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Zinc Deficiency in Autism spectrum Disorder- A Case-control study.

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ABSTRACT
Background: Autism spectrum disorder (ASD) is a neuro-developmental disorder affecting communication and behavior. There is a wide variation in the type and severity of symptoms in people with ASD. The prevalence of the disorder is increasing day by day. According to WHO, every 1 out of 160 kids is diagnosed with ASD. The etiology of the disease is still unknown. Environmental factors such as heavy metal exposure due to industrialization or polluted conditions might cause a disbalance of minerals leading to neurodevelopmental disorder. The deficiency of elements like zinc, copper, and magnesium might play some role in the causation of autism spectrum disorder. As the etiology of ASD is not known, there have several studies to find the cause, and zinc deficiency is found to be associated. However, the relationship between ASD and Zinc is yet to be established, and zinc as a treatment and prevention of ASD needs further research. **Methods:** A case-control study was conducted at a tertiary care hospital in Assam for one year. The study group comprised 15 children diagnosed with ASD (10 boys and five girls) from 2 to 8 years attending randomly selected therapy centers at Assam.
The control group consisted of 15 neurotypical children who had not been diagnosed with neurological disorders aged from 2 to 8 years, randomly selected from the general population of the same area. The hair samples were evaluated for zinc in the Environmental Chemistry Laboratory, IASST, Guwahati, by Atomic absorption Spectrometry. **Results:** A total of 15 cases and 15 controls were taken up for study with a mean age of 4.2years and 4.8 years in the case and control groups, respectively. The results were statistically analyzed using the Graphpad Prism version. The mean zinc concentration in the case group was 116.2ppm, and the mean zinc concentration in the control group was 170.7ppm with a p-value of 0.035, which was statistically significant. **Conclusion:** Decreased Zinc content was observed in the hair samples of the children with ASD compared to the control group. These findings suggest that zinc deficiency may epigenetically contribute to the pathogenesis of Autism, and a nutritional approach may yield a novel hope for its treatment and prevention.
Keywords: Autism Spectrum Disorder (ASD), Zinc.

I. INTRODUCTION:

Autism spectrum disorder (ASD) is a neuro-developmental disorder affecting communication and behavior. Symptoms of Autism may appear in the first two years of life, but it is often diagnosed later. There is a wide variation in the type and severity of symptoms people with ASD experience. The American Psychiatric Association created a Diagnostic and Statistical Manual of Mental Disorder (DSM-5) for the diagnosis of ASD, according to which people with ASD have difficulty in communication and interaction, restricted interest and repetitive behaviors, as well as an inability to function appropriately at school, work and other areas of life. Although it is a lifelong ailment, the symptoms, and quality of life improve with early diagnosis, treatment, and behavioral therapy. Thus all children should be screened for Autism for an early diagnosis.

The prevalence of the disorder is increasing day by day. According to WHO, every 1 out of 160 kids is diagnosed with ASD. The etiology of the disease is still unknown. Some researchers blame environmental changes, whereas some believe that genetics and epigenetics might have some role in the causation of the disease. Environmental factors such as heavy metal exposure due to industrialization or polluted conditions might cause a disbalance of minerals leading to neurodevelopmental disorder. Trace elements have a significant influence on neurotransmitters. The deficiency of elements like zinc, copper, and magnesium might play some role in the causation of autism spectrum disorder.

The importance of zinc in human nutrition and health is recognized early in the 1960s. For

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zinc nutritional status assessment, serum zinc alone is limited because its levels are influenced by factors other than zinc intakes, like hypoalbuminemia, infection, acute stress, and pregnancy. In addition, serum zinc levels are subject to diurnal variation and fasting status. Hence we considered other modalities to estimate the zinc status by measuring zinc concentration in hair samples.

There have been limited human trials with prenatal zinc supplementation, with most studies beginning zinc supplementation during gestation. Prenatal zinc supplementation has been shown to improve autonomic function in children versus controls, which was noticeable during gestation. Maternal zinc deficiency has been shown to increase obstetric complications, and zinc deficiency may be involved in the increased obstetric risk associated with higher maternal age in a low socioeconomic group.

Zinc and the nervous system have been reviewed recently. Zinc has essential functions in the nervous system to maintain the structure, cell-signaling, and enzymatic co-factors. Zinc is a required co-factor for DNA and RNA polymerases; histone catalyzes DNA ligase. As such, zinc is involved in most aspects of protein synthesis within the CNS and is an independent factor in gene expression.

Zinc has been implicated in olfactory, cerebellum, and hippocampal development, and even mild zinc deficiency has been shown to affect memory and learning. It has also been demonstrated that transient gestational zinc deficiency can affect memory and learning that persists into adulthood. The lack of population-based longitudinal studies hampers the generalizations of the aetiopathogenesis of ASD. Taken together, the studies conducted do, though, suggest zinc deficiency may be expected in ASD.

Aims and Objectives: The study aimed to assess the Zinc status in children with an autism spectrum disorder**.**

To compare the Zinc concentration in hair samples of case and control groups.

Materials and Methods: It was a case-control study conducted at a tertiary care hospital in Assam for one year.

Each child's parents or legal guardians signed a written protocol consent to participate in the study.

The study group comprised 15 children diagnosed with ASD (10 boys and five girls) from 2 to 8 years attending randomly selected therapy centers at Assam.

The control group consisted of 15 neurotypical children who had not been diagnosed with neurological disorders aged from 2 to 8 years, randomly selected from the general population of the same area.

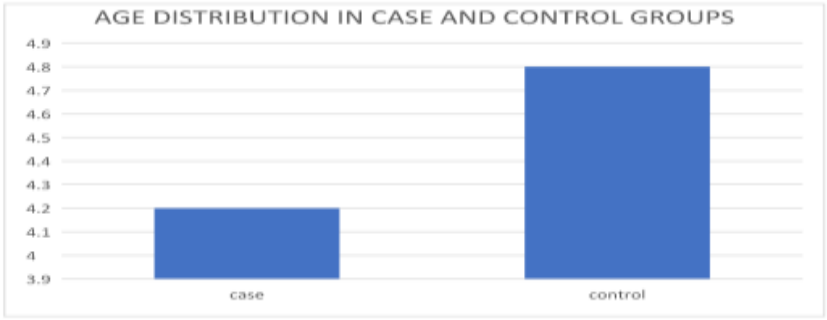
The hair samples were evaluated for zinc in the Environmental Chemistry Laboratory, IASST, Guwahati, by Atomic absorption Spectrometry.

Sample collection and processing:

- Hair samples from both cases and control were taken from 6 different areas of the occipital part of the head.
- The hair samples were washed properly.
- After the hair samples are dried, they are weighted for approx 0.1g.
- Hydrogen peroxide was added just to wet the hairs and kept for approx 3 hours.
- 2N nitric acid (HNO_3) was added, followed by perchloric acid ($HClO_4$), and digested in a fume hood at about 50°C.
- The samples were allowed to cool at room temperature, and approx 1 ml of H_2O_2 was added and heated again at 50°C until the volume was reduced to 2.5 ml.
- The vessels were cooled, and the contents were then filtered separately using Whatman filter paper and transferred to clean 100ml volumetric flasks by rinsing the vessel several times with distilled water.

II. RESULTS:

Age Distribution



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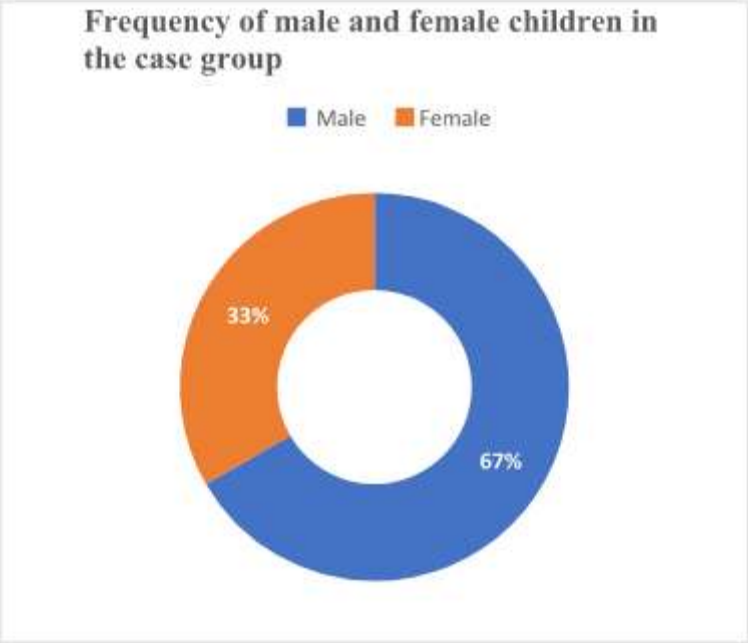
The mean age in the case group is 4.2 years, and the mean age in the control group is 4.8 years.

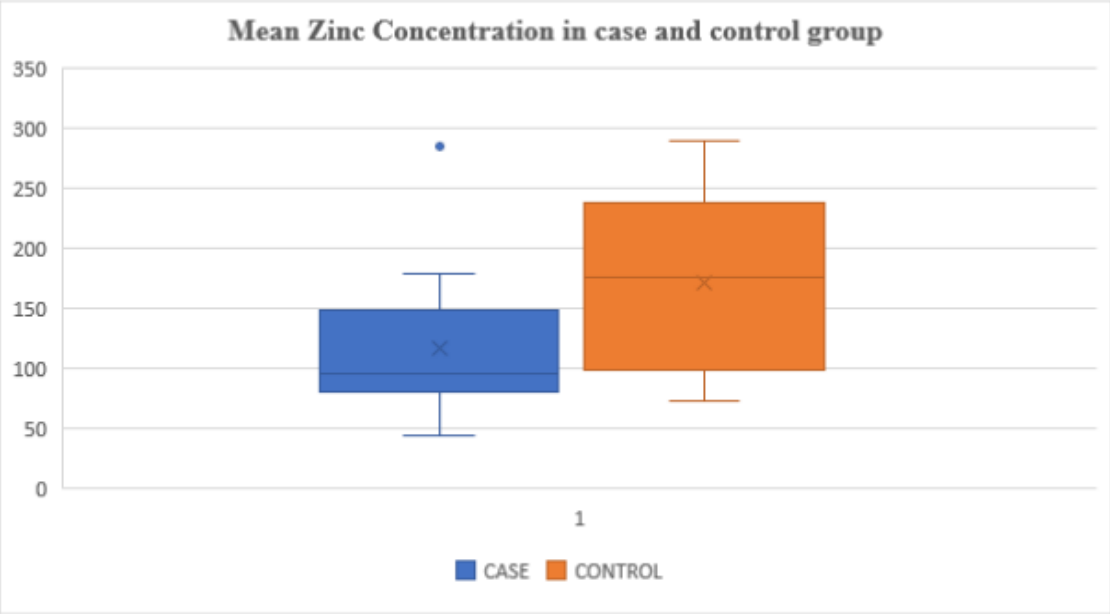
Sex distribution

The study group comprised 15 children diagnosed with ASD, ten boys(67%) and five girls(33%).
The control group comprised 15 children with nine boys(60%) and six girls(40%)



Zinc concentration in case and control group

Mean zinc concentration	case 116.2ppm	control 170.7ppm
P value	0.035	



III. CONCLUSION:

Decreased Zinc content was observed in the hair samples of the children with ASD compared to the control group. These findings suggest that zinc deficiency may epigenetically contribute to the pathogenesis of Autism, and a nutritional approach may yield a novel hope for its treatment and prevention.

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