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Vitamin D Deficiency in Patients with Attention Deficit Hyperactivity Disorder

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Author's contribution

The sole author designed, analyzed, interpreted and prepared the manuscript.

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Short Research Article

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ABSTRACT

Objective: This study aimed to investigate the connection between childhood Attention Deficit Hyperactivity Disorder (ADHD) and the level of Vitamin D in the blood.
Materials and Methods: The study was undertaken in 2018 on children in the age group of 4-13 years. Twenty two children diagnosed with ADHD were selected, along with a control group comprising twenty two healthy children showing no symptoms of ADHD or any other neurological disorder or liver or kidney disease or any endocrine problem. Anyone using Vitamin D supplements was excluded from the study. Venous blood samples were acquired from the subjects and serum Vitamin D level was measured.
Results: The mean average level of Vitamin D in the research subjects exhibiting ADHD (18.60±6.33 ng/ml) was found to be lower than the control group (34.34±8.19) (*P-value* < 0.0005).
Conclusions: This study has shed some light on the role played by Vitamin D in maintaining the antioxidant status of the brain. The study has shown that the Vitamin D is much lower in children diagnosed with ADHD. Vitamin D increases the expression of the enzyme, Gamma-Glutamyl Transferase (GGT). This enzyme is involved in the metabolism of Glutathione, which is considered an important antioxidant in the brain.

Keywords: ADHD; glutathione; neurological disorder; Vitamin D.

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1. INTRODUCTION

Attention-Deficit Hyperactivity Disorder (ADHD) is a neurological disorder diagnosed on the basis of hyperactivity, inattention and impulsivity. There is no way to detect ADHD by laboratory tests at present and the diagnosis is based on observation of certain behavioral symptoms. It is known from previously published literature that Attention-Deficit Hyperactivity Disorder (ADHD) has a prevalence of 5.3-7.1% among children and adolescents [1]. Before the age of 12, ADHD is characterized by three main symptoms: attention deficiency, impulsivity, and hyperactivity [1,2]. Aggression, anti-social behavior, conflict with peers, and social non adjustment are also clinical symptoms of ADHD [2,3]. At present, the primary treatment method is drug therapy but this has limited success since 30% of patients do not respond to therapy (Fig. 1). Hence, more effective strategies are required [4,5].

ADHD is less common in those parts of the world that receive plenty of sunshine [6]. Exposure to sun and phototherapy are used as treatments for ADHD [7,8]. Numerous studies have investigated the role of nutrition also in the development of ADHD. These studies have found that vitamins and minerals present in breast milk are essential for the newly born child. They protect the child from developing neurological disorders [9-12]. Lately, the attention of researchers has been drawn to the role played by nutrition in the treatment of ADHD as well [10-13]. Many studies have tried to understand the role of micronutrients such as iron [14-16], omega-3 fatty acids [17] and zinc [18,19] in the control and prevention of symptoms of ADHD (Fig. 2). Unfortunately, the role of Vitamin D has been ignored in these studies even when Vitamin D deficiency is known to be associated with various neurological disorders [20-22]. Vitamin D deficiency is common in the Persian Gulf countries despite the easy availability of sunlight. The findings from a previously conducted study have shown that 80% of young girls in Saudi Arabia suffer from Vitamin D deficiency [23].

An important role played by Vitamin D is in the regulation of serum Calcium level in the body. However, it also plays a significant role as signal second messenger in many organs of the body. Hence, it is recommended that Vitamin D levels be checked regularly for pregnant women and newly born babies [24]. The deficiency of Vitamin D, during fetal development, accounts for a number of post-natal neurological disorders [25] (Fig. 3). Additionally, it has been hypothesized that the lack of Vitamin D in both the developing baby and the newly born child adversely affects the development of the brain [25]. The current study was conducted to measure serum Vitamin D levels in children diagnosed with ADHD.

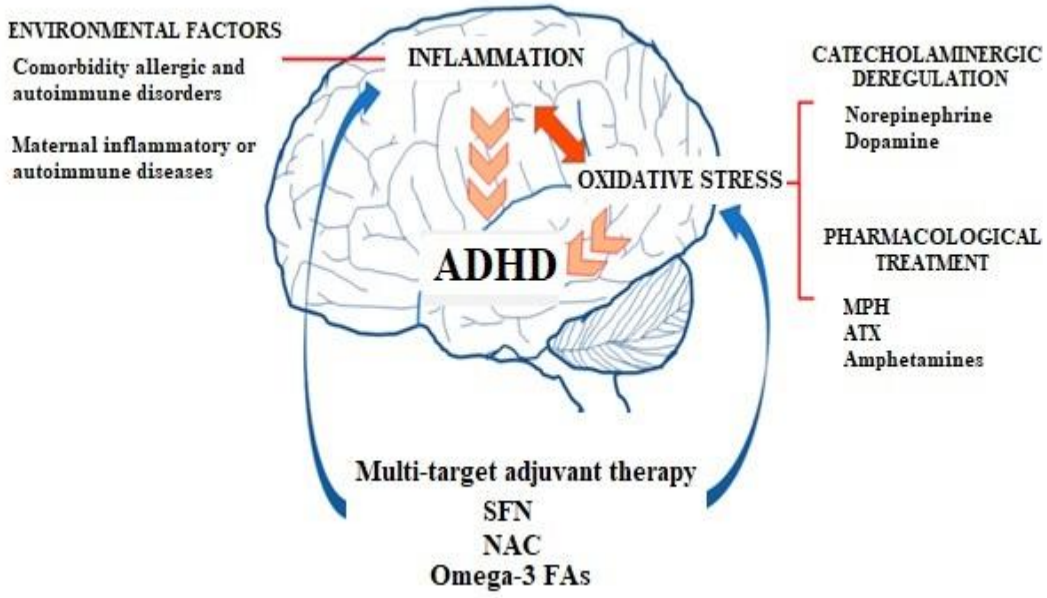

Fig. 1. Summary of the factors that can lead to ADHD and its current treatment options

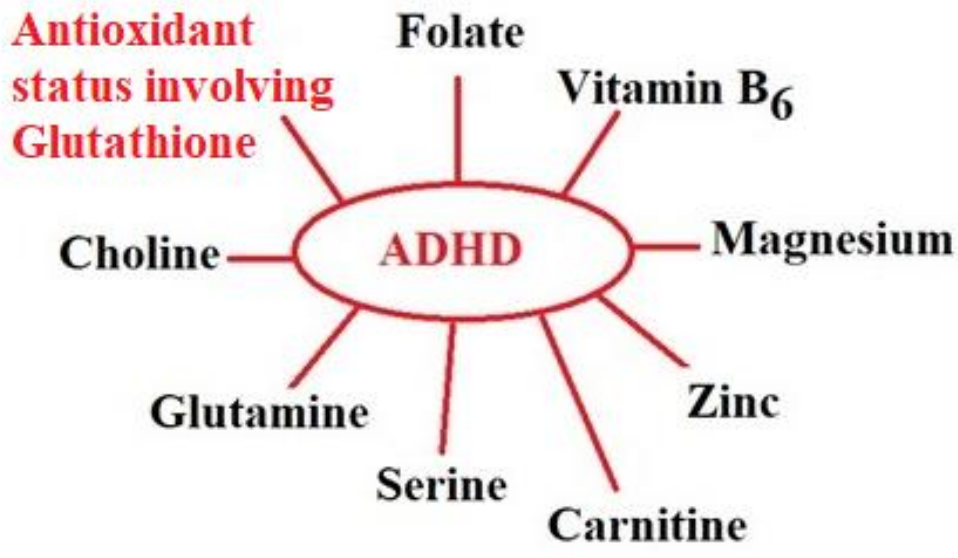

Fig. 2. Schematic showing the dependence of ADHD on various nutritional factors and metabolites such as the antioxidant, Glutathione

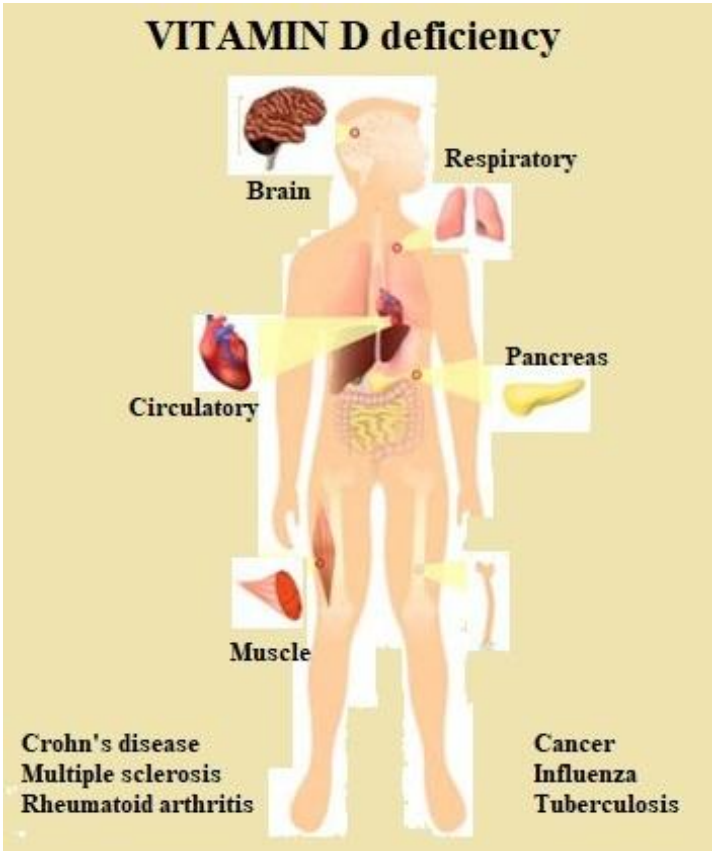

Fig. 3. The effect of Vitamin D deficiency on the human body

2. MATERIALS AND METHODS

The study employed 22 children diagnosed with ADHD as research subjects in the age range of 4-13 years and a control group comprising 22 healthy children in the same age group. The demographic data was collected at the time of referral. The diagnosis for ADHD was confirmed using information gathered from personal interviews with the children and their parent(s) and using the criteria described in the Diagnostic Statistical Manual of Mental Disorders (DSM-IV) [26]. Any child suffering from liver or kidney disorder or any other endocrine disease, or anyone using Vitamin D supplements, was excluded from the study. Also excluded were children diagnosed with mental retardation, autism and seizures. Three mL blood samples were obtained from each subject. Vitamin D_2 (25-hydroxy cholecalciferol) levels were measured using the DIA source kit and ELISA.

2.1 Statistical Analysis

The data was analyzed using SPSS version-16 (Chicago, IL, USA) by t-test and chi square test and any correlation was considered as significant at α-level ≤0.05.

3. RESULTS AND DISCUSSION

For this study, Vitamin D_2 level < 10 ng/mL was classified as being severely deficient (Table 1); Vitamin D_2 level in the range between 10-20 ng/mL was classified as being deficient, Vitamin D level in the range between 20-30 ng/mL was classified as being insufficient and a Vitamin D level > 30 ng/mL was classified as being normal. The analysis has shown a difference in serum Vitamin D_2 levels between the ADHD and control groups (*P-value*=0.04) (Table 2). In fact, no research subject in the ADHD group had a normal Vitamin D level. 31.8% of the children in the control group had high serum Vitamin D_2 level whereas 61.4% were classified as normal. None of the children in either of the two groups had a Vitamin D_2 level high enough that could result in toxicity (Vitamin D_2 level >100 ng/mL).

Vitamin D is a neurosteroid and its deficiency results in many neurological disorders [20-22]. Many studies have shown the role played by Vitamin D deficiency in development of neurological disorders [27-33]. Additionally, Vitamin D up-regulates the level of the enzyme, Gamma-Glutamyl Transferase (GGT), also known as Gamma-Glutamyl Transpeptidase. GGT causes the formation of Glutathione, which is an important antioxidant factor in the brain [34]. Lack of Vitamin D during development of the fetus, in the first few days after birth and during childhood, affects nerve differentiation, formation of axon synapses and development of brain structure and function (20).

The results (Table 3) show that children suffering from ADHD exhibited Vitamin D deficiency more frequently than the control group. Additionally, the mean value of serum Vitamin D_2 level in the ADHD group (18.60±6.33 ng/ml) was lower than that of the healthy control group (34.34±8.19). This finding confirms the result of a similar study conducted in Turkey where a significant difference (*P-value* < 0.05) in serum Vitamin D level between ADHD and control groups was demonstrated [35]. Another study reporting 1331 ADHD cases of adolescents less than 18 years of age showed that the Vitamin D level in serum of research subjects was lower than that of the control group. In this study, 8.15% of the ADHD subjects possessed normal serum Vitamin D level [36].

In a study conducted in New Zealand employing 80 ADHD patients over the age of 16, it was found that 27% of the subjects suffered from Vitamin D deficiency. After the use of Vitamin D as a supplement for 8 weeks, many of the subjects reported a lessening of the symptoms of the disease. However, a study in England found no association between ADHD and Vitamin D level [37]. When other supplements such as Zinc, Vitamin B_{12}, Iron and Folic acid were investigated, they were found to have no effect [38].

Table 1. Normal range of Vitamin D level in the blood

Vitamin D status	**Blood level** (**ng/mL**)
Severe deficiency	Less than 10
Deficiency	10-20
Insufficiency	20-30
Normal	Other 30
Overdose	Over 100

Table 2. Comparison of serum Vitamin D levels of ADHD patients and control group

Group	Severe Vitamin D deficiency	Vitamin D deficiency	Normal Vitamin D level	Total
ADHD	2 (9.1%)	20 (90.1%)	0 (0%)	22 100%)
Control	0 (0%)	7 (31.8%)	15 (38.2%)	22 (100%)
Total	2 (4.5%)	27 (61.4%)	15 (34.1%)	44 (100%)

*P-value < 0.0005

Table 3. Correlation among the various groups

Group	Mean	SD
ADHD	18.6	6.3
Control	34.3	8.2
Total	26.5	10.8

*P-value < 0.0005

4. CONCLUSION

This study has shown that a very high percentage of children exhibiting ADHD suffered from Vitamin D deficiency also. Some of the healthy children in the control group as well exhibited Vitamin D deficiency. It is possible that the low Vitamin D level in children suffering from ADHD causes the expression of the enzyme, Gamma-Glutamyl Transferase (GGT) to become reduced in the ADHD group. GGT is known to produce the antioxidant, Glutathione, which determines the antioxidant status of the brain.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author's.

ETHICAL APPROVAL

The study was approved by the Ethics Committee of Prince Abdallah Ibn Musaed Hospital (Arar, Saudi Arabia).

COMPETING INTERESTS

Author has declared that no competing interests exist.

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