



Assessment The Effect of Heavy Metals on Autism Patients

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Abstract :

This study aims to analyze the potential impact of heavy metals, such as lead, mercury, and cadmium, on patients with autism spectrum disorder. It provides a theoretical review of studies that have demonstrated the relationship between heavy metal accumulation and the behavioral and neurological effects of autism. This study relies on an analysis of data on exposure to these elements, such as food or pollution, and how they are measured to obtain the causes related to the autism spectrum disorder.

1. Autism Disorder

It is difficult to find an agreed-upon definition of autism disorder. This is because many researchers have focused on this disease or disorder, referring to it as a complex neurodevelopmental disorder that a child experiences before the age of three and persists throughout their life. It is a widespread disease or disorder that has negative effects on a child's development. It is both a mental and social disability, characterized by deficits in social behavior, communication, and imaginative play. Stereotypical and repetitive behaviors and interests are also present. Attention Deficit Disorder (ADD) is a co-morbidity with this disorder. (1) Abdul Rahman Suleiman defined autism disorder as: "Avoidance or exaggerated response to auditory and visual stimuli, a special interest in certain cognitive experiences, the presence of abnormalities and strange patterns in speech and language, unusual motor behavior, resistance to environmental change, and extreme expression of emotions and moods." (2) Autism is also known as rumination or self-stimulation, which refers to a severe disturbance in communication with others and a behavioral disturbance that affects children in early childhood, approximately between three and three and a half years of age. We note that these children do not speak intelligible, meaningful language, and are withdrawn, emotionally dull, and uninterested in others. They may be interested in and attached to animals and non-human objects. (3) The aforementioned terms and definitions all aim to describe a specific category that shares the same characteristics: autistic disorder, which is the latest term

to be popularized for the autistic child. Kanner is considered the first to use the first method to diagnose autism, i.e., autism. He explains the following points, which are characteristics that define autism and autism, and he determined that the first two characteristics are the criteria for diagnosing autism:

1. Severe impairment in emotional communication with others.
2. Love of routine (extreme aversion to any change in one's daily routine).
3. Strong and abnormal attachment to objects. 4- Appearing as a deaf-mute child.

5- Demonstrating or maintaining some good cognitive abilities. (4)

One of the most widely accepted definitions is the one proposed by the National Association for Autistic Children in 1978, which defined autism as a disorder or syndrome of mental manifestations that usually appear before the child reaches three years of age (i.e., 30 months), and includes the following:

- A disturbance in the rate and sequence of development.
- A disturbance in sensory response to external stimuli.
- Deficits in speech, language, and cognitive skills.
- Excessive attachment and affiliation to people, events, and things. (5)

2-Causes of Autism

Scientists and researchers have yet to determine a precise and definitive cause of autism, as this condition remains an open subject for study and research. Studies indicate that autism results from complex factors, primarily including genetics and environmental influences. (6)

A- Genetic Factors:

Genes are believed to play a major role in the susceptibility to autism. Research has shown a link between autism and certain genetic changes, such as chromosomes. These changes may impact brain development and function, leading to problems with language, communication, and movement. Studies have indicated that the incidence of this disease in twins has reached 100% if one of them is affected. (7)

There are also those who believe that autism is the result of a defect or disorder in certain genes. Autism has been linked to a weakness in a specific type of chromosome. Furthermore, it has been found that 2% of families of children with autism have relatives who suffer from the same type of disorder, indicating a strong genetic link. This confirms that genes may contribute to the transmission of this disorder among family members, reinforcing the hypothesis that genetic influence is a primary factor in the

emergence of autism. The prevalence of this disorder is also higher among identical twins than among fraternal twins. (8)

B- Psychological factors:

Kanner indicates that autism is the result of a defect in social communication in autistic children during childhood. Due to poor social upbringing, the child withdraws from their surroundings and becomes introverted due to their failure to adapt to their surroundings, resulting in a disruption in the linguistic and cognitive skills that were normal at birth. Kanner stated that there are a number of factors that negatively impact children, such as parents' tendencies toward their children and a family social environment devoid of emotions. Deficiencies in verbal communication between parents and children can cause a child to withdraw from their surroundings and become self-absorbed, leading to autism. (9) Recent studies have indicated that parental abuse has no relation to autism. The view that links autism to parental characteristics is no longer acceptable today, as the focus has shifted toward studying the cognitive aspects and developmental disorders suffered by autistic children themselves. This shift is evidence of the importance of understanding children's developmental characteristics in explaining the nature of autism, away from previous assumptions that placed responsibility on parents.

3-Environmental Factors:

Numerous studies indicate a close relationship between autism and the effects of environmental pollution, particularly exposure to certain chemicals. Environmental factors can play a significant role in increasing the likelihood of developing autism, especially when the environment surrounding the pregnant mother is polluted. These factors are believed to affect the fetus during pregnancy, contributing to the onset of autism symptoms later in life. Most of the causes of this pollution are due to modern lifestyles, where pollution sources are numerous. Prominent examples include:

1- Environmental Pollution in Densely Populated Areas:

Areas with dense population centers are more susceptible to pollution resulting from industrial activities. For example, the presence of factories that release harmful chemical pollutants or oil refineries leads to the spread of pollutants in the air and water. These pollutants not only affect the surrounding environment but can also reach pregnant women, leading to harmful effects on the health of fetuses.

2- Malnutrition and deficiency of essential nutrients:

A deficiency of essential vitamins and minerals can lead to deformities and health disorders in children. This is because a balanced diet plays a vital role

in physical and mental development. When a child's diet lacks iron, calcium, and proteins, vital bodily functions may be significantly affected, causing problems such as anemia or a weakened immune system.

3- Pregnancy at an advanced age:

Pregnancy after the age of 35 increases the likelihood of giving birth to children with health problems. This is due to several biological factors.

4- Excessive smoking or drug and alcohol use by pregnant women. These habits can cause deformities in children. (10)

4-Biochemical Factors:

Studies indicate that seizures associated with autism may be the result of a dysfunction in the brain's interaction with nerve signals that require attention and concentration. This dysfunction may arise from an imbalance in neural activity between different parts of the brain, especially in the cerebral cortex, which is a major center for processing nerve signals. This imbalance leads to difficulty in the brain responding normally to the surrounding environment.

(11) Key Peptidase Enzymes From a biochemical perspective, research has shown that there is a decrease in the levels of key enzymes in people with autism. These enzymes play an important role in the digestive system, particularly in the use of the hormone secretin, which is essential for digestive functions. It is believed that a disturbance in this system may lead to the appearance of digestive symptoms common among children with autism. (8)

5-Symptoms of Autism

Researcher Wendy Brown indicated in her study that the symptoms associated with autism include multiple aspects that can be classified into main axes, such as:

A- Social Aspect:

Children with autism suffer from disturbances in social interaction, manifested in an inability to understand social cues such as facial expressions and gestures, and a lack of desire or ability to build relationships with others. The autistic child appears to live in his or her own world, indifferent to those around him or her.

B- Language Developmental Disorders:

Children with autism suffer from a marked delay in language development. They may have a very limited ability to speak or may completely lack language skills, making it difficult for them to express their needs or feelings.

C- Deficits in Cognitive Skills and Imagination:

The autistic child suffers from difficulties in cognitive processes such as perception, thinking, and imagination. These difficulties affect the understanding of abstract ideas or interacting with the environment in innovative ways.

D- Motor Coordination Disorder:

Some children with autism have problems with coordination and coordination. This may manifest in difficulty performing fine motor movements such as writing and grasping objects.

E- Stereotyped Repetitive Behaviors:

Children with autism often engage in repetitive, routine behaviors such as repeating certain movements (rocking or spinning) or arranging objects in an exaggerated manner. These behaviors provide them with a sense of comfort and stability in the face of change. (12)

6-Types of Autism

A- Asperger's Syndrome (13)

Asperger's syndrome is currently recognized as part of the autism spectrum, and was previously classified as the least severe form. People with Asperger's syndrome are characterized by average or above-average intelligence and the ability to complete tasks efficiently and interact in daily life. However, they face difficulties with communication skills. Symptoms of Asperger's syndrome include:

- 1- Weakness in social interaction: Difficulty building social relationships and forming friendships.
- 2- Avoidance of human contact: Failure to look into others' eyes while speaking.
- 3- Difficulty understanding nonverbal cues: such as facial expressions and body language.
- 4- Repetitive behaviors and activities: Insisting on a specific daily routine and repeating the same actions.
- 5- Understanding speech literally: Difficulty understanding jokes, sarcasm, or metaphors.
- 6- Speaking too loudly and standing too close to people without leaving personal space.

B- Pervasive Developmental Disorder (PDD): (13)

This is one of the autism spectrum disorders and is also called atypical autism. The symptoms of this type are more severe than those of Asperger's syndrome and include the following:

- 1- Noticeable impairment in social communication.
- 2- Weak language skills or delayed language development.
- 3- Difficulty adapting to new changes.
- 4- Tendency to repeat certain behavioral patterns.
- 5- Atypical and unnatural responses to sounds, smells, or touch.

C- Childhood Disintegrative Disorder (CDD): (14)

This is considered the rarest form of autism. This type is characterized by normal developmental stages in the child's early years, followed by a rapid loss and decline in many of the linguistic, mental, and social skills they have acquired.

Symptoms of this disorder often appear after the child reaches the age of 3, but it can be diagnosed at any time before the age of 10. The exact cause of this disorder is still unknown. Symptoms include the following:

- 1- A decline in communication skills, i.e., a child who was previously able to say two or more sentences stops speaking.
- 2- A decreased desire or acceptance of physical contact despite previously accepting it.
- 3- Hallucinations, where the child may tell his parents or those around him that he sees, hears, or smells things that do not exist.
- 4- The child loses many previously acquired skills, such as motor abilities, social skills, and language skills.

7- Autism Disorder:

This is one of the most severe cases of the autism spectrum, and its symptoms are similar to those of Asperger's syndrome and atypical autism, but are more severe. Examples of symptoms of autism disorder include:

- 1- Noticeable difficulty with communication and social interaction.
- 2- Following repetitive behavioral patterns.
- 3- Anger attacks.
- 4- Sleep problems.
- 5- Disturbed eating habits.

Heavy metals

A heterogeneous group of elements with diverse functions and chemical properties. Heavy metals primarily belong to the transition elements in the periodic table. Heavy metals are those elements with densities five times greater than that of water.

Research has demonstrated a relationship between exposure to heavy metals such as cadmium (Cd), lead (Pb), and mercury (Hg), and an increased risk of neurodevelopmental disorders. Exposure to these metals can negatively

impact fetal growth and development, even at low levels of exposure. The prenatal period is highly sensitive to the effects of toxic substances, as the blood-brain barrier is incomplete, facilitating the passage of toxins into the fetal brain and affecting the development of the nervous system and neuronal migration. Heavy metals can easily cross the placental barrier, leading to negative effects on the developing brain. (16)

Studies show that autism can be influenced by various environmental factors, most notably exposure to toxic chemicals that affect neurological and behavioral development, especially during critical stages of nervous system development. These substances include environmental toxins that may cause neurological damage through various mechanisms, such as disruption of immune regulation, lipid metabolism, and impact on mitochondrial function. (15)

Research has also confirmed a link between heavy metal levels in children with autism and elevated levels of amino acids and glutamate receptors in nervous system cells, indicating a neurochemical imbalance in the body. Furthermore, it has been confirmed that there is a link between exposure to environmental endocrine-disrupting compounds (EDCs) during pregnancy and an increased risk of autism spectrum disorder (ASD). These compounds include heavy metals whose levels have been measured in maternal amniotic fluid, where elevated levels of elements such as lead, mercury, and cadmium have been found. (17)

8-Heavy metal saturation:

This topic has begun to gain significant traction in autism. A study measured the levels of heavy metals in the blood of 18 children with autism and found that 16 of them had levels exceeding acceptable limits. The reason for this saturation is environmental contamination with these metals, which enter the body through inhalation, oral ingestion, or other means. Some children have poor detoxification processes, which leads to the presence of these toxins in large quantities in the blood and their entry into the diaphragm, which is not fully developed in children. When these metals enter the brain, brain cells, enzymes, and nerve receptors are damaged, leading to an autoimmune reaction. (18)

8.1 The Effect of Heavy Metals on Autism Patients and Its Relationship to Oxidative Stress

Oxidative stress is a condition resulting from an imbalance between the production of free radicals and the body's ability to neutralize them using antioxidants.

Studies indicate that oxidative stress plays a major role in the development of autism spectrum disorders, especially when exposed to heavy metals such as lead, mercury, and cadmium, which enhance the production of free radicals and cause damage to neurons.

8.2 Oxidative Stress and the Mechanisms of Heavy Metal Effects

- Enhancing Free Radical Production

Heavy metals such as lead and mercury stimulate the production of reactive oxygen species (ROS), unstable molecules that damage lipids, proteins, and DNA. Mercury has the ability to disrupt mitochondrial function, increasing ROS production. (19)

- Reducing the effectiveness of antioxidants

Heavy metals negatively affect antioxidant enzymes, such as glutathione, one of the main antioxidants in the brain. Studies have shown that children with autism have lower levels of glutathione compared to healthy children, making them more susceptible to cell damage due to oxidative stress. (20)

8.3 The effect of cadmium on oxidative stress

Cadmium causes oxidative stress by disrupting the balance between oxidative and antioxidant enzymes, leading to damage to neural tissue. For example, a 2020 study showed that children's exposure to cadmium was associated with increased markers of oxidative stress in the brain, a factor that increases the likelihood of autism symptoms. (21)

8.4 Oxidative stress and its relationship to autism symptoms:

- Impaired neurological function

Oxidative stress leads to the destruction of neuronal cell membranes and vital proteins, affecting the transmission of nerve signals. Oxidative stress has been shown to play a major role in the neurological changes associated with autism. (22)

- Increased neuroinflammation

Oxidative stress stimulates the release of inflammatory cytokines, which increases the severity of neurological symptoms. Such as impaired social communication and stereotypical behaviors.

- Impact on cognitive skills

Accumulating damage resulting from oxidative stress leads to decreased cognitive performance in children with autism. Oxidative stress has been found to be associated with decreased learning ability in autistic patients. (23) Oxidative stress appears to be a central factor in the relationship between heavy metals and autism spectrum disorders. Increased free radicals resulting from exposure to lead, mercury, and cadmium lead to neuronal damage,

contributing to the behavioral and neurological symptoms associated with autism.

8.4 The Effect of Heavy Metals on Mitochondria and the Immune System in Autism Patients

Mitochondria are the most important cellular organs responsible for energy production and play a crucial role in maintaining neurological health. However, exposure to heavy metals such as lead, mercury, and cadmium significantly affects mitochondrial function, leading to increased free radicals and oxidative stress.

Lead and mercury affect mitochondria by disrupting enzymes responsible for energy production (such as respiratory chain enzymes), reducing the cells' ability to generate the energy needed to perform their vital functions. Mercury directly affects mitochondria, disrupting electron transport within the mitochondria and increasing the production of free radicals. (24)

When cells are exposed to oxidative stress caused by heavy metals, damage occurs to mitochondrial membranes and the proteins embedded within them, leading to a disruption in the energy production mechanism. A study has confirmed that exposure to lead can disrupt the ability of mitochondria to generate energy, contributing to impaired neurological function and increased behavioral symptoms associated with autism. (25)

The immune system plays a fundamental role in defending the body against microbes and harmful substances, but heavy metals can negatively impact the immune system's ability to regulate the inflammatory response. Heavy metals, such as mercury and lead, over-activate the immune system, increasing levels of inflammation in the body. This can lead to chronic inflammation in the brain, which is linked to the development of behavioral symptoms and autism. Studies have shown that children with autism exposed to high levels of mercury showed elevated levels of inflammatory cytokines such as TNF- α and IL-6, which contribute to neuroinflammation (26). The immune system in the brain (which includes microglia) can be significantly affected by exposure to heavy metals. In chronic heavy metal poisoning, the brain's immune system secretes high levels of inflammatory cytokines, contributing to the neurodevelopmental disorders associated with autism. One study confirmed that children exposed to high levels of heavy metals had an abnormal immune response in the brain, which contributed to increased severity of behavioral and cognitive symptoms (27).

8.5 Diagnostic and Treatment Methods for Heavy Metal Influence on Autism Patients

Diagnosing the effects of heavy metals on autism patients requires the use of a range of modern methods, including laboratory tests, neuroimaging, and behavioral assessment tools.

Toxicology and heavy metal screening tests.

Blood and urine tests are the most common methods for detecting heavy metals in the body.

Urine tests are more accurate for detecting heavy metals, as these substances are excreted in the urine after a period of toxicity. Urine analysis can be used to detect toxins stored in the body using "metal toxicology screening" (28)

- Neurological assessment

Neuroimaging techniques such as magnetic resonance imaging (MRI) can show structural changes in the brain caused by heavy metal poisoning, or functional magnetic resonance imaging (fMRI) to determine the effects of heavy metals on brain structure and cognitive and linguistic functions. (29)

- Behavioral and psychological assessment

Physicians assess the patient's behavioral and cognitive symptoms using autism assessment scales, such as the Children's Autism Rating Scale (CARS). This scale is used to determine the extent to which autism affects a child's behavior and is based on 15 behavioral traits, including communication, social interaction, sensory responses, and more.

The Autism Interaction Rating Scale (ADOS) is an internationally recognized behavioral assessment tool used to determine the severity of autistic symptoms. For example, one study indicated that children exposed to high levels of mercury were more likely to develop autism symptoms. They are more likely to exhibit severe autistic behaviors, such as limited communication and social isolation. (30)

8.6 Treatment Methods

- Detoxification

- Using detoxification agents (chelation therapy): Chelation therapy is the process of removing heavy metals from the body using agents that bind to these metals and remove them from the body. Among the medications used are:

-DMSA (Dimercaptosuccinic Acid), used to treat lead poisoning, especially in children.

-EDTA (Ethylene diamine tetra acetic acid), used to treat acute lead poisoning.

-DMPS (Dimercapto-1-propane sulfonate), used for mercury poisoning. Treatment must be performed under strict medical supervision to avoid complications.

- Supporting nutrition and natural detoxification.

This is achieved by increasing the consumption of foods rich in antioxidants:

- Vitamin C (such as oranges and strawberries)
- Vitamin E (such as nuts and seeds)
- Glutathione, an antioxidant that promotes detoxification.

Also, by enhancing the diet with fiber-rich foods:

- Such as leafy greens, oats, and whole grains to improve the elimination of toxins through the digestive system.
- Taking zinc and magnesium supplements to compensate for any deficiency resulting from poisoning.

- Behavioral and Rehabilitative Interventions:

Cognitive behavioral therapy, occupational therapy, and speech therapy help reduce the neurological and behavioral symptoms associated with autism when exposed to heavy metals. Children are trained in communication skills and social behaviors to improve their lives.

8.6 Environmental Strategies:

Reducing exposure to heavy metals in the environment (such as controlling sources of environmental pollution). Exposure can occur through contaminated water or unhealthy foods. Removing these sources is the essential step in treatment. Controlling exposure to these sources is achieved through the use of personal protective equipment, selecting non-toxic materials, and verifying food safety. These are important methods for treating heavy metal poisoning.

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