# A survey on the parents awareness of the relationship of heavy metals: lead and mercury to autism in Saudi Arabia

Asia Alharbi<sup>1</sup>, Nawaf Almuntashiri<sup>1.2</sup>, Osama Alsahafi<sup>1.2</sup>, Salma Alsayed<sup>1.3</sup>, Hamzah Alzahrani<sup>1</sup>, Walla A. Elwani<sup>4</sup>

<sup>1</sup>Master Student of Toxicology & Forensic Science, University of Jeddah, Saudi Arabia <sup>2</sup>Bachelor of Pharmaceutical Science, Makkah Health Affairs, Ministry of Health, Saudi Arabia <sup>3</sup>Bachelor of Medical Laboratory Technology, Prince Muhammed Bin Abdul-Aziz Hospital, National Guard Health Affairs , Saudi Arabia <sup>4</sup>Department of Biochemistry , Faculty of Science , University of Jeddah, Saudi Arabia

**Abstract:** Autism spectrum disorder (ASD) is a neurodevelopmental disorder that causes behavior abnormalities. ASD is prevalent in 1-2% of the population worldwide affecting males four times more as compared to the females. In the current study, data of 158 autistic children was collected from various regions of Saudi Arabia. A questionnaire-based cross-sectional study was conducted to determine the effect of lead and mercury on autism in Saudi Arabia. The results showed that ASD was affected males three times more than the females. Children of age 6-10 were found to be more affected with ASD than other age groups. Factors involved in the onset of autism included exposure to environmental pollutants, use of canned foods, dental amalgam fillings, obesity and smoking. Most of the parents were found to be unaware of the role of heavy metals in ASD and sources of these pollutants. Additionally, testing for the presence of heavy metals was done in only 14.3% of the studied children. These results show that there is a lack of awareness and insufficient knowledge about autism among parents. Thus, there is a need for creating further awareness among the people regarding toxic effect of heavy metal pollutants and sources of these pollutants.

Keywords: Autism disorder, lead, mercury, toxicity.

#### 1. Introduction

The Autism or more specifically known as the Autism Spectrum Disorder (ASD) is a type of neurodevelopmental disorder whose signs and symptoms can be different from one affected individual to the other <sup>21</sup>. The latest definition of ASD has been given by the team of child psychiatrists in the "American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5)<sup>20</sup>. The signs and symptoms of ASD appear before the age of 3 year, however it may be diagnosed later. Most of the people affected with this disorder are able to speak, live normally and remain free of symptoms until adulthood <sup>5</sup>.Mostly the characteristic signs and symptoms revolve around the problems in the social interaction and bizarre repetitive behaviors <sup>23</sup>.

Previously language delay or speech difficulties were also considered as the part of ASD diagnosis <sup>21</sup>. The prevalence of ASD in the recent surveys is estimated as 1-2% worldwide in which male gender is affected almost 4 time more as compared to the female gender <sup>21</sup>. Prevalence of autism in United States of America and United Kingdom was found to be 1.7% and 1%, respectively. However, prevalence was higher in the Asian countries ranging from 1.81% - 2.6% <sup>18</sup>.

The increase in the prevalence of ASD might be due to advancements in the diagnostic process or might be due to increased industrialization. Previously autism was considered as having a genetic heterogeneity with complex mechanisms taking part in hereditary process<sup>15</sup>. Recently scientists and researchers noted that 80% of the total individuals affected by ASD have normal genetic makeup while 20% of the individuals which show some defects in genes do not show common mutations <sup>15</sup>. Due to

such findings, scientists had believed that ASD is a multifactorial disorder and environmental factors also play an important role in its pathophysiology along with the defects at the genetic level <sup>15</sup>. The abnormally high levels of toxic elements such as lead and mercury might induce harmful effect on for the neurodevelopment <sup>4</sup>. These elements also even can play hazardous role in the presence of their safe levels. Thus, no level of these metals can be considered as safe<sup>13</sup>.

The problem with lead and mercury toxicity arises from the industrialization of the modern world. House paints and different kind of color polishes are the continuous source of lead toxicity. Presence of mercury in certain foods such as sea foods and smoking agents causes toxic levels of this metal around us <sup>15,20,9</sup>. Interestingly, researchers have been reported that that high levels of mercury in the obese mothers is linked with increased chances of developing autism in their fetuses <sup>19</sup>. Another important study has been conducted by Kern et al <sup>15</sup> on the association of neurotoxic metals in developmental brains and the incidence of neurodevelopmental disorders such as autism .

It has been concluded that accumulation of toxic elements such as lead and mercury might cause damage to the developing brain, and this damage is highly observed on male compared to female <sup>8</sup>. This difference related gender was attributed to the fact that female has more glutathione in the brain for detoxifying the bad impact of toxic metal. Additionally, female has an efficient mechanism to protect brain from neurotoxins due to increased detoxification process and reduced oxidative stress as a beneficial effect of estrogen and progesterone <sup>8</sup>.

These findings positively correlate with the high prevalence of autism in male in comparison to female. Considering these facts, significance of genetic testing for autism needs to be explored. Additionally, the role of lead and mercury toxicity must be highlighted. Notably, more efforts are required to increase public awareness about the importance of diagnosis and environmental factors linked to autism for treating this lifelong disorder. This investigation is particularly needed for the developing countries as the lack of autism data is clearly noted.

#### 2. Methods

A questionnaire study was conducted to determine the parents awareness of the relationship of heavy metals: lead and mercury to autism in Saudi Arabia. The electronic questionnaire was distributed through the social media, and 168 family having autistic children were participated in this study. The questionnaire questions were designed by reviewing the articles showing any linkage between neurotoxic metals (lead & mercury) and autism.

The questionnaire was divided to three categories of questions, the first one was about patients' demographic information questions (patient's gender, patient's age range and actual patient's age when diagnosed), the second category was about ASD factors information questions (is the patient diagnosed by any genetic testing, is the patient's family lived near industrial area, did the mother exposed to mercury dental filling, is the mother obese, did the mother took any kind of canned sea food during pregnancy and is there a smoker in the family) and the third category was about community awareness questions (are the parents aware of the effect of mercury and lead on autism, are the parents aware of the sources of heavy metals and did the patient had a heavy metals testing). The questionnaire data were analyzed using SPSS version 21 and results through the Pie charts.

#### 3. Results

In this study, 24 out of 168 autistic children were tested for presence of heavy metals, and 12 of these 24 tested children were subjected to treatments.

# **3.1. Patients Demographic Information**

# 3.1.1. Patients' Gender



Figure 3.1.1. The gender of Autism Children involved in this study.

Within all 168 data questionnaire of Autism children, 77.4 % of them (130 out 168) were male and 22.6% (38 out 168) were females (Fig 3.1.1).



3.1.2. Patient's Age Range

Figure 3.1.2. The age distribution of Autism children involved in this study.

The data shows that 25% (42 out 168) of Children with autism were between one to five years old. In addition, 25.6% (43 out 168) were more than 11 years and 49.4% (83 out 168) were between 6 to 10 years (Fig 3.1.2).

# 3.1.3. Actual Patient's Age when diagnosed.



Figure 3.1.3. The percentage of the actual age distribution of Autism children when diagnosed by ASD involved in this study.

The data shows that 82.1% (138 out 168) of patients were between one to five years old. Moreover, 7.7% (13 out 168) were between 6 to 10 years, 3.6% (6 out 168) were more than 11 years and 6.5% (11 out 168) were patient's family didn't know (Fig 3.1.3).

# **3.2. ASD factors Information**



3.2.1 Is patient diagnosed by genetic testing?

# Figure 3.2.1. The distribution of percentage of the ASD children diagnosed by genetic testing involved in this study.

The majority of ASD children 55.4% (93 out 168) had not carried out genetic testing. In addition, the autistic's family did not know if genetic testing done or not 26.8% (45 out 168) and few of Children with autism were carried out genetic testing 17.9% (30 out 168) (Fig 3.2.1).



#### 3.2.2. Is the patient's family lived near industrial area?

Figure 3.2.2. The Percentage of the autistic family exposed to industrial and environmental pollutants involved in this study.

The majority of ASD autistic family 73.8 % (124 out 168) had not lived near industrial area or environmental pollutant whereas 13.1% (22 out 168) confirmed that their environmental was polluted. In addition, 13.1% (22 out 168) did not know if their environmental polluted or not (Figure 3.2.2).

#### 3.2.3. Did the mother expose to mercury dental filling?



Figure 3.2.3. Mothers' exposure to mercury dental filling during pregnancy involved in this study.

The data shows that 43.5% (73 out 168) the mothers had not exposed to mercury dental filling during pregnancy while 20.8% (35 out 168) were exposed. Moreover, 35.7% (60 out 168) of the mothers did not know if she was exposed or not (Fig 3. 2.3).

#### **3.2.4.** is the mother obese?



Figure 3.2.4. The distributed percentage of obese mothers during pregnancy in this study.

The data shows 73.2% (123 out 168) of the mothers were not obese while 26.8% (45 out 168) were obese (Fig 3.2.4).



# 3.2.5. Did the mother took any kind of canned sea food during pregnancy?

Figure 3.2.5. The Percentage of the mothers who have a child with autism and eating canned sea food during pregnancy involved in this study.

Majority of the mother 53.6% (90 out 168) with an autistic child eat sometimes canned sea food during pregnancy, while 10.7% (18 out 168) always eat canned sea food, In addition, 9.5% (16 out 168) did not take canned sea food and 26.2% (44 out 168) did not know if she had been eaten a canned food or not (Fig 3.2.5).

#### **3.2.6.** Is there a smoker in the family?



Figure 3.2.6. The percentages of smoker in the autistic family involved in this study.

The data shows 54.2% (91 out 168) having smokers in the autistic families whereas 45.8% (77 out 168) have not (Fig 3.2.6).

# 3.4. Community awareness







Data demonstrated the lack of parent's awareness on the effect of mercury and lead on autism with 93.5 % (157 out 168), while 6.5% (11 out 168) had aware (Fig 3.4.1).



#### 3.4.2. Are the parents aware of the sources of heavy metals?

Figure 3.4.2. Parents' awareness about the source of exposure of mercury and lead in this study.

Data illustrated the lack of parent's awareness on the source of exposure to mercury and lead with 93.5 % (157 out 168), while 6.5% (11 out 168) had aware (Fig 3.4.2).



#### 3.4.3. Did the Patient Had A Heavy Metals Testing?

Figure 3.4.3. Percentage of the children with autism having a heavy metals test.

Data shows that most of the autistic children had not carried out the heavy metals test with 85.7% (144 out 168), while 14.3% (24 out 168) had carried out the test (Fig 3.4.3).

#### 1. Discussion

This study analyzed the prevalence of ASD in the Kingdom of Saudi Arabia, factors related to onset of autism and the awareness of community about the factors causing autism. The current study showed that males were more affected as compared to females. Previous studies have also shown high incidence of autism in males as compared to females <sup>10,7</sup>. Loomes <sup>1</sup> reasoned that this gender difference was due to the reason that females remain under-recognized and diagnosed late as compared to males. This camouflaging effect is more prevalent in the females who have no visible intellectual disability because such females are mostly missed in the conventional diagnostic procedures <sup>11</sup>. Therefore, under-

diagnosis may be a reason for results showing high autism prevalence in Saudi male patients as well. Children of 6-10 years were more affected as compared to other age groups. However, most of the cases were diagnosed in the early age of 1-5 years.

A previous study on by Al-Salehi and Al-Hifthy <sup>24</sup> showed that mean age of autism diagnosis in Saudi autistic children was 6.3 years. An early diagnosis (1-5 years) observed in this study may be due to improved medical facilities accessible to people in urban areas. Only 17.9% of the studied autistic children were diagnosed by genetic testing. Due to recent advances in molecular diagnostics, genetic testing can be very useful to understand the etiology of disease and therefore, should be performed in the hospitals <sup>22</sup>. Genetic testing may also help to diagnose both males and female with equal efficiency <sup>2</sup>. However, the results of this study showed that parents who has autistic children were unaware of the significance of genetic testing in the diagnosis of autism.

This study showed that mothers of autistic children were exposed to environmental pollutants and sea canned food during pregnancy. This agrees with previous studies which demonstrated that consumption of preserved sea food items, industrial and environmental pollution have a significant role towards the onset of autism <sup>14</sup>. In this study, maternal dental amalgam filling and obesity were also found to be linked with autism as reported previously <sup>16,17</sup>.

The results of current study showed that around half of the autistic children (54%) had a smoker in their family. Smoke also deposits metals like cadmium to the children <sup>6</sup>. In a recent study by Khalil <sup>3</sup>, exposure to secondhand smoke was found to cause autism in male children. This study revealed that parents were not aware of the factors that cause autism and there was a clear lack of parents' awareness about the prevalence of this disease. For instance, 94% parents were unaware of the effect of mercury and lead on autism. Similarly, 94% parents did not know about the sources of heavy metal toxicants. Due to lack of awareness about heavy metal toxicity, children with autism do not undergo for heavy metal testing. The study demonstrated that only 14.3% of the autistic children were tested for the level of heavy metals in their bodies.

Previous studies have shown that high levels of heavy metals like lead and mercury are present in the blood of autistic children <sup>13,20</sup>. Contamination of the environment, primarily drinking water, with heavy metals is the result of rapid industrialization. Therefore, there is a need to raise concern about contribution of heavy metals to various health related issues <sup>12</sup>.

#### 2. Conclusions

It is concluded that prevalence of autism in Saudi Arabia is a rising concern. Females may be under-recognized for autism diagnosis that resulted in data showing high prevalence in males. It may also be concluded that suitable medical facilities were available in Saudi Arabia that resulted in early diagnosis of disease. However, genetic testing was not frequently performed for the diagnosis. Exposure to environmental pollutants, consumption of canned sea foods, obesity, dental amalgam fillings and smoking were found to have a role in the incidence of autism. Clearly, parents were not aware about the role of heavy metal toxicity in the development of autism and the sources of these heavy metals causing the disease. Due to this unawareness, most of the autistic children never undergo a test for analysis of heavy metals. It can be concluded that there is insufficient knowledge and a lack of awareness about autism related heavy metals particularly mercury and lead among parents who has autistic children. Therefore, as parents are the primary caregivers for their children, significant efforts should be done at raising knowledge levels amongst them, through awareness campaigns.

#### 3. Recommendations

- Parents or guardians should pay attention to the behavioral changes in males and females and should take them to hospital as soon any symptom is found.
- To understand the etiology of disease, genetic testing should be promoted in the autistic children.
- Prospective parents should avoid the risk factors like exposure to environmental pollutants, use of canned foods, dental amalgam fillings, obesity and smoking.
- Children with autism should be tested for heavy metals not only to evaluate the link between metals and disease but also to understand the causes of autism.

#### 4. Acknowledgements

Authors desiderate a grateful thank to Dr. Waleed Alharbi for facilitating this study.

#### References

- Discovery.ucl.ac.uk. (2019). Gender differences in children and adolescents with high-functioning autism spectrum disorders - UCL Discovery. [online] Available at: http://discovery.ucl.ac.uk/1519664/ [Accessed 3 Aug. 2019].
- [2] Wiśniowiecka-Kowalnik, B. and Nowakowska, B. (2019). Genetics and epigenetics of autism spectrum disorder—current evidence in the field. Journal of Applied Genetics, 60(1), pp.37-47.
- [3] Khalil, N., Kaur, B., Lawson, A., Ebert, J. and Nahhas, R. (2018). Secondhand smoke exposure is associated with autism spectrum disorder in US males but not in females: Results from the National Survey on Children's Health. Environmental Disease, 3(1), p.8.
- [4] Lee, M., Chou, M., Chou, W., Huang, C., Kuo, H., Lee, S. and Wang, L. (2018). Heavy Metals' Effect on Susceptibility to Attention-Deficit/Hyperactivity Disorder: Implication of Lead, Cadmium, and Antimony. International Journal of Environmental Research and Public Health, 15(6), p.1221.
- [5] Lord, C., Elsabbagh, M., Baird, G. and Veenstra-Vanderweele, J. (2018). Autism spectrum disorder. The Lancet, 392(10146), pp.508-520.
- [6] Qin, Y., Jian, B., Wu, C., Jiang, C., Kang, Y., Zhou, J., Yang, F. and Liang, Y. (2018). A comparison of blood metal levels in autism spectrum disorder and unaffected children in Shenzhen of China and factors involved in bioaccumulation of metals. Environmental Science and Pollution Research, 25(18), pp.17950-17956.
- [7] Tromans, S., Chester, V., Kiani, R., Alexander, R. and Brugha, T. (2018). The Prevalence of Autism Spectrum Disorders in Adult Psychiatric Inpatients: A Systematic Review. Clinical Practice & Epidemiology in Mental Health, 14(1), pp.177-187.
- [8] Kern, J., Geier, D., Homme, K., King, P., Bjørklund, G., Chirumbolo, S. and Geier, M. (2017). Developmental neurotoxicants and the vulnerable male brain: a systematic review of suspected neurotoxicants that disproportionally affect males. Acta Neurobiologiae Experimentalis, 77(4), pp.269-296.
- [9] Li, H., Li, H., Li, Y., Liu, Y. and Zhao, Z. (2017). Blood Mercury, Arsenic, Cadmium, and Lead in Children with Autism Spectrum Disorder. Biological Trace Element Research, 181(1), pp.31-37.
- [10] Palmer, N., Beam, A., Agniel, D., Eran, A., Manrai, A., Spettell, C., Steinberg, G., Mandl, K., Fox, K., Nelson, S. and Kohane, I. (2017). Association of Sex With Recurrence of Autism Spectrum Disorder Among Siblings. JAMA Pediatrics, 171(11), p.1107.
- [11] Ratto, A., Kenworthy, L., Yerys, B., Bascom, J., Wieckowski, A., White, S., Wallace, G., Pugliese, C., Schultz, R., Ollendick, T., Scarpa, A., Seese, S., Register-Brown, K., Martin, A. and Anthony, L. (2017). What About the Girls? Sex-Based Differences in Autistic Traits and Adaptive Skills. Journal of Autism and Developmental Disorders, 48(5), pp.1698-1711.
- [12] Rehman, K., Fatima, F., Waheed, I. and Akash, M. (2017). Prevalence of exposure of heavy metals and their impact on health consequences. Journal of Cellular Biochemistry, 119(1), pp.157-184.
- [13] Saghazadeh, A. and Rezaei, N. (2017). Systematic review and meta-analysis links autism and toxic metals and highlights the impact of country development status: Higher blood and erythrocyte levels for mercury and lead, and higher hair antimony, cadmium, lead, and mercury. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 79, pp.340-368.
- [14] Ye, B., Leung, A. and Wong, M. (2017). The association of environmental toxicants and autism spectrum disorders in children. Environmental Pollution, 227, pp.234-242.
- [15] Kern, J., Geier, D., Sykes, L., Haley, B. and Geier, M. (2016). The relationship between mercury and autism: A comprehensive review and discussion. Journal of Trace Elements in Medicine and Biology, 37, pp.8-24.
- [16] Li, M., Fallin, M., Riley, A., Landa, R., Walker, S., Silverstein, M., Caruso, D., Pearson, C., Kiang, S., Dahm, J., Hong, X., Wang, G., Wang, M., Zuckerman, B. and Wang, X. (2016). The Association of Maternal Obesity and Diabetes With Autism and Other Developmental Disabilities. PEDIATRICS, 137(2), pp.e20152206-e20152206.
- [17] Mortazavi, G., Haghani, M., Rastegarian, N., Zarei, S. and Mortazavi, S.M.J., (2016). Increased release of mercury from dental amalgam fillings due to maternal exposure to electromagnetic fields as a possible mechanism for the high rates of autism in the offspring: introducing a hypothesis. Journal of biomedical physics & engineering, 6(1), p.41

www.ijasrjournal.org

- [18] Poovathinal, S., Anitha, A., Thomas, R., Kaniamattam, M., Melempatt, N., Anilkumar, A. and Meena, M. (2016). Prevalence of autism spectrum disorders in a semiurban community in south India. Annals of Epidemiology, 26(9), pp.663-665.e8.
- [19] Skalny, A., Skalnaya, M., Bjørklund, G., Nikonorov, A. and Tinkov, A. (2016). Mercury as a possible link between maternal obesity and autism spectrum disorder. Medical Hypotheses, 91, pp.90-94.
- [20] Mohamed, F., Zaky, E., El-Sayed, A., Elhossieny, R., Zahra, S., Salah Eldin, W., Youssef, W., Khaled, R. and Youssef, A. (2015). Assessment of Hair Aluminum, Lead, and Mercury in a Sample of Autistic Egyptian Children: Environmental Risk Factors of Heavy Metals in Autism. Behavioural Neurology, 2015, pp.1-9.
- [21] Lai, M., Lombardo, M. and Baron-Cohen, S. (2014). Autism. The Lancet, 383(9920), pp.896-910.
- [22] Griesi-Oliveira K, Sertié AL.(2017). Autism spectrum disorders: an updated guide for genetic counseling. Einstein (Sao Paulo). 2017 Apr-Jun;15(2):233-238.
- [23] Yassa, H. (2014). Autism: A form of lead and mercury toxicity. Environmental Toxicology and Pharmacology, 38(3), pp.1016-1024.
- [24] Al-Salehi, S., Al-Hifthy, E. and Ghaziuddin, M. (2009). Autism in Saudi Arabia: Presentation, Clinical Correlates and Comorbidity. Transcultural Psychiatry, 46(2), pp.340-347.