
بسم الله الرحمن الرحيم

RISK FACTORS for AUTISM SPECTRUM DISORDER

دکتر شاهرخ امیری
فوق تخصص روانپزشکی کودک و نوجوان
استاد دانشگاه علوم پزشکی تبریز

Genetic Risk Factors

- Autism is the most highly heritable of all mental disorders, exceeding that of schizophrenia or bipolar disorder.
- Twin and family studies have convincingly demonstrated that genetic factors play a role in disorders throughout the autism spectrum.

- Recent studies have shown that the concordance rates in monozygotic twins is between 60% and 90%.
- In those instances where the twins were discordant for autism, the nonautistic twin often had impairments in communication and social interaction as well as stereotypic behaviors, though not at a sufficient level to merit a diagnosis.

- In a recent study , the heritability of ASD was found to be approximately 50%. (2014)
- Both maternal and paternal age can influence the likelihood of ASD. (Mothers older than 30 years, Fathers older than 32 years)(Even grandfathers' age was important)

- Neither study addressed the question of whether late marriage played a role in determining the outcome.
- Men or women who themselves might have Asperger's disorder, or the wider variant of autism disorder, might marry later because of their social limitations or overall "oddity." Such individuals would be at greater risk of having a child with ASD than would other parents in the cohort.

- A number of known genetically caused syndromes include autism spectrum disorder as part of a broader phenotype.

- The most common of these inherited disorders is **fragile X syndrome**, an X-linked recessive disorder that is present in 2 to 3 percent of individuals with autism spectrum disorder

- **Tuberous sclerosis**, another genetic disorder characterized by multiple benign tumors, inherited by autosomal dominant transmission,Is found with greater frequency among children with autism spectrum disorder.

- Up to 2 percent of children with autism spectrum disorder also have tuberous sclerosis.

- Researchers who screened the DNA of more than 150 pairs of siblings with autism spectrum disorder found evidence of two regions on **chromosomes 2 and 7** containing genes that may contribute to autism spectrum disorder.
- Additional genes hypothesized to be involved in autism spectrum disorder were found on **chromosomes 1 6 and 1 7**

- Family studies have demonstrated increased rates of autism spectrum disorder in siblings of an index child

- Siblings of a child with autism spectrum disorder are also at increased risk for a variety of developmental impairments in communication and social skills, even when they do not meet criteria for autism spectrum disorder.

- In families with one autistic child, there is a 10% recurrence risk of autism and a 20–25% risk of other neurodevelopmental disorders in siblings.

- The recurrence risk increases to 36% in families with two autistic children.

- fragile X syndrome and tuberous sclerosis complex together are estimated to account for < 10% of cases of autism (monogenic cause).
- Advances in genetic technology have now made it possible to identify genetic aetiologies in 25–35% of people with autism

- Family and twin studies suggest that autism spectrum disorder has a significant heritable contribution; however, it does not appear to be fully penetrant.
- Although up to 1 5 percent of cases of autism spectrum disorder appear to be associated with a known genetic mutation, in most cases, its expression is dependent on multiple genes.

- The concordance rate of autistic disorder in two large twin studies was 36 percent in monozygotic pairs versus 0 percent in dizygotic pairs in one study and about 96 percent in monozygotipairs versus about 27 percent in dizygotic pairs in the second study.

- High rates of cognitive impairments, in the nonautistic twin in monozygotic twins with perinatal complications, suggest that:
- Contributions of perinatal environmental factors interact with genetic vulnerability differentially in autism spectrum disorder.

Immunological Factors

- Several reports have suggested that immunological incompatibility(i.e., maternal antibodies directed at the fetus) may contribute to autistic disorder.
- The lymphocytes of some autistic children react with maternal antibodies, which raises the possibility that embryonic neural tissues may be damaged during gestation. These reports usually reflect single cases rather than controlled studies, and this hypothesis is still under investigation.

- The heterogeneity in expression of symptoms in families with autism spectrum disorder suggests that there are multiple patterns of genetic transmission.
- Studies indicate that both an increase and decrease in certain genetic patterns may be risk factors for autism spectrum disorder.
- In addition to specific genetic factors, gender plays a strong role in the expression of autism spectrum disorder.

Prenatal and Perinatal Factors

- A higher-than-expected incidence of prenatal and perinatal complications seems to occur in infants who are later diagnosed with autism spectrum disorder.

- The most significant **prenatal factors** associated with autism spectrum disorder in the offspring are **advanced maternal and paternal age at birth, maternal gestational bleeding**, **gestational diabetes**, and **firstborn baby**.

- **Perinatal risk factors** for autism spectrum disorder include: **umbilical cord complications**, **birth trauma**, **fetal distress**, **small for gestational age**, **low birth weight**, **low 5-minute Apgar score**, **congenital malformation**, **ABO blood group system or Rh factor incompatibility** and **hyperbilirubinemia**

- Many of the obstetrical complications that are associated with risk for autism spectrum disorder are also risk factors for hypoxia,which may be an underlying risk factor itself.
- There is not sufficient evidence to implicate any one single perinatal or prenatal factor in autism spectrum disorder etiology, and a genetic predisposition to autism spectrum disorder may be interacting with perinatal factors.

Psychosocial Theories

- Studies comparing parents of children with autism spectrum disorder with parents of normal children have shown no significant differences in child-rearing skills.
- Kanner's early speculations that parental emotional factors might be implicated as contributing to the development of autism spectrum disorder have been clearly refuted.

A recent study by Dr Malek , Dr Amiri 2015

- Asthma, epilepsy, macrocephaly, hearing/vision impairments, allergy to milk/wheat, side effects of rubella vaccination, language disorders in the immediate family members and siblings, parents' low levels of education, and lack of breastfeeding until the age of two were more prevalent in children with AD

- Based on the logistic regression results, mothers' low education [Exp (B) =4.59, CI=2.13-9.87, $p<0.001$] and lack of breastfeeding until the age of two [Exp (B) =2.91, CI=1.54-5.50, $p<0.01$] were the predictors of AD.

- Significance variables recognized by the Fisher's exact test were included in the logistic regression model and mother's low level of education [Exp(B)=4.59, C.I. for EXP(B)=2.13-9.87, $p<0.001$] was introduced as predictors of AD where breastfeeding until the age of two [(Exp(B)=2.91, C.I. for EXP(B)=1.54-5.50, $p<0.01$] was introduced as a protective factor