A Review on Autism Spectrum Disorders and Lead Toxicity: An Indian perspective

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Abstract: Background: Environmental chemicals and autism have been the subject of a growing number of epidemiological publications over the past decade. These studies are important because it is now understood that environmental factors play a dominant role in causing autism and because they address modifiable risk factors, primary prevention of autism may be possible with better understanding. **Purpose:** The purpose of this review is to discuss the importance of environmental influences and environmentally vulnerable physiology in autism spectrum disorders (ASDs). **Study design:** Review. **Conclusion:** This review studies an association between environmental toxicants (lead) and autism spectrum disorders (ASD). Children exposed to these toxicants show traits of ASD and have been reported with high body burdens of these toxicants which highlights the need for further research.

Keywords: Lead toxicity, Cerebral palsy, BLLs (blood lead levels), Autism spectrum disorders (ASDs), CDC

1.Introduction:

The term autism spectrum disorder refers to an individual who has a particular set of difficulties in social communication, repetitive behaviors, highly restricted interests, and/or sensory behavior that begins during early childhood. Autism is a "spectrum disorder," which means a child's symptoms might exist in many ways, from mild to severe. A child with autism may have difficulty communicating and interacting with others. A child with autism is characterized by rigid and repetitive patterns of behavior and interests, along with early-emerging impairments in social and communication skills. In addition, it can also cause a child to perform repetitive movements, to become upset when their daily routine changes, and to react in an unusual way to certain situations. Early signs of autism are seen in some children as young as 12 months. A child with autism may be sensitive to touch, certain smells, loud noises, temperature extremes, and even certain colors. Autism is more common in boys than in girls.

Facts about autism:

- Autism can affect any child - One in 110 children has autism, and there are many theories about the cause, but no definitive answer.
- Cause of autism is unknown - It is not known exactly how a child develops autism, but several theories exist about it.

Early intervention, such as behavioral and speech therapy, can improve a child's abilities to learn and communicate. [1,2] Lead is a naturally occurring metal that has a wide variety of industrial applications and health effects. It is a constant environmental contaminant. Lead accumulates in the body and impairs a variety of cellular processes. It can also cause negative neurodevelopment effects. Several symptoms are frequently quiet which composed lead exposure which is a frequently unrecognized and underestimated threat for prevalent neurocognitive disorders [3]. For various centuries, lead has been utilized for a variety of purposes. During the industrial revolution, the use of lead became widespread. Use of lead-based paints, gasoline, and meal containers resulted in acute environmental contamination. Lead toxicities were well documented in Egyptian papyrus rolls which described its use for homicidal purposes. The toxic clinical effects of lead poisoning in kids were linked to lead-based paint utilized in the early 20th century [4]. The lead exposure in utero, infancy or early childhood resulted in slower mental development and brought lower intelligence later in childhood which can continue later. The effects of lead are more toxic on developing nervous system of kids than on a developed or matured brain [5]. Lead toxicity in the early life can bring on lifelong brain damage which leads to - Cerebral palsy. Cerebral palsy (CP) is a group of disorders that attacks and changes a person's movement ability, balance and posture. Anyhow, in few kids' viral infections, lead poisoning, or head injuries that happen early life can result in acquired CP [6]. The process of quick growth, development, and differentiation in the developing brain are interfered by lead. Elevated lead levels may bring on permanent damage [7]. The incidence of lead poisoning peaks at around 18 to 30 months of age for most children. On the contrary, ongoing and repetitive oral exploratory behaviors may bring on a doubled risk and later causes elevating of BLLs (blood lead levels) amongst kids who have developmental delays, that is autism or pervasive developmental delay [1].

2.Neurotoxicity of lead

As a neurotoxin, lead can cause metabolic and infrastructural disturbances at the molecular and cellular levels of a developing nervous system. Children are much more sensitive to the negative effects of lead on their development than adults are because of the vulnerability of their nervous system, the postnatal continuation of neuronal maturation, and the increased permeability of neuronal structures to lead's entry [8]. Numerous studies have demonstrated adverse neurodevelopmental, neurobehavioral, and cognitive effects of prenatal and postnatal lead exposure [9,10]. Observations have shown that lead exposure has long-term effects on intellectual and academic achievement, even after apparently low exposure levels with BLL less than 10 µg/dL [11,12].

3.Monitoring Blood Lead Levels

Measurement of BLLs is the essential principal technique of determining if notable absorption of lead has occurred or not. The rate of BLL decrease can count on both, the duration of the BLL rise and the quantity of lead in the child's body. After a period of 7 days of treatment, a course of chelation therapy with succimer results in a quick drop in BLL. Anyhow, BLLs of those treated recover after treatment ends, and roughly 7 weeks after an initial course of therapy, BLLs of treated patients may arrive nearly 75% of prechelation levels [8]. After completion of chelation therapy, CDC recommends reevaluating children's BLLs 7 to 21 days [9]. Usual causes of increasing BLLs involves failure to address risk in the child's environment, inappropriate environmental lead abatement techniques, and continued use of imported pottery, cosmetics, or folk medicines that are polluted with lead. However, medical conditions resulting in bed rest or lookalike immobilization [10], or in acidosis [11], can bring on children's BLLs to rise unexpectedly, or fail to fall.

2.1. Confirmation of BLL by Venous Sample.

Any screening BLL overhead 10 Fg/dL must be confirmed with a venous sample. The time frame for confirmation depends upon the initial BLL (Table 3.3). Overall, the higher the screening BLL, the rapid the confirmatory test. However, an earlier diagnostic confirmation may be indicated if a child is less than 12 months old, or if over there is bounds to assume that the BLL is rising rapidly.

Recommended Schedule for Obtaining a Confirmatory Venous Sample: [12]

Screening test result (µg/dL)	Perform a confirmation test within:
10-19	3 months
20-44	1 week-1 month[a]
45-59	48 hours
60-69	24 hours
> 70	Immediately as an emergency lab test

a. The higher the BLL on the screening test, the more urgent the need for confirmatory testing.

2.2. Follow-Up Venous Blood Lead Testing

Medical management involves follow-up blood lead testing. Table 3.4 presents the recommended frequency of follow-up tests. This table is to be utilized as guidance. Case managers and PCPs should give consideration for one individual patient characteristics and caregiver capabilities and adjust the frequency of follow-up tests accordingly.

Schedule for Follow-Up Blood Lead Testing[a]

Venous blood lead level (µg/dL)	Early follow-up (first 2-4 tests after identification)	Late follow-up (after BLL begins to decline)
10-14	3 months[b]	6-9 months
15-19	1-3 months[b]	3-6 months
20-24	1-3 months[b]	1-3 months
25-44	2 weeks-1 month	1 month
> 45	As soon as possible	Chelation with subsequent follow-up

a. Seasonal variation of BLLs exists and may be more apparent in colder climate areas. Greater exposure in the summer months may necessitate more frequent follow ups.
b. Some case managers or PCPs may choose to repeat blood lead tests on all new patients within a month to ensure that their BLL level is not rising more quickly than anticipated.

4. Association between early childhood lead exposure and Autism in childhood.

Autism spectrum disorders (ASDs) is a set of complicated neurodevelopment disorders common in kids and is increasing at a regular rate in current years. There are numerous environmental agents that have been recommended for playing a role factor to ASD pathogenesis, which considers big metals (Hg and Pb), persistent biological pollutants (DDT, PBDEs and PCBs) and emerging chemicals (phthalates and BPA). These three main categories of toxicants could be the reason for ASD in children. There're a lot of evidence supporting the etiological link between exposure to environmental toxicants and the development of ASD. Kids exposed to these toxicants in the environment present signature traits of ASD and have been reported with increasing body burdens of these chemicals and/or their metabolites. Symptoms of ASD manifest during the initial three years of life as social deficits, intercommunication difficulties, and cognitive delays. Humans are primarily exposed to Pb by means of ingestion of putrid meal and water while kids are subjected to accidental ingestion of Pb paint. Stomachache, vomiting, extraordinary pale skin, or brain

damage related symptoms like seizures, papilledema is most well-known ones. Other symptoms add socio-behavioral disabilities, slurred speech, and mental retardation. Epidemiological studies reported that Pb exposure during childhood relates to cognitive and intelligence quotient (IQ) deficits, moreover behavioral abnormalities. In addition, a significant rise in Pb 7 concentrations in both hair and nail samples from kids with ASD has been observed when compared to a healthy control group. Study shows that elevated levels of Pb and Hg in the body are correlated with symptoms of developmental disorders in children. Thus, leading to the conclusion that poisoning involving these heavy metals may lead to the development of ASD in children. The Childhood Autism Rating Scale (CARS) was utilized to examine the autistic symptomatology [13,14].

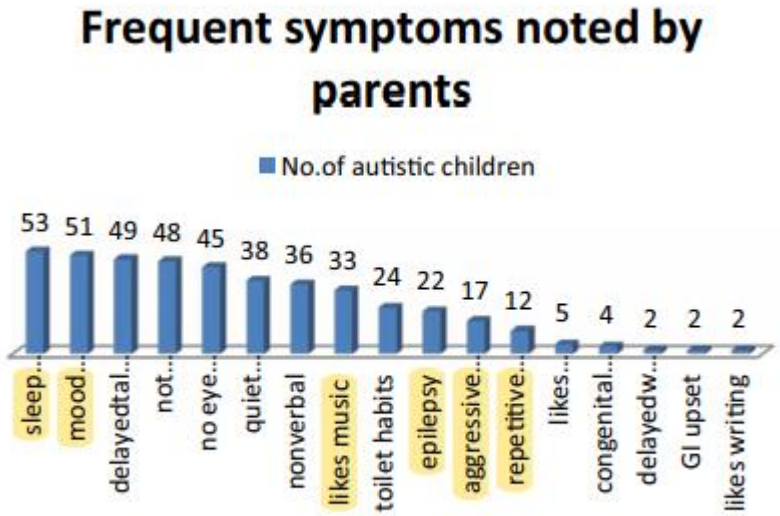

Fig. 1 Symptoms frequently noted by the parents

5. Current Limitations

Existing knowledge on this topic are mostly from cross-sectional constructs and BLL measurements that occurred either simultaneous to or after the ADHD diagnosis, therefore the temporal relationship between lead exposure and ADHD could not be set up. Exact neurotoxicological pathways by which lead exposure impose ADHD risk remains unclear. The accurate etiology of ASDs still remains unidentified. In the case of research into relationships between metals content material in the hair and neurodevelopment disorders, tests should be conducted within larger social groups (preferably international) and appropriate control methods should be adopted to prohibit data manipulation by means of any local influence

6. Conclusion

Innovative preventive approaches should be directed to control or remove sources of lead in environment are necessary to save the children from getting exposed and affected. Comprehensive toxicology databases must be developed with details of all environmental chemicals, their health effects on humans and sensitive laboratory methodologies to identify clinically significant exposures and their clinical manifestations**.** Additionally, research shall be conducted to identify biomarkers for autism in different stages of clinical presentation that can provide better insights into the pathogenesis of this disease especially in children with confirmed lead exposure. Identifying and implementing important preventive measures for effective reduction of lead exposure is also must. Establishment of advanced tertiary and quaternary care medical centers that can efficiently detect heavy metal toxicities much earlier and treat those suspected of having developmental or behavioral problems. Research should be focused on sex-specific biological pathways associating perinatal exposure to pollutants in those with ASDs. Investigating common environmental chemicals in terms of their most common routes of exposure and concentrations at which they cause neurodevelopmental damage is absolutely necessary. Future studies shall focus to characterize the pathophysiology of autism that can help to classify this disease as those due to toxic exposure or due to other causes.

7. Conflict of interests

Authors declare no conflict of interests

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Author profile

With a bachelor's degree in genetics, microbiology, and biochemistry, I have a knack for solving problems and working with innovative ideas in the field. I believe in teamwork while also being a good leader, I strive to advance the field of my study and look forward to every opportunity to learn.