

## Autism Spectrum Disorder (ASD); The Past, The Present, and The Future

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### Abstract

Autism Spectrum Disorder (ASD) is one of the most puzzling disorders for which not only no exact cause has been identified but also no definitive cure has been found yet. Over the last few decades, its prevalence showed a dramatic rise; an observation that encouraged many researchers across the globe to try to explore all its aspects from etiology to diagnosis and treatment. Although autistic caregivers as well as physicians and researchers would like to know the exact cause of ASD and find a definitive cure for it, this goal still seems to be distant. Accordingly, the realistic achievable goal in dealing with ASD is to try to direct all the available resources to help its sufferers to improve their skills and functioning and get the utmost benefits of their strengths aiming at improving their quality of life. Socioeconomic support for autistic caregivers is also essential to empower them in helping their children across their journey for a better tomorrow. Lastly, we must believe that “whenever and wherever there is help, there is hope”.

**Keywords:** Autism Spectrum Disorder (ASD); History of ASD; DSM 5; Heritability and ASD; ASD environmental risk factors; Epigenetics; Diet and ASD

### Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder that is characterized by persistent impairment of social communication and reciprocity across multiple contexts as well as restricted, repetitive, and stereotypic patterns of behavior, interests, and or activities. Manifestations of ASD must be encountered early in life (<30-36 months of age) although they might not be fully developed until later when the social demands far exceeds the child abilities. Meanwhile, they should lead to clinically significant impairment in social, occupational, or other crucial domains of functioning. The diagnosis might be difficult as the child gets older because he or she learns how to hide some critical diagnostic manifestations [1,2]. ASD has many specifiers that make each child suffering from it unique and necessitate individualization of diagnosis and management plan [1].

### Autism Spectrum Disorder (ASD); the journey from the past to the present

Historically, late in the first decade of the twentieth century, Eugen Bleuler used the term autism to describe some schizophrenic symptomatology. That term was derived from the Greek word “autos” that means “self” to reflect the status of a person who has impaired social reciprocity, hence lives isolated. Later, in 1940s, the term “autism” was used to refer to children suffering from social and or emotional problems. By that time, Leo Kanner from USA called several children with tendency to remove themselves from their surrounding societies “autistics”. Concurrently, Hans Asperger from Germany described similar cases suffering from the same problem that later was identified as Asperger syndrome [3,4].

Autism has been identified as a separate disorder from schizophrenia only in 1960s and since then to 1970s it has been treated using electroconvulsive therapy, LSD, and behavioral modification techniques depending on all types of punishment but from 1980s to 1990s till the present; behavior therapy using positive reinforcement, environmental restructuring for learning, and communication skills training have become the main therapeutic modalities for ASD [4-6].

### Prevalence and gender differences

Autism spectrum disorder is still considered as a mysterious disease that unfortunately has a drastic increase of its prevalence over the last few decades [7]. In some reports; it was claimed to affect 10-20 per 10000 children [8] but astonishingly, in 2012, the Centers for Disease Control and Prevention (CDC) found the prevalence of ASD in United States to be 1 in 68 children with a male: female ratio of 4.5:1 [9]. Meanwhile, in a recent Egyptian community based study (2016) [10], 23.8% of studied toddlers in enrolled Primary Health Care Units were suspected to have ASD and needed further professional evaluation with a male: female ratio of 3:1.

The foregoing reported drastic increase in ASD prevalence could be attributed to the broadening of its diagnostic criteria that might have resulted in exaggeration of the numbers of included children under the diagnostic umbrella of ASD [11]. Also, none can deny the impact of increased awareness all over the world about how to pick autistic manifestations as well as the negative influence of exposure to some environmental hazards on such significant rise of ASD prevalence [12].

On the other hand, recently, it has become clear that sex hormones play a significant role in our brains whether males or females through genomic and non-genomic receptors. Estrogens protectively influence many neurobehavioral functions as mood, cognition, coordination, pain, regulation of blood pressure, and opioid sensitivity. Accordingly, gender differences do occur for many of these functions normally and aberrantly; a fact that is indicative of a better understanding of gender

impact on neurobehavioral functions in health and diseases like ASD and schizophrenia that are more prevalent in males [13].

### **What is behind the occurrence of Autism Spectrum Disorder?**

Although autism has been identified as a separate disorder which starts to manifest early in life since 1960s, its exact cause is still unknown but what is known nowadays beyond any doubt that it results from the interaction between nature and nurture. Genetic susceptibility in the form of polygenes leads to many biological derangements (nature) favoring the negative neuro-pathological impact of many environmental hazards (nurture) [14, 15]. It is worthy to mention that parenting style (e.g. refrigerator mother) once claimed to be behind the occurrence of ASD was proved not to be true [16].

Genetic factors are crucial for the development of ASD as heritability estimates from family and twin studies suggested that about 90% of variance could be attributed to such factors [17]. Monozygotic twins are much more concordant for ASD than dizygotic twins [18]. On almost every chromosome, at least one ASD linked locus has been identified; more linked to it than others are those on X, 2, 3, 7, 11, 15, 17, and 22. It seems that such linked genes are crucial for the normal development of neuro-circuits concerned with communication, social reciprocity, and emotional expression which are impaired in autistics [19]. On the other hand, about 20% of autistic children were found to suffer from comorbid genetic conditions as Down syndrome, fragile X syndrome, phenylketonuria, tuberous sclerosis, Smith Lemli Opitz syndrome, and others [20].

Also, it is worthy to mention that at the time of zygote formation, the older the parental age, the higher the risk of occurrence of ASD especially on the paternal side because production of sperms occurs throughout life that makes them more vulnerable to be negatively influenced by mutations [21].

However, the significant increase of the prevalence of ASD along the last few decades cannot solely be explained by the genetic susceptibility; a fact that encouraged many researchers across the globe to define the causes behind such terrifying increased prevalence. Environmental factors are accused to be the precipitating factors interplaying with the genetic make-up of affected individuals via epigenetic mechanisms [22,23].

Such environmental factors include antenatal exposure to teratogens (like maternal thyroxin deficiency, maternal hypotension, gestational diabetes, maternal stress, maternal drug intake like valproic acid and thalidomide, etc.), perinatal hazards (as prematurity, low birth weight, intra-partum hypoxia, etc.), and neonatal complications (like respiratory distress syndrome, intracranial hemorrhage, indirect hyperbilirubinemic encephalopathy, etc.) [24-30]. interestingly, some autistic mothers have been proved to have antibodies against fetal brain proteins which cross the placenta and interfere with the development of fetal brain with subsequent development of ASD [31,32].

On the other hand, deficiency of vitamin D, which is an immunomodulator, strong antioxidant guarding against oxidative stress, and natural protector against mutations because of its DNA repair promoting features, has been found to be one of the potential causes of autism [27,33-35].

Meanwhile, some autistic patients have difficulty in digesting gluten and casein with subsequent formation of gliomorphin and

caseomorphin peptides, which when absorbed, due to increased gut permeability (leaky gut syndrome) in those patients, lead to behavioral changes like impaired social and communication abilities and tendency for withdrawn behavior. Such impact of these peptides is claimed to be due to their similarity to opiates chemically [36].

Furthermore, intoxication with heavy metals like mercury, lead, and aluminum are considered as environmental risk factors for ASD development [37-39].

### **ASD diagnostic criteria; the present versus the past**

Recently in 2013, the Diagnostic and Statistical Manual of Mental Disorders; the 5th edition (DSM 5) was published [1]. According to it, there is just ASD, with a spectrum of severity of its manifestations from mild to severe. These manifestations include deficits in social communication and interaction that are persistent across many situations as well as patterns of behavior, interests, and or activities that are restricted, ritualistic, and repetitive. Individualization of diagnosis is based on the presence or absence of many specifiers that allow a rich clinical description of the sufferers. These specifiers include intellectual impairment, structural language impairment, association with other conditions (medical, genetic, or environmental), and association with another neurodevelopmental, mental, or behavioral disorder.

Before DSM 5 publication and according to DSM IV TR diagnostic criteria [40], there were different types of Autism Spectrum Disorders that included "autistic disorder, Asperger disorder, and pervasive developmental disorder-not otherwise specified (PDD-NOS)". As an example to highlight the difference in diagnosis from the past to the present, cases who were previously diagnosed as Asperger disorder according to DSM IV TR diagnostic criteria, are diagnosed nowadays as ASD without impairment of language or intellect [1].

### **Diagnosis of Autism Spectrum Disorder (ASD)**

Early diagnosis of ASD is crucial for implementation of early intervention, searching for an identifiable cause or a risk factor, and providing proper counseling concerning recurrence risk. For diagnosis of ASD, evaluation is often a two stages process. Stage I entails general developmental screening of all toddlers during their primary health care visits while stage II entails professional evaluation of any cases suspected to have ASD during stage I by a multidisciplinary team that includes a developmental pediatrician, a speech pathologist, an occupational therapist, a child psychologist, and a child psychiatrist. Stage II professional multidisciplinary team assessment has to focus on evaluation of autistic core symptomatology, cognitive and linguistic abilities, and adaptive, sensory, and motor skills [41,42].

For detection of any possible cause and to exclude any differential diagnosis, a battery of laboratory testing and electrophysiological evaluation might be needed [2,42].

### **Differential diagnoses**

ASD has many differential diagnoses which include many conditions like structural language disorder, intellectual disability, acquired epileptic aphasia, selective mutism, psychosocial deprivation, hearing impairment, and visual impairment [43].

## Prevention

Creating awareness about the risk factors for developing ASD could play a significant role in reducing its prevalence. Also, genetic counseling concerning recurrence risk in siblings is vital even when no risk factor is identified. Risk of recurrence ranges from 2% to 8% when a family has only one child with idiopathic ASD [44].

## Therapeutic modalities for Autism Spectrum Disorder (ASD)

The goal of treatment of autistic cases is to improve their functional abilities and the quality of their lives and provide support to their caregivers as there is no definitive cure for ASD has been identified till now. In order to achieve this goal; early intervention (from birth to 36 months) to enable the child to talk, walk, and interact with others, is crucial [41,45].

The available therapeutic modalities for ASD include behavioral and communication techniques, dietary intervention, medications, and complementary and alternative approaches [2,45].

Applied Behavioral Analysis (ABA) is an approach that reinforces positive behaviors and discourages negative ones aiming at improving the autistic child deficient skills. On the other hand, Developmental, Individual Differences, Relationship-Based Approach (DIR) concentrates on development of emotional and interaction skills while Treatment and Education of Autistic and related Communication-handicapped Children (TEACCH) depends on visual cues to teach different skills. Furthermore, for an autistic person to live independently, occupational therapy is needed [46,47].

Autistics who have troubles with their sensory input (sights, sounds, and smells) could benefit from sensory integration therapy. On the other hand, speech therapy will help them to communicate verbally and non-verbally. Meanwhile, the Picture Exchange Communication System (PECS) teaches autistics to use picture symbols to ask and answer questions [46,47].

On the other hand, elimination of gluten and casein from the diet of autistic children has been recognized as a line of their treatment and proved to benefit many of them. Caregivers claimed that it improved their children learning and communication abilities, behavior and sleep patterns, concentration, eye to eye contact, and chronic diarrhea. Also, removal of food allergens as artificial additives, flavors, and colors was associated with behavior improvement. Meanwhile, vitamins and minerals supplementation improves the nutritional status of some autistic children as they commonly suffer from deficiencies of many of them especially vitamin B6, vitamin D, and magnesium but megavitamins are better avoided to eliminate the possibility of overdose [36,48,49].

Medications might help in overcoming some associated difficulties encountered with ASD as irritability, aggression, repetitive behavior, poor attention, anxiety, and or depression [45].

Finally, complementary and alternative approaches in the form of art, music, sports, animal therapy, etc. may improve communication and learning abilities of autistic children [11,50,51].

## Future Scope

Although autistic caregivers as well as physicians and researchers would like to know the exact cause of ASD and find a definitive cure for it, this goal still seems to be distant. Accordingly, the realistic achievable goal in dealing with ASD is to try to direct all the available

resources to help its sufferers to improve their skills and functioning and get the utmost benefits of their strengths aiming at improving their quality of life. Socioeconomic support for autistic caregivers is also essential to empower them in helping their children across their journey for a better tomorrow [49]. Lastly, we must believe that “whenever and wherever there is help, there is hope”.

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