



## Khaled Saad<sup>1\*</sup> and Abdulrahman A Al-Atram<sup>2</sup>

<sup>1</sup>Pediatric Department, Faculty of Medicine, Assiut University, Egypt.

<sup>2</sup>Department of Psychiatry, College of Medicine, Almajmaah University, KSA

**Dates:** Received: 17 May, 2017; Accepted: 21 June, 2017; Published: 22 June, 2017

**\*Corresponding author:** Khaled Saad, Associate professor of Pediatrics, Faculty of medicine, University of Assiut, Assiut 71516, Egypt, Tel: +20-100-608-0182; Fax: +20-88-236-8371; E-mail: ksaad8@yahoo.com

<https://www.peertechz.com>

## Editorial

# Autism and Vitamin D

## Editorial

Autism spectrum disorder (ASD) is a complex neurodevelopmental syndrome. It begins before three years of age. ASD is characterized by pervasive deficits in social interaction, impairment in verbal and nonverbal communication, and stereotyped patterns of interests and activities. The increasing incidence of ASD in the pediatric population and the lack of successful curative therapies make ASD one of the most challenging disorders for medicine [1,2]. The pathogenesis of ASD is bewildering. The chemosensory immune system participates in neurodevelopment, regulating neuronal proliferation, synapse formation and plasticity, along with removing apoptotic neurons [3]. Hundreds of studies over the last 4 decades have reported altered immune responses in autistic individuals. We found significant inverse relationships between serum 25-OH vitamin D levels and the frequencies of dendritic cells (DCs) population in children with ASD [1]. Vitamin D has an important role in brain homeostasis, neurodevelopment, ageing, and significantly, in gene regulation. Also, it has been shown to bind to more than 2700 genes and to regulate the expression of more than 200 of them [2,4-6]. Many studies suggested that vitamin D has an important role as a neuroactive steroid, which can affect neuronal differentiation, axonal connectivity and brain structure and function. Moreover, vitamin D deficiency during pregnancy is linked with several adverse effects in the fetus [2,7]. Growing data have shown an association between the risk for ASD and vitamin D insufficiency in patients with ASD. Our previous study [6] showed that more than half of children with ASD had vitamin D deficiency, and about one third had vitamin D insufficiency. We found a significant negative relationship between serum 25-OH vitamin D levels and severity of autism [6]. Feng et al. [8], performed a recent

trial of vitamin D<sub>3</sub> in ASD children. The study found significant inverse correlations between serum 25 (OH)D levels and ABC total scores and language subscale scores. Vitamin D<sub>3</sub> was intramuscularly administered at a dosage of 150,000 IU per month (3 injections) and orally administered at a dosage of 400 IU/day (in total 3 months). After vitamin D therapy, the symptom scores were significantly reduced on the CARS and ABC. Furthermore, the study suggested that treatment effects were more pronounced in younger children with ASD [8]. We conducted a double-blind, randomized clinical trial on 109 Egyptian children with ASD. We assessed the effects of vitamin D supplementation on the core symptoms of autism in children. ASD patients were randomized to receive vitamin D<sub>3</sub> or placebo for four months. The levels of 25-OH vitamin D were measured before and vitamin D therapy. The autism severity and social maturity of the children were assessed by the Childhood Autism Rating Scale (CARS), Aberrant Behavior Checklist (ABC), Social Responsiveness Scale (SRS), and the Autism Treatment Evaluation Checklist (ATEC). The ASD children generally tolerated well the supplementation with vitamin D. The autism symptoms of the children improved significantly, following 4 months of vitamin D<sub>3</sub> therapy [4]. Vitamin D has an important role in the regulation of both innate and adaptive immune responses. While affecting the immune system at multiple levels, the main target of vitamin D in immune population is the DCs. In DCs, vitamin D can generate invitro a stable maturation-resistant tolerogenic phenotype, with low expression of HLA-DR, low expression of costimulatory molecules and increased interleukin 10 (IL-10)/IL-12p70 ratios that are maintained even after removal of the compound [1,9]. Significantly, introduction of an antigen in parallel with vitamin D can induce antigen-specific tolerogenic DCs with the ability to induce infectious tolerance, changing the behavior of other proinflammatory mature DCs through the induction of antigen-specific regulatory T cells, and causing the perpetuation of the tolerogenic response. In addition, 1,25(OH)<sub>2</sub>D<sub>3</sub>-conditioned fully differentiated DCs lose their ability to activate autoreactive T cells, stimulating instead the generation of regulatory T cells, Tregs [9-11]. Reintroduction of such 1,25D<sub>3</sub>-DCs in vivo leads to immune modulation [10], which represents a reliable strategy for the promotion or restoration of antigen-specific tolerance through vaccination strategies. Although the immunomodulatory properties of vitamin D on DCs phenotype and function are well outlined,

the intracellular and molecular mechanisms leading to these effects strongly suggest olfaction [11].

We need additional wide-scale studies to critically validate the efficacy of vitamin D and its biochemical mechanism in ASD.

## References

1. Saad K, Zahran AM, Elsayh KI, Abdel-rahman AA, Al-Atram AA, et al. (2017) Frequency of Dendritic Cells and their expression of Costimulatory Molecules in Children with Autism Spectrum Disorders. *Journal of Autism and Developmental Disorders*. In press. [Link: https://goo.gl/Gz6Ro4](https://goo.gl/Gz6Ro4)
2. Bjorklund G, Saad K, Chirumbolo S, Kern JK, Geier DA, et al. (2016) Immune dysfunction and neuroinflammation in autism spectrum disorder. *Acta Neurobiol Exp (Wars)*. 76: 257-268. [Link: https://goo.gl/d64AyT](https://goo.gl/d64AyT)
3. Wang TT, DU L, Shan L, Jia FY (2014) Research advances in immunological dysfunction in children with autism spectrum disorders. *Zhongguo Dang Dai Er Ke Za Zhi*. 16: 1289-93. [Link: https://goo.gl/kJhFFS](https://goo.gl/kJhFFS)
4. Saad K, Abdel-rahman AA, Elserogy Y, Al-Atram AA, El-Houfey AA, et al. (2016) Randomized-Controlled Trial of Vitamin D Supplementation in Children with Autism Spectrum Disorder. *J Child Psychol Psychiatry*. [Link: https://goo.gl/NJYVwm](https://goo.gl/NJYVwm)
5. Cannell JJ, Grant WB (2013) What is the role of vitamin D in autism? *Dermatoendocrinology* 5: 199-204. [Link: https://goo.gl/6QC9Xf](https://goo.gl/6QC9Xf)
6. Saad K, Abdel-Rahman AA, Elserogy YM, Al-Atram AA, Cannell JJ, et al. (2016) Vitamin D status in autism spectrum disorders and the efficacy of vitamin D supplementation in autistic children. *Nutr Neurosci* 19: 346-351. [Link: https://goo.gl/NNdKMM](https://goo.gl/NNdKMM)
7. Eyles DW, Burne TH, McGrath JJ (2013) Vitamin D effects on brain development, adult brain function and the links between low levels of vitamin D and neuropsychiatric disease. *Front Neuroendocrinol* 34: 47-64. [Link: https://goo.gl/UpbXSa](https://goo.gl/UpbXSa)
8. Feng J, Shan L, Du L, Wang B, Li H, et al. (2016) Clinical improvement following vitamin D3 supplementation in Autism Spectrum Disorder. *Nutr Neurosci* 20: 284-290. [Link: https://goo.gl/tQTqnK](https://goo.gl/tQTqnK)
9. van Halteren AG, van Etten E, de Jong EC, Bouillon R, Roep BO, et al. (2002) Redirection of human autoreactive T-cells Upon interaction with dendritic cells modulated by TX527, an analog of 1,25 dihydroxyvitamin D (3). *Diabetes* 51: 2119-2125. [Link: https://goo.gl/pdLHQA](https://goo.gl/pdLHQA)
10. Ferreira GB, Gysemans CA, Demengeot J, da Cunha JP, Vanherwegen AS, et al. (2014) 1,25-Dihydroxyvitamin D3 promotes tolerogenic dendritic cells with functional migratory properties in NOD mice. *J Immunol* 192: 4210-4220. [Link: https://goo.gl/rAksGY](https://goo.gl/rAksGY)
11. Ferreira GB, Vanherwegen AS, Eelen G, Gutiérrez AC, Van Lommel L, et al. (2015) Vitamin D3 Induces Tolerance in Human Dendritic Cells by Activation of Intracellular Metabolic Pathways 10: 711-725. [Link: https://goo.gl/Dqo5zg](https://goo.gl/Dqo5zg)