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Role of Vitamin (D) Deficiency in Children with Autism Spectrum Disorder

Mohammed Hussen Sheikh[1*], Manal Mohammed E. Alhawiti[2], Shaykhah Salman A. Alderaan[3], Daher Mushref Daher Alshehri[4], Shahad Abdulaziz S. Alzahrani[5], Aseel Ali T. Albalawi[2], Reem Awadh N. Alharbi[6], Faisal Ibrahim S. AlSukairan[7], Hamad Saad M. Alkhaldi[7], Zainab Ali H. Alarab[8], Abdullah Hassan F. Alsuayri[9] and Marwan Fahad H. Altemani[10]

[1]Department of Pediatric, University of Tabuk, Saudi Arabia.
[2]Medical Intern, University of Tabuk, Saudi Arabia.
[3]University of Tabuk, Saudi Arabia.
[4]King Khalid University, Saudi Arabia.
[5]King Abdulaziz University, Saudi Arabia.
[6]Sulaiman Alrajhi University, Saudi Arabia.
[7]Imam Mohammed Bin Saud University, Saudi Arabia.
[8]King Faisal University, Saudi Arabia.
[9]University of Bisha, Saudi Arabia.
[10]Internal Medicine Resident, King Salman Armed Force Hospital, Saudi Arabia.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

The disorder of the automatic spectrum is a neurodolevating disorder characterized by a decrease in social interactions, communication and stereotypical disorders and repeated behaviors with various degrees of gravity. A number of systematic reviews and meta- analyses have described prenatal and perinatal factors, as well as factors related to maternal nutrition and lifestyle. There is evidence to support the importance of vitamin D in the normal structure and function of the nervous

**Corresponding author: E-mail: msheikh@ut.edu.sa;*

system. The effects of VD administration during pregnancy on the mother and conception before and after birth have been repeatedly investigated. It has been found that preventing VD can reduce the risk of autism.

Keywords: Vitamin D; deficiency; risk factors; autism; children.

1. INTRODUCTION

Autism is a general disorder among children and children with an estimated frequency of occurrence reached from 20.0 to 116.1 per 10,000 people [1].

Some recent studies have suggested that early environmental factors, such as maternal metabolic syndrome during pregnancy, viral and bacterial infections, air pollution, influence of various drugs and nutritional deficits, can play a significant role in the risk of autism. However, in recent years, VD has been shown to have significant additional skeletal activity beyond the classically recognized activities [2]. Adequate intake of VD appears to be important to physical and mental health worldwide, as evidenced by evidence that VD deficiency may be associated with several diseases such as infections; asthma; inflammatory bowel disease; obesity; metabolic syndrome; neuropsychiatric symptoms, including autism spectrum disorders (ASD) [3].

1.1 Objectives

The study aims to summarize the updated evidence regards autism spectrum disorders in children, epidemiology, risk factors, relation with vitamin D deficiency and the role of vitamin D administration.

2. EPIDEMIOLOGY OF AUTISM SPECTRUM DISORDERS IN CHILDREN

A 2012 review commissioned by WHO estimated that the global prevalence of ASD was about 1%, with a more recent review estimating the prevalence to be 1·5% in developed countries [4]. Increases in prevalence estimates in the USA over the past several decades have now mostly plateaued and probably can be largely accounted for by improved awareness and services, differences in documentation, and the inclusion of milder cases without intellectual disability [5]. Only two rigorous studies of adult epidemiology of ASD have been done, both in the UK, and also provided estimates of about 1%, with many adults never having received a formal diagnosis [6].

3. RISK FACTORS

Many risk factors for ASD have been suggested. A number of systematic reviews and meta-analyses have described prenatal and perinatal factors, as well as maternal dietary and lifestyle factors.

3.1 Maternal Risk Factors of ASD

The mother's lack of VD is associated with a high risk of ASD. There is evidence that the prevalence of ASA in children born to mothers with hypothetical reduced VD skin synthesis during pregnancy has been seen as evidence that vitamin D deficiency is closely related to the development of ASA [7].

Older mothers (≥40 years old) and fathers' age (≥50 years old) were independently associated with ASD risk and short interspecies interval (<24 months) in several studies [8].

Several studies have investigated drug abuse by mothers during pregnancy. Prenatal exposure to valproic acid is associated with an increased risk of ASA. For antidepressants, including selective serotonin reuptake inhibitors, despite previous concerns, well-controlled studies [9,10] have not shown a clear risk.

3.2 Infant Related Risk Factors of ASD

Preterm birth (95^{th} percentile of birth weight) is independently associated with an increased risk of ASA, although it is unclear whether these factors are causal or risk markers. However, these children should be monitored for ASD in later infancy and early childhood. No consistent association was found between Caesarean section or assisted conception and ASA risk [9]. The 4,444 babies who were pregnant in winter and babies born to dark-skinned women who immigrated to high-latitude countries were more likely to be diagnosed with ASD than babies who were pregnant in summer. They were babies born to white-skinned immigrants. However, For a variety of reasons, the results of these studies are still inconclusive, and recent research does not seem to link the labor season to ASD [11].

Several studies have reported insufficient VD status in children with ASD. The reduction in absorption and exposure to ultraviolet radiation is believed to be a possible cause. A meta-analysis of 11 studies in 2016 showed that the serum concentration of active VD in ASD cases was significantly lower than that in the control group [12].

4. RELATIONSHIP BETWEEN VITAMIN D AND BRAIN STRUCTURE AND FUNCTION IN ASD

There are multiple pieces of evidence supporting the importance of vitamin D in the normal structure and function of the nervous system. A large number of studies have shown that vitamin D receptor VDR is widely present in adult brain neurons, peripheral neurons and non-neuronal brain cells. The highest concentrations are located in areas of the nervous system that are required for critical functions [13]. For example, it has been found that the expression of VDR in the prefrontal cortex and hippocampus is increased, and these areas are closely related to learning, memory and executive control. In addition, VDR has been detected in areas rich in dopaminergic neurons, indicating that there may be a link between VD and dopaminergic neurotransmission. Finally, it has been reported that VDR expression regulates the structure of the fully mature brain, because an increase in VDR is associated with a decrease in cell proliferation and an associated increase in programmed cell excretion [14].

The detection of VDR in nerve tissue is considered to be evidence that VD plays an important role in regulating the structure and function of the nervous system during development and maturation [15].

VD deficiency is related to many significant structural and functional changes in the brain. When VD deficiency causes severe and permanent structural and functional damage, these are very important in the early stages of nervous system development. When they occur in adults, these changes are usually mild and limited to functional brain abnormalities [16].

4.1 The Role of Vitamin D Administration in ASD

The effect of taking VD during pregnancy on mothers and prenatal and postnatal concepts has been repeatedly studied. It has been found that VD prevention can reduce the risk of autism [17].

A specially planned study was conducted to evaluate the impact of VD prevention during pregnancy on the risk of ASD in children. Pregnant women who have given birth to ASA children are prescribed a dose of 5,000 IU/day, and children receive 1,000 IU/day from birth to their third birthday. Of the children born to women taking supplements, only one in ten was diagnosed with ASD, which is significantly lower than expected because of the prevalence of new ASD cases among children born to mothers of children with previous ASDs. The disease rate is 20% [18].

There are more than 160 human autoimmune diseases, and autism seems to be one of them. A number of studies have shown that most autoimmune diseases are related to vitamin D deficiency. Therefore, vitamin D is a potential starting point for the treatment of autoimmune diseases such as autism [19].

Up to 25% of children with autism have seizures.

In a recent public study, 8 of 13 patients with epilepsy were severely deficient in vitamin D. The researchers then gave all 13 test subjects a single dose of 40,000-200,000 IU of vitamin D3, and then 2,000-2,600 IU of vitamin D3 daily for 3 months to correct their vitamin D deficiency based on their weight. This intervention reduced seizures by 40%. A subject started with a vitamin D level of less than 4 ng/ml, and his level increased to 43.1 ng/ml after treatment; after 3 months, his total number of seizures decreased from 450 to 30 [20]. Limitations of the study include the small number of patients and the lack of placebo. However, this study is certainly worthy of a randomized controlled follow-up study and emphasizes the importance of correcting vitamin D deficiencies in patients with epilepsy (including autistic patients with seizures) [21].

Neurotrophic factor is a protein that induces the development, function and survival of nerve and brain cells. VD can increase neurotrophic factors up to 5 times.

Therefore, vitamin D seems to be closely related to the regulation of neurotrophic factors [22].

Garcion and colleagues and others report that vitamin D up-regulates glutathione levels in the

brain. Garcion and colleagues concluded that vitamin D is closely involved in the glutathione cycle by up-regulating γ-glutamyl transpeptidase through calcitriol, which is involved in glutathione metabolism. Once glutathione is used, it will be divided into two and needs to be remodeled. This is the rate-limiting step of glutathione production and is carried out by γ-glutamyl transpeptidase [23].

5. CONCLUSION

A number of systematic reviews and meta-analyses have described prenatal and perinatal risk factors of autism, as well as maternal dietary and lifestyle factors. There are several evidences that prove the importance of vitamin D in proper structure and function of nervous system. Impact of vitamin D administration during pregnancy as a prophylaxis may reduce the risk of autism.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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