predominantly hyperactive, which can denote reduced cognitive activity of the child due to reduced magnesium levels.

A systematic review determined that serum/plasma magnesium concentration, red blood cell concentrations (RBC-mag), and urinary magnesium can be used to evaluate the status of magnesium and supplementation of the same in the deficient part helps to show its efficacy as a diagnostic test.¹⁸ Baza et al., in his study tried the management of ADHD with magnesium supplements and apparently found improvement in the clinical symptoms.¹⁹

Our study clearly showed that there was a significant drop in the serum calcium, magnesium and ferritin levels in the severe stage of the disease process and also in individuals who were inattentive in nature in comparison to the other group individuals. However there were elevated levels noted across all the minerals in the hyperactive individuals. This shows that these minerals can be used as diagnostic parameters to diagnose as well as stage the disease process.

Management of ADHD, still remains a controversy but the most common treatment protocol includes medications to improve the symptoms of ADHD in no combination with psychological counseling, which is followed by continuous reinforcement to obtain the maximum effect. However, these traditional treatments have not provided with the best results and the search for alternative therapies for management of ADHD, and the research to understand the causative factors and influencing the disease process remains at bay.^{20,21}

The four most common factors cited for ADHD & its progression are delayed reach to the professional, stigma, ignorance, and lack of access to specialized care.²²

It is also important to provide training with respect to ADHD especially for the pediatricians, general practitioners (GPs), teachers, and the social workers. Further to address the concerns and acceptability of the parents at a very early stage it is important to educate the families in relation to the symptoms and their management levels.²²

CONCLUSION

Diagnostic markers have been vital in prediction of the disease process and assessment of the same. However, it becomes difficult to use them as a precise marker without substantial evidence. Therefore, we conclude that serum ferritin, calcium and magnesium levels are elevated in ADHD patients and can be used as reliable markers to assess the status of the affected individual. These minerals have showed a significant increase in the group but nonetheless there remains a need for more studies to provide substantial evidence to make them a reliable diagnostic marker.

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