

Association "neurotoxicity" of Toxic Metal Mercury in Hair with Autism Spectrum Disorders in Children

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Abstract— Autism spectrum disorder is a complicated neurological disease that is identified by the occurrence of two defining characteristics present in people with ASD, notably social deficits and repetitive and stereotypical behaviors. This review aims to systematically investigate the relationship between the levels of toxic and trace element Hg in hair and the developments of ASD. The objective of this review is to Methodically investigate the connection Amidst ASD emergence, also hair levels of hazardous, also trace elements Hg. Through Original articles that reported on the amounts of trace elements Hair was incorporated. The majority of studies' interests change grave not harmful state of being gathered or focused components in the hair of kids with neurodevelopmental disorders like ASD. A survey of field medicine describes demonstrated mercury exposure, whether organic, or inorganic can result in the development of characteristics symptoms that characterize or are frequently observed in autism spectrum disorders (ASD). The (DSM-IV) diagnostic criteria of autism include deficits with interpersonal relationships, having trouble expressing oneself, and engaging in behaviors that are both stereotypical and repetitious, all of which be brought on by mercury.

Keywords— Autism, Mercury, Autism spectrum disorder, trace element toxic

I. INTRODUCTION

The autism spectrum describes a range of conditions classified as neurodevelopmental disorders in the fifth revision of the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5). These conditions are typified by sensory problems, stereotyped or repetitive behaviors and interests, social impairments and communication challenges, and occasionally cognitive disabilities [1]. Through, last ten years have seen an increase in the prevalence of autism worldwide, interest the critical need for this research. As a result, extensive study is being conducted to determine the variables that lead to the development of ASD. Genetic and environmental pollution-related factors will become a focus of interest [2].

Some possible sources of heavy metal poisoning include chemical products, fertilizers, industrial paint, building materials, fish that is high in mercury, silver dental fillings, and mercury-containing preservatives (thiomersal) in vaccines. Lead may be found in the dirt near roads and can still be found in paint from older houses. Children eating paint chips or those with pica may develop toxic lead levels [3]. The concentrations of trace elements in hair from normal children differ from patterns observed in both autistic and autistic-like children.

Furthermore, some studies, suggested that mercury hair analysis may have potential use as a diagnostic tool for autism [4]. Studies have shown that there is a biological possibility and epidemiological evidence showing a direct relationship between increasing doses of mercury from thimerosal-containing vaccines and neurodevelopmental disorder [5].

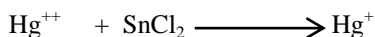
Our review will concentrate on the connection between ASD and mercury exposure by an extensive search of the literature for unique human studies, research on biomarkers for mercury exposure, and epidemiological studies. The search for relevant literature on mercury and ASD comprises published original research papers from PubMed and Google Scholar. To find more studies, references listed in the publications that were found were also looked up. Children with ASD may benefit from scalp hair as a sample to measure their mercury levels. Mercury in hair a main sample used to assess the relationship between mercury and ASD, is noninvasively obtained, and represents long-term exposure to mercury [6]. However, in order to prevent possible contamination during the pre-analytical stage, it is crucial to gather and prepare hair samples correctly. At a growth Assess of about (1.5 cm per month), scalp hair can reveal information about exposure to mercury over time [7].

II. METHODS

Analysis of Hair Hg: Atomic Absorption Spectrometry (AAS)/hydride system is one of the most sensitive analytical methods for determining trace elements, and it is used to test mercury. The determination is based on



the synthesis of atomic mercury at room temperature following a reaction with a strong reducing agent, such as sodium borohydride or tin (II) chloride (stannous chloride) SnCl_2 [8].



In future research, we will measure mercury in the hair of autistic children practically by Atomic Absorption Spectrometry.

III. RESULT AND DISCUSSION

Farida El-baz et al 2009 [8] revealed that the hair mercury level in the autistic group was significantly greater than in the age and sex-matched healthy control group. This was consistent with the findings of (Fido et al). [9], who reported that autistic children had higher levels of hair mercury than non autistic children. Adams et al. [10] observed that toxic metal excretion pathways may significantly vary among study subjects diagnosed with moderate to severe ASD as opposed to participants diagnosed with a mild ASD. This may be of a particular importance when examining hair toxic metal concentrations in young children because previous studies have suggested that hair toxic concentrations may be related to toxic metal excretion rates. Emerging evidence supports the theory that some ASDs may result from a combination of genetic/biochemical susceptibility, specifically a reduced ability to excrete mercury (Hg), and exposure to Hg at critical developmental periods [11]. They suggested that autistic children retain mercury in their bodies due to impairment in detoxification pathways [12,13]. However, Ip et al. found no difference in mercury levels in hair and blood of autistic children compared with non autistic normal children [14].

The environmental protection agency (EPA) warns that pregnant women can be exposed to methyl mercury by the consumption of contaminated fish or the use of dental amalgam, and their offspring may have developmental and neurological abnormalities[15].

Because mercury (Hg) is considered to have the most significant impact on ASD owing to its neurotoxic properties. Additionally, the cumulative exposure to multiple toxic elements may have synergistic effects, exacerbating the neurotoxic impact and complicating the understanding of individual element contributions to ASD. Thiomersal, an organic compound of mercury used as a preservative in vaccines such as Measles-Mumps-Rubella and as an antiseptic and antifungal agent, has historically been suspected to contribute to a substantial number of autism cases. Metabolic issues with toxic elements in children with autism are thought to be associated with oxidative stress, diminished methylation and transsulfuration potential, and mitochondrial dysfunction. Additionally, elevated levels of porphyrins are found in the urine of children with autism, indicative of the body's mercury load [16].

Many animal studies have attempted to determine the neurological mechanisms linking Hg and ASD. Experiments on monkeys show that Hg levels in the brain increase after exposure, and that it is necessary to evaluate the effects of

its presence on neurological structures. After administering organic Hg to monkeys, the half-life of Hg in the brain varied considerably in different brain regions. In the thalamus, Hg levels remained the same, and in the pituitary gland, they doubled six months after exposure. Stereologic and autometallographic studies showed that the persistence of Hg in the brain was accompanied by a significant increase in the number of microglia, while the number of astrocytes decreased [17].

An active neuroinflammatory process was detected in the brains of ASD patients, including a marked activation of microglia. Hg-mediated modulation of cytokine production (IL-6, TNF- α) could have an adverse impact on ASD patients, leading to autoimmune brain response, IgG accumulation in the brain, and CD4+ T cell infiltration [18]. It is also shown that some cognitive and sensory deficits can be associated with Tryptophan-Kynurenine metabolic system in the human brain[19]., Jafari et al. [20] reported significantly lower Hg levels in hair for cases compared to controls, they also reported higher Hg levels in whole blood and RBCs for ASD cases compared to controls. Shiani et al. [21] observed that, in their meta-analysis involving 13 trials, 952 patients had significantly higher Hg levels than 650 controls. These results corroborate previous findings of earlier research showing that ASD cases had higher mercury levels than controls, {but the current meta-analysis included a significantly greater number of partakers samples, including plasma samples. Understanding the critical period of exposure to potential risk factors is crucial for comprehending the pathophysiological process of neurodevelopmental illnesses [22]. During pregnancy, the placenta, in one of its roles, prevents the passage of pathogenic me-diators, thus protecting the fetus [23]. However, this barrier cannot prevent the transfer of several pollutants [24]. Therefore, the developing fetus and infant are at poten-tial risk of environmental toxic effects as a result of their immature system [25]. Studies investigating the status of trace elements and their correlation with ASD employ a range of exposure biomarkers, including hair mineral analysis, blood, urine, and teeth compartments. Autism is also conceptualized as a manifestation of mercury (Hg) poisoning. Certain micronutrients, like copper (Cu), are implicated in the development of ASD. The imbalance of essential micronutrients can disrupt the physiological equilibrium, potentially leading to neurodevelopmental disorders. The role of nutritional status and dietary habits in ASD development also warrants further exploration. Conversely, zinc (Zn) is recognized for its protective role against neurodevelopmental issues, participating in detoxification and antioxidation processes, involving, for example, metallothioneins [26].

It is believed that exposure to environmental variables, particularly grave compounds, participates in the pathogenesis of autism spectrum disorder (ASD) due to the increasing incidence of autism (Table 1). Table 1 explains in detail the complex interactions between different grave metal (Hg), their molecular forms, and the mechanisms by which they cause ASD. It is supported by references [27,28,9,29,30,31,32]. meticulously elucidates the intricate relationships between various toxic metal Hg, their chemical forms, and the mechanisms through which they contribute to ASD. This table provides a comprehensive synthesis of the

multifaceted impacts of these metal Hg on individuals diagnosed with ASD, offering insights into the complex interplay between environmental exposure and neurodevelopmental disorders. Children are more susceptible to exposure to environmental toxins due to their higher absorption rates and lower detoxification capacities compared to adults. Mercury (Hg) is considered to have the most significant impact on ASD owing to its neurotoxic properties. Additionally, the cumulative exposure to multiple toxic elements may have synergistic effects, exacerbating the neurotoxic impact and complicating the understanding of individual element contributions to ASD. Thiomersal, an organic compound of mercury used as a preservative in vaccines such as Measles-Mumps-Rubella and as an antiseptic and antifungal agent, has historically been suspected to contribute to a substantial number of autism cases. Metabolic issues with toxic elements in children with autism are thought to be associated with

oxidative stress, diminished methylation and transsulfuration potential, and mitochondrial dysfunction. Additionally, elevated levels of porphyrins are found in the urine of children with autism, indicative of the body's mercury load [33]. The lower concentration of mercury in the newborn hair of autistic children suggests a change in mercury metabolism, which could be brought on by a reduced capacity for mercury excretion. This is in line with the use of larger doses of oral antibiotics, which may have a comparable effect in humans. These antibiotics are known to decrease mercury excretion in rats by altering the gut flora. A further factor contributing to the high prevalence of chronic gastrointestinal issues in autistic individuals may be the increased use of oral antibiotics during infancy [34].

Table 1:-Toxic Metal (Hg).Their Chemical Forms, and Mechanisms Contributing to ASD][27-29,33].

Metal	Chemical Form	Mechanism of ASD Contribution
Hg (Mercury)	-	Higher levels of antineuronal antibodies; neurological, motor, immune, and sensory dysfunctions. Exposure can occur through fish contaminated with methylmercury or through fungicides used as grain preservatives in bread. Children with ASD exhibit higher levels of Hg in primary teeth and blood. Hg induces metallothionein dysfunction, related to Zn deficit.
	Mercury ions (Hg ²⁺)	Nephrotoxic and causes damage to muscle tissue.
	Methylmercury (CH ₃ Hg ⁺)	"Most toxic form, can cross the blood-brain barrier due to its lipophilic nature, binding to neurons and causing high neurotoxicity. Main sources for humans include fish, bacteria, and algae, leading to the biotransformation of elemental Hg to methylmercury.

IV. CONCLUSIONS

At the present time, with environmental pollution and harmful emissions surrounding ,research on metals is always needed, with special alertness to the speciation forms and concentrations of metals, as well as the courses, also duration of exposure, because metals have varying effects on different molecular targets. By means of tentative investigation Since behaviors are the result of neurological processes, probably would have possible results in interfering with these underlying processes ,show rapprochement both at the molecular and behavioral levels. Consequently, So, what exactly neural mechanism causes ASD outcomes to occur as well as how so many genetic and non-genetic factors could be involved in the same process protrude. Interestingly, oxidative stress, inflammation, synapse development, synaptic communication, brain connection, gut-brain signaling are among the essential molecular components of ASD that are impacted by metals. Therefore, As a result, one could speculate that a primary pathology of ASD may be a trace metal imbalance, characterized by either the presence of toxic metals and/or the overload or lack of essential metals, particularly Accumulation of mercury in hair.

CONFLICT OF INTEREST

Authors declare that they have no conflict of interest.

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