International Journal of Applied Chemical and Biological Sciences (2022), 3(6), 1-6
ISSN 2582-788X

REVIEW PAPER

Article Identifier: https://identifier.visnav.in/1.0001/ijacbs-22i-28001/

ADHD and its association with Environmental toxins and Nutritional deficiencies

Karan Gupta [1]*, Yamini Sharma [2], Akanksha Gupta [3], Mujtaba Hussain Shah [4], Maria Gabriela Zurita [5], Aadrika Kashyap [6] and Vineeta Singh [7]

[1] Post Graduate Institute of Medical Education and Research, Chandigarh, India
[2] Avalon University School of Medicine, Youngstown, Ohio/Curacao Campus, USA
[3] Bhagat Phool Singh Government Medical College for Women, Sonipat, Haryana, India
[4] Noorda College of Osteopathic Medicine, Utah, USA
[5] Universidad Especialidades Espíritu Santo, Samborondon, Ecuador
[6] Seth GSMC and KEM hospital, Mumbai, India
[7] Adesh Institute of Medical Science and Research, Bathinda, Punjab, India

* For correspondence: karangupta084@gmail.com

Received on: 28 September 2022 *Published on: 13 November 2022*

ABSTRACT

ADHD a neurobehavioral disorder associated with nutritional, mineral deficiency and environmental toxins. Environmental toxins play a large role in prenatal and early childhood ADHD development. ADHD is a prevalent and highly impairing condition which has frequent concurrence with other psychiatric disorders, creating an enormous burden for the individual, their family, and the community. Recent studies have reported that ADHD children present higher urine concentrations of chromium, manganese, cobalt, nickel, copper, molybdenum, tin, barium, and lead. There is also significant link between ADHD and deficiency of essential minerals such as iron, zinc, magnesium and omega 3 fatty acids. Although effects of toxins are being constantly studied, the conclusive evidence of their possible associations with ADHD requires more research in this field.

Keywords: ADHD, attention deficit hyperactivity disorder, environmental toxins, iron deficiency, zinc deficiency.

1. INTRODUCTION

The prevalence of Adult Onset Hyperactivity Disorder (ADHD) has grown remarkably in children, adolescents and adults. The clinical presentation of a patient comprises of impulsivity, inattention and hyperactivity at different levels of the spectrum. According to the recent data, the prevalence of ADHD varies between 5.9% to 7.1% in children and 1.2% to 7.3% in adults, depending upon the geographical area [1-2]. The point prevalence of ADHD in primary school age children is higher among the males as compared to females (3:1)[3].

The usual age of onset of ADHD in children is from 7 to 17 years old but, it is important to mention that ADHD is also present in adults. According to the recent studies, the number of adults with ADHD has increased over the last 20 years. The major part of this increase is due to the

permanence of symptoms of ADHD in the adults in 76% of diagnosed patients [4]. ADHD is a prevalent and highly impairing condition which has frequent concurrence with other psychiatric disorders, creating an enormous burden for the individual, their family, and the community.

DSM-V specifies three subtypes of ADHD– predominantly inattentive, hyperactive-impulsive type and combined type. The hyperkinetic disorder mentioned in ICD-10 is similar to the combined type of ADHD with severe impairment.

2. Environmental factors associated with ADHD

Although previously cited evidence indicates that ADHD is a predominantly familial disorder, environmental toxins play a large role in prenatal and early childhood ADHD development. These include prenatal exposure to various substances, exposure to heavy metals and chemicals and nutritional deficiencies [5].

2.1. Gestational and Perinatal factors

Premature birth is one of the most important risk factors associated with ADHD. The estimated increased risk of ADHD in premature babies is reported to be 2.6 to 4 times of term born babies [6]. The most important reason for this being the inflammation in the central nervous system of the babies which releases free radicals and other chemical mediators of inflammation which affect the neurogenesis and halt the cortical expansion [6].

The adequate dietary intake of polyunsaturated fatty acid docosahexaenoic acid (DHA) during pregnancy, promotes the proliferation and differentiation of neural progenitor cells. Decreased levels of DHA intake during the Brain development has been associated with ADHD and other neurodevelopmental disorders [7].

The exposure of pesticides during pregnancy is another environmental factor associated with ADHD. There was direct indication of increased incidence of ADHD in children with prenatal exposure of polychlorinated biphenyl (PCB) and p,p'-dichlorodiphenyldichloroethylene in prospective cohort [8]. In a study conducted by Braun et al. mothers who were exposed to environmental and industrial toxins upon sampling the umbilical cord blood of the newborns for chemicals, 217 out of 237 were toxic chemicals and harmful to brain leading to neurological dysfunctions and associated with worse mental and psychomotor development. These toxins were dimethyl phosphate, Polycyclic hydrocarbons and Bis-phenol [9]. Children exposed to pesticides metabolites like dimethyl phosphate were more likely to meet diagnostic criteria for ADHD. The children with levels higher than the median had twice the odds of ADHD [10].

In the multiple population based cohort studies conducted by Motlagh *et al*. (2010) and Nomura *et al*. (2010) there has been consistent finding of higher incidence of ADHD in the children where the mother is smoking during their pregnancy [11-12].

2.2. Heavy Metal Exposure

The assessment of school children aged 6-7 years old with ADHD presented higher levels of mercury in saliva. However, when including all age groups, only a mild tendency of increased risk was observed [13]. Whereas, Nicolescu *et al*. (2010) in a study conducted on Romanian children did not find an appreciable association between mercury levels and ADHD symptom scores [14].

In a study addressing the relationship between ADHD and manganese in drinking water, higher incidence of inattentive type of ADHD was seen. High concentration of manganese is also associated with low learning quotient [15]. In a separate study by Farias *et al*. (2010)

Table 1. Possible association with Environmental toxins and Nutrient Deficiencies in Children with ADHD

Name	Association with ADHD
Mineral deficiency	
Iron	Yes
Zinc	Yes
Omega 3 fatty acid	Yes
Vitamin c	Yes
Toxins and heavy metal	
Manganese	Yes
Organchlorines	Yes
Mercury	Inconclusive
Bisphenol	Yes
Lead	Yes

the association between inattentive and combined subtype and higher manganese levels were found in the children [16].

Multiple studies have shown a direct correlation between high blood lead levels and ADHD. Few studies cite the direct risk as high as fourfold increase in risk of ADHD [9]. There has been rising evidence of reduced cortical grey matter due to toxic lead exposure during the post natal neurodevelopmental phase of life. Levels of lead in children's deciduous teeth have been associated with hyperactivity, inattention and impulsivity [17]. A study conducted on children by Liu et al. from a lead-contaminated region reported that high blood levels of cadmium, lead, and manganese are positively correlated with ADHD [18].

A recent study published by Li *et al*. (2020) reported that ADHD children present higher urine concentrations of chromium, manganese, cobalt, nickel, copper, molybdenum, tin, barium, and lead [19].

3. NUTRITION DEFICIENCY AND ADHD

Children with ADHD have decrease levels of zinc, iron and omega 3 fatty acids in RBC and plasma [20]. At adequate concentrations, iron is an essential cofactor in the production of serotonin, norepinephrine, and dopamine. In a study conducted on individuals with insufficient serum ferritin, adding iron supplements with conventional medication reveals beneficial effects on ADHD symptoms without significant adverse side effects. There have been progressive improvements in ADHD symptoms comparable to stimulants in children with low serum ferritin taking 80 mg of oral iron over 12 weeks [21-22].

A large number of studies have shown correlation of decrease levels of zinc in children with ADHD, most of which have been conducted in Asia and Europe [23]. Neurotoxins also contribute to zinc deficiency, as byproducts of plastic degradation bind and deplete zinc stores. There have been significant differences in ADHD rating scale after zinc replacement. There was 37% of reduction in optimal amphetamine dose after 30 mg zinc supplementation in most of the patients [24].

Vitamin C is also an essential factor in collagen synthesis pathway, promoting the integrity of myelin sheaths and enhancing neural signaling. Further research supports addition of vitamin C with both conventional ADHD medications and nutritional supplements, particularly Omega-3 fatty acids, for antioxidant protection and enhanced efficacy [25].

4. DISCUSSION

While ADHD remains a complex etiology, the purpose of this review article is to describe some of the related factors which are associated with ADHD. In this article, we present the evidence of association between environmental toxins and mineral deficiency linked to pathogenesis of ADHD. The evidence remains strong that there is integration between environmental toxins and mineral deficiency in association to ADHD. It is indicated that children who were exposed to environmental toxins in utero in moderate to high level were at increased risk of developing ADHD later in life.

There is also significant link between ADHD and deficiency of essential minerals such as iron, zinc, magnesium and omega 3 fatty acids. While evaluating sections of this review, there might be other underlying factor that could have association with ADHD and further research is needed. All of the above mentioned factors produce significant changes in brain functions that cause certain symptoms that are experienced by individuals with ADHD. It was difficult to determine the strength of evidence with association between certain chemicals and ADHD. However, timing of toxin exposure during prenatal or during childhood may play an important role with regards to ADHD symptoms. Thereby, measurement of the exposure in a given time period may alter the result of a given study. However, some associations might exist between ADHD and other toxins which have not yet been investigated. Although effects of toxins are being constantly studied, the conclusive evidence of their possible associations with ADHD requires more research in this field. In future, it would be of value to gather more evidence of associations between environmental toxins and nutritional deficient in ADHD.

5. CONCLUSION

Elimination of environmental toxin in prenatal and early childhood and, nutritional supplementation by intake of diets rich in iron, zinc and magnesium have shown significant improvements in ADHD rating scale. Substantial improvement in child's performance has been confirmed by teachers at school and by parents at home with added supplements in ADHD patients. Currently there is lack of substantial evidence to support supplementation as a monotherapy for the treatment of ADHD patients. However, supplementation may improve medication response and overall well-being, especially in the patients with deficiencies. Although, several nutritional deficiencies have emerged among individuals with ADHD, orthomolecular approaches to treatment remain contingent upon biochemical individuality to tailor interventions on a case-by-case basis. Nutritional psychiatric advancement should begin with full genetic and biochemical assessments, including food sensitivity analyses, to identify specific imbalances that require correction. The use of comprehensive panels can also help to recognize significant individual variations in metabolism and digestion that confirms the correct selection and dose of vitamin and mineral supplements.

6. CONFLICT OF INTEREST

The authors have declared that there is no conflict of interest.

7. SOURCE/S OF FUNDING

NA

8. REFERENCES

1. Melissa L. Danielson, Rebecca H. Bitsko, Reem M. Ghandour, Joseph R. Holbrook, Michael D. Kogan & Stephen J. Blumberg (2018). Prevalence of Parent-Reported ADHD Diagnosis and Associated Treatment among U.S. Children and Adolescents. *Journal of Clinical Child & Adolescent Psychology*, **47*(2)***: 199-212

2. Huss M., Duhan P., Gandhi P., Chen C.W., Spannhuth C., Kumar V (2017). Methylphenidate dose optimization for ADHD treatment: Review of safety, efficacy, and clinical necessity. Neuropsychiatr. Dis. Treat. **13**: 1741–1751.

3. Ougrin D, Chatterton S, Banarsee R (2010). Attention deficit hyperactivity disorder (ADHD): review for primary care clinicians. *London J Prim Care (Abingdon)*. ***3(1)***: 45-51.

4. Ortíz León S., Jaimes Medrano A.L (2016). Trastorno por déficit de atención en la edad adulta y en universitarios. *Revista de la Facultad de Medicina de la UNAM*. **59**: 6–14.

5. Barkley RA (2002). Major life activity and health outcomes associated with attention-deficit/hyperactivity disorder. *J Clin Psychiatry*. **63*(12)***: 10–15.

6. Aylward G.P (2005). Neurodevelopmental outcomes of infants born prematurely. *J. Dev. Behav. Pediatr.* **26:** 427–440.

7. Gharami K., Das M., Das S (2015). Essential role of docosahexaenoic acid towards development of a smarter brain. *Neurochem. Int.* **89:** 51–62.

8. Sagiv SK, Thurston SW, Bellinger DC, (2010). Prenatal organochlorine exposure and behaviors associated with attention deficit hyperactivity disorder in school-aged children. *Am J Epidemiol*. **171**: 593–601.

9. Joe M. Braun, Robert S. Kahn, Tanya Froehlich, Peggy Auinger, and Bruce P. Lanphear 2006. Exposures to Environmental Toxicants and Attention Deficit Hyperactivity Disorder in U.S. Children, *Environmental Health Perspectives,* **114**: 12.

10. Bouchard MF, Bellinger DC, Wright RO, Weisskopf MG (2010). Attention-deficit/hyperactivity disorder and urinary metabolites of organophosphate pesticides. *Paediatrics*. **125960**: 1270-7.

11. Motlagh MG, Katsovich L, Thompson N, (2010). Severe psychosocial stress and heavy cigarette smoking during pregnancy: an examination of the pre- and perinatal risk factors associated with ADHD and Tourette syndrome. *Eur Child Adolesc Psychiatry*. **19**: 755–764.

12. Nomura Y, Marks DJ, Halperin JM (2010). Prenatal exposure to maternal and paternal smoking on attention deficit hyperactivity disorders symptoms and diagnosis in offspring. *J Nerv Ment Dis.* **198**: 672–678.

13. Barry M.J., Almotawah F., Pani S.C., Ingle N.A (2010). A Comparison of Salivary Mercury Levels in Children with Attention Deficit/Hyperactivity Disorder When Compared to Age-matched Controls: A Case-control Observational Study. *J. Contemp. Dent. Pract.* **21**: 129–132.

14. Nicolescu R, Petcu C, Cordeanu A, (2010). Environmental exposure to lead, but not other neurotoxic metals, relates to core elements of ADHD in Romanian children: performance and questionnaire data. *Environ Res*. **110**: 476–483.

15. Schullehner J., Thygesen M., Kristiansen S.M., Hansen B., Pedersen C.B., Dalsgaard S (2020). Exposure to Manganese in Drinking Water during Childhood and Association with Attention-Deficit Hyperactivity Disorder: *A Nationwide Cohort Study. Environ. Health Perspect*. **128**: 97004.

16. Farias AC, Cunha A, Benko CR, (2010). Manganese in children with attention-deficit/hyperactivity disorder: relationship with methylphenidate

exposure. *J Child Adolesc Psychopharmacol*. **20**:113–118.

17. Chan T.J., Gutierrez C., Ogunseitan O.A (2015). Metallic Burden of Deciduous Teeth and Childhood Behavioral Deficits. *Int. J. Environ. Res. Public Health*. **12**: 6771–6787.

18. Liu W., Huo X., Liu D., Zeng X., Zhang Y., Xu X (2014). S100beta in heavy metal-related child attention-deficit hyperactivity disorder in an informal e-waste recycling area. *Neurotoxicology*. **45**: 185–191.

19. Li Y., Cha C., Lv X., Liu J., He J., Pang Q., Meng L., Kuang H., Fan R (2020). Association between 10 urinary heavy metal exposure and attention deficit hyperactivity disorder for children. Environ. Sci. Pollut. Res. Int. **27**:31233–31242.

20. Greenblatt JM, Delane DD (2017) Micronutrient Deficiencies in ADHD: A Global Research Consensus. *J Orthomol Med*. **32*(6)***

21. Konofal E, Lecendreux M, Arnulf I, Mouren M (2004). Iron Deficiency in Children with Attention-Deficit/Hyperactivity Disorder. *Arch Pediatr Adolesc Med.* **158*(12)***: 1113–1115.

22. D'Amato TJ (2005). Is Iron Deficiency Causative of Attention-Deficit/Hyperactivity Disorder? *Arch Pediatr Adolesc Med*. **159*(8)***: 787–788.

23. Akhondzadeh S, Mohammadi MR, Khademi M (2004). Zinc sulfate as an adjunct to methylphenidate for the treatment of attention deficit hyperactivity disorder in children: a double blind and randomized trial. BMC Psychiatry. **8**; 4-9

24. Konofal E, Lecendreux M, Arnulf I, Mouren M (2004). Iron Deficiency in Children With Attention-Deficit/Hyperactivity Disorder. *Arch Pediatr Adolesc Med*, **158*(12)***: 1113–1115.

25. Joshi K, Lad S, Kale M, Patwardhan B, Mahadik SP, Patni B, Chaudhary A, Bhave S, Pandit A (2006). Supplementation with flax oil and vitamin C improves the outcome of Attention Deficit Hyperactivity Disorder (ADHD). Prostaglandins Leukot Essent Fatty Acids. **74*(1)***: 17-21.