

# Comprehensive Review of Autism Spectrum Disorder: Etiology, Early Signs, and Diagnostic Assessment

Tejasri Reddy Ananthula (MBBS)<sup>1</sup>, Akash Kumar CJ (MBBS)<sup>2</sup>, Phanindra Goud Vilasagaram (MBBS)<sup>3</sup>

tejasrireddyananthula[at]gmail.com

cjakashkumar[at]gmail.com

phani007.med[at]gmail.com

**Abstract:** *Autism Spectrum Disorder (ASD) is a complex neurodevelopmental disorder characterized by challenges in social communication and interaction, restricted interests, and repetitive behaviours. This review article provides an extensive examination of ASD, covering its etiology, early signs and symptoms, and diagnostic assessment. By synthesizing current research findings, this review aims to enhance understanding of ASD and facilitate early detection, accurate diagnosis, and effective interventions.*

**Keywords:** Autism Spectrum Disorder, etiology, early signs, symptoms, diagnostic assessment, neurodevelopmental disorder, social communication, repetitive behaviours.

## 1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder characterized by difficulties in social communication and interaction, as well as restricted interests and repetitive behaviours (1). It affects individuals across various age groups, impacting their daily functioning and overall quality of life. Early recognition and accurate diagnosis of ASD are crucial for initiating appropriate interventions and support. Paediatricians play a vital role in the early identification of ASD, as they are often the first point of contact for parents. In recent years, increased awareness and understanding of ASD, along with advancements in diagnostic tools and assessment approaches, have improved the early detection and diagnosis of the disorder. This comprehensive review article aims to provide an in-depth exploration of the etiology of ASD, early signs and symptoms, and diagnostic assessment approaches. By synthesizing the available data and research findings, this review aims to enhance our understanding of ASD and contribute to early detection, accurate diagnosis, and effective interventions for individuals with ASD.

### Definition and Diagnostic Criteria for Autism Spectrum Disorder

Autism Spectrum Disorder (ASD) is diagnosed based on a set of criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM - 5) (2)(3)(4)(5)(6)(7). To receive an ASD diagnosis, individuals must meet specific criteria related to social communication and interaction, as well as restricted and repetitive behaviors. The diagnostic criteria include:

#### 1) Difficulties in Social Emotional Reciprocity

Individuals with ASD exhibit challenges in social interaction, such as trouble with social approach, engaging in back-and-forth conversations, sharing interests with others, and expressing or understanding emotions. They may have difficulty initiating or sustaining social interactions and struggle with reciprocal communication.

#### 2) Difficulties in Nonverbal Communication

Individuals with ASD may demonstrate difficulties in nonverbal communication used for social interaction. This includes abnormal eye contact, atypical body language, and difficulty understanding and using nonverbal cues like facial expressions or gestures for communication.

#### 3) Deficits in Developing and Maintaining Relationships

ASD is characterized by deficits in developing and maintaining relationships with others, beyond those with caregivers. Individuals with ASD may lack interest in forming social connections, have difficulties responding appropriately in different social contexts, and struggle with sharing imaginative play with peers.

In addition to the above criteria, the DSM - 5 also specifies that individuals must exhibit at least two of the following four types of restricted and repetitive behaviors, interests, or activities:

- **Stereotyped Speech and Repetitive Movements:** This includes repeating words or phrases, engaging in repetitive motor movements, using objects or phrases in a repetitive manner, or displaying echolalia.
- **Rigidity and Resistance to Change:** Individuals with ASD often demonstrate a rigid adherence to routines, rituals, or patterns of behavior. They may have an extreme resistance to change and become significantly distressed when faced with even minor disruptions to their established routines.
- **Highly Restricted Interests:** People with ASD may exhibit a strong attachment to unusual objects or develop intense, focused interests in specific topics or activities. These interests often surpass what is considered typical or age-appropriate.
- **Sensory Reactivity:** Individuals with ASD may display increased or decreased reactivity to sensory input. This can manifest as a lack of response to pain, a strong dislike or sensitivity to certain sounds, excessive touching or smelling of objects, or a fascination with spinning objects.

By using the DSM - 5 criteria (8), clinicians can maximize diagnostic sensitivity and specificity, especially in preschool children who may present with early signs of ASD. Globally, the prevalence of autism varies, with studies reporting a range of estimates (9). However, the median prevalence is approximately 100 cases per 10,000 individuals, with a male - to - female ratio of around 4.2. (10) (11) (12), (13), (14). Many individuals with ASD face challenges in communication, social interaction, and functioning effectively in various areas of life. This places significant burdens on parents and caregivers, who often experience decreased parenting efficacy, increased stress, and higher rates of mental and physical health problems compared to parents of typically developing children or children with other developmental disorders (15).

### Early Signs and Symptoms: Indicators of Abnormal Brain Development

Autism Spectrum Disorder (ASD) encompasses a range of related disorders characterized by impairments in reciprocal social interaction, communication, and the presence of repetitive and inflexible behavior (16). The early symptoms of ASD can manifest in the first few months of life, providing valuable clues about atypical developmental trajectories and potential challenges ahead. (17)(18). These early signs and symptoms include delayed speech and language development or a lack of responsiveness when the Child's name is called. Other notable differences may involve social orienting, joint attention(19) (the ability to share attention with others), imitation, affect regulation, increased negative affect, ambiguous affective expressions, and reduced use of gestures(20)(21).

Various domains of development can exhibit atypicalities in individuals with ASD. In the visual domain, there may be abnormalities in visual tracking, prolonged fixation on objects (22), and intense visual inspection(23). Motor skills may be delayed, with decreased activity levels, delayed fine and gross motor skills, and the presence of atypical motor mannerisms (24) Play behaviors may also demonstrate delays, such as limited toy play, delays in motor imitation, and repetitive actions with toys, Social - communication abilities may be affected, presenting as atypical eye gaze, difficulties in orienting to one's name, impaired imitation, reduced social smiling, diminished social interest and affect, and a reduced expression of positive emotions (25). Language development may be delayed, including delays in babbling, particularly in back - and - forth social babbling, as well as delays in verbal comprehension and expression, and gesturing, as assessed through standardized measures (26). General cognitive development may also show signs of slower acquisition of new skills, as indicated by declining standard scores in certain domains (27), in a subset of toddlers subsequently diagnosed with ASD. [(23), (25), (27), (28), (29), (30), (31)]

Recognizing these early signs and symptoms is crucial for early detection and intervention, as it allows for the implementation of targeted strategies to support developmental progress and improve outcomes for individuals with ASD (32). By understanding the specific domains affected during early childhood, clinicians, caregivers, and educators can design interventions that

address the unique challenges faced by children with ASD and promote their social, communicative, cognitive, and motor development.

## 2. Etiology and Risk Factors

Autism Spectrum Disorder (ASD) is a complex disorder that arises from the interplay of genetic and environmental factors (33). The genetic component of ASD is significant, with the disorder being highly heritable and involving a remarkable genetic heterogeneity (34). Over 800 ASD predisposition genes have been identified thus far, encompassing various biological processes such as chromatin remodelling, gene transcription regulation, cell growth and proliferation, ubiquitination, and neuronal - specific processes like synaptic organization, dendritic morphology, and axonogenesis. [(34), (35)] While there are fewer common single - gene mutations and chromosomal abnormalities associated with ASD, it is believed that multiple interacting genes of modest effect contribute to the risk. Genome - wide linkage analysis has identified several susceptibility loci and positional and functional candidate genes that potentially confer a risk for ASD. [(36)(37)(38)] Interestingly, many of these genes implicated in ASD also contribute to the genetic risk for other neurodevelopmental disorders like intellectual disability, schizophrenia, specific language impairment, epilepsy, and attention deficit hyperactivity disorder (ADHD). Understanding the specificity of these genes in relation to ASD remains a crucial challenge, necessitating further advances in research. (39)

Environmental factors also play a role in the pathogenesis of autism through their epigenetic effects. (40) These factors can be categorized into prenatal, natal, and postnatal risk factors. Prenatal risk factors(41) include advanced parental age, particularly paternal age, which has been identified as one of the most significant risk factors for autism [(42)(43)(44)(45)]. Maternal physical health conditions such as metabolic syndrome, bleeding, and maternal infections during pregnancy have also been associated with an increased risk of autism in children(46). Maternal mental health, parental behaviour, and communication patterns have shown associations with the formation of children's personality and emotions, as well as the risk of mental disorders including autism(47). Maternal prenatal medication use has been linked to a 46% increased risk of autism in the fetus (48)(49)(50)(51). Studies examining the relationship between parental education and the risk of autism have yielded variable conclusions, with some confirming a correlation between lower levels of parental education and autism risk, while others indicate a stronger correlation between higher levels of parental education and the incidence of autism. (52) Natal risk factors include abnormal gestational age, with both preterm (<35 weeks) and post term pregnancy (>42 weeks) associated with a significantly increased risk of autism (53) (54) (55) (56). Fetal complications such as fetal distress and umbilical cord complications, including fetal nuchal cord and cesarean delivery, have been implicated in hypoxia (lack of oxygen) during birth, potentially increasing susceptibility to autism. In the postnatal period, low birth weight, jaundice, and postnatal infections, including meningitis, mumps, varicella, unknown fever, and ear infections within the first 30 days of

life, have been correlated with a higher risk of autism. (57) (58) (59).

Understanding the interplay between genetic and environmental factors in the etiology of ASD is crucial for elucidating the underlying mechanisms and developing targeted interventions. Further research is needed to unravel the specific genetic contributions and interactions, as well as the precise impact of environmental factors on autism risk. Such knowledge can ultimately inform strategies for early detection, prevention, and personalized interventions for individuals with ASD.

#### Diagnostic Assessment and Evaluation: Key Considerations in Autism Spectrum Disorders

Pediatricians play a pivotal role in the early recognition of autism spectrum disorders (ASDs) as they often serve as the primary point of contact for parents seeking medical guidance (60)(61)With increased awareness of the early signs of ASD due to widespread media coverage, parents are more likely to express concerns to their child's pediatrician if they observe any published indicators. Over the past two decades, professionals specializing in autism have emerged, introducing the term autism spectrum disorders to encompass the diverse range of clinical characteristics that define this condition (60) (62).

Neuropathology and neuroimaging studies have contributed to our understanding of ASD by highlighting fundamental differences in brain growth and organization in individuals with ASD. (63)(64)(65)These differences are believed to originate in the prenatal period and persist throughout early childhood into adulthood. (66)(67) Notably, research has shown that children with ASD often exhibit increased head circumference and brain volume(68)(69)(70), with one study reporting larger - than - normal brain volumes in 90% of toddlers with ASD(71)(72)(73)(74)(75)(76) However, the challenge in recognizing ASD lies in the wide heterogeneity of features(78)(79)(80)observed among individual children.

When assessing for ASD, specific behavioural markers(81) can aid in early identification (82). These markers include a lack of appropriate gaze, absence of warm and joyful expressions in eye contact, a missing back - and - forth pattern of vocalizations between infant and parent typically observed around six months of age (where infants with ASD may continue vocalizing without regard for the parents speech) (81). Furthermore, children with ASD may display limited recognition of their mothers, fathers, or consistent caregiver's voice, coupled with a disregard for vocalizations while maintaining a keen awareness of environmental sounds. Delayed onset of babbling past nine months of age, decreased or absent use of prespeech gestures (such as waving, pointing, and showing), and a lack of expressions like oh oh or & huh are additional signs to consider(83). Furthermore, children with ASD may exhibit a lack of interest or response to neutral statements. (82)

By recognizing these early behavioural indicators, healthcare professionals can facilitate early detection and timely interventions, leading to improved outcomes for children with ASD. Understanding the complex and diverse presentation of ASD is essential in guiding diagnostic

assessments and evaluating the unique needs of each individual. Through comprehensive and multidisciplinary approach, we can enhance our diagnostic capabilities and provide targeted support to optimize the development and well - being of individuals with ASD.

### 3. Conclusion

In conclusion, this comprehensive review article provides a synthesized overview of existing research on autism, encompassing a wide range of topics related to the disorder. Through a thorough examination of various studies and publications, the review has explored crucial aspects such as the diagnostic process, etiological factors, prevalence rates, behavioral characteristics.

The findings from this review underscore the significance of early detection and intervention in improving outcomes for individuals with autism spectrum disorder (ASD). Early diagnosis enables the implementation of tailored interventions, leading to better social, communicative, and adaptive skills development. It highlights the need for increased awareness among healthcare professionals, educators, and parents to recognize early signs and ensure timely support.

Furthermore, the review emphasizes the multifactorial nature of autism, with genetic and environmental factors interacting to contribute to its complex etiology. While significant strides have been made in identifying specific genes associated with ASD, more research is required to fully comprehend the interplay between genetics and environmental influences in the development of the disorder.

### References

- [1] *Autism spectrum disorder: definition, epidemiology, causes, and clinical evaluation.* **Hodges H, Fealko C, Soares N.** s1, s. 1.: Translational Pediatrics, 2020, Vol.9.55 - 65.
- [2] *Potential Impact of DSM - 5 Criteria on Autism Spectrum Disorder Prevalence Estimates.* **Matthew J. Maenner, PhD, Catherine E. Rice, PhD, Carrie L. Arneson, MS, Christopher Cunniff, MD, Laura A. Schieve, PhD, Laura A. Carpenter, PhD, Kim Van Naarden Braun, PhD, Russell S. Kirby, PhD, Amanda V. Bakian, PhD, and Maureen S. Durkin, PhD, DrPH.3,** s. 1.: JAMA Psychiatry, 2014, Vol.71.292 - 300.
- [3] *How will DSM - 5 affect autism diagnosis? A systematic literature review and meta - analysis.* **Kristine M Kulage 1, Arlene M Smaldone, Elizabeth G Cohn.8,** s. 1.: Journal of Autism and Developmental disorders, 2014, Vol.44.
- [4] *A Comparison of DSM - IV - TR and DSM - 5 Diagnostic Classifications in the Clinical Diagnosis of Autistic Spectrum Disorder.* **Yaylaci F, Miral S.1,** 2017, Journal of Autism and Developmental disorders, Vol.47, pp.101 - 109. PMC27747464. .
- [5] *Application of DSM - 5 criteria for autism spectrum disorder to three samples of children with DSM - IV diagnoses of pervasive developmental disorders.* **Huerta M, Bishop SL, Duncan A, Hus V, Lord**



- C.10, s. 1.: The American Journal of Psychiatry, 2012, Vol.169. PMC6003412.
- [6] *S. The effects of DSM5 autism diagnostic criteria on number of individuals diagnosed with autism spectrum disorders: a systematic review.* **Sturmey P, Dalfern S.** 249 - 252, s. 1.: Journal of Autism and Developmental disorder, 2014, Vol.1.
- [7] *Rates of Autism Spectrum Disorder Diagnosis Under the DSM - 5 Criteria Compared to DSM - IV - TR Criteria in a Hospital - Based Clinic.* **Hartley - McAndrew M, Mertz J, Hoffman M, Crawford D.** 34 - 38, s. 1.: Pediatric Neurology, 2016, Vol.57. PMID: 26869267.
- [8] *Diagnostic and Statistical Manual of Mental Disorders.* **Asken, Michael J., Dave Grossman, and Loren W. Christensen.** 10, Arlington, VA.: "American Psychiatric Association., 2013, Vol.45.
- [9] *Prevalence of Autism Spectrum Disorder Among Children Aged 8 Years - Autism and Developmental Disabilities Monitoring Network, 11 Sites, United States, 2014.* **Baio J, Wiggins L, Christensen DL, Maenner MJ, Daniels J, Warren Z, Kurzius - Spencer M, Zahorodny W, Robinson Rosenberg C, White T, Durkin MS, Imm P, Nikolaou L, Yeargin - Allsopp M, Lee LC, Harrington R, Lopez M, Fitzgerald RT, Hewitt A, Pettygrove S, Const. SS - 6,** s. 1.: Morbidity and Mortality Weekly Report, 2018, Vol.67.
- [10] *Prevalence of autism spectrum disorders - - autism and developmental disabilities monitoring network, six sites, United States, 2000.* **Investigators, Autism and Developmental Disabilities Monitoring Network Surveillance Year 2000 Principal.** 1, s. 1.: MMWR Surveillance Summaries, 2007, Vol.56.
- [11] *Prevalence of autism spectrum disorders - - autism and developmental disabilities monitoring network, 14 sites, United States, 2002.* **Investigators, Autism and Developmental Disabilities Monitoring Network Surveillance Year 2002 Principal.** 1, s. 1.: MMWR Surveillance Summaries, 2007, Vol.56.
- [12] *Prevalence of autism spectrum disorders - Autism and Developmental Disabilities Monitoring Network, United States, 2006.* **Investigators, Autism and Developmental Disabilities Monitoring Network Surveillance Year 2006 Principal.** 10, s. 1.: MMWR Surveillance Summaries, 2009, Vol.58.
- [13] *Prevalence of autism spectrum disorders - - Autism and Developmental Disabilities Monitoring Network, 14 sites, United States, 2008.* **Investigators, Autism and Developmental Disabilities Monitoring Network Surveillance Year 2008 Principal.** SS03, s. 1.: Morbidity and Mortality Weekly Report (MMWR) Surveillance Summaries, 2012, Vol.61.
- [14] *Prevalence of autism spectrum disorder among children aged 8 years - autism and developmental disabilities monitoring network, 11 sites, United States, 2010.* **Investigators, Developmental Disabilities Monitoring Network Surveillance Year 2010 Principal and (CDC), Centers for Disease Control and Prevention.** SS02, s. 1.: MMWR Surveillance Summaries, 2014, Vol.63.
- [15] *Parent and family impact of autism spectrum disorders: a review and proposed model for intervention evaluation.* **Karst JS, Van Hecke AV.** 3, s. 1.: Clinical Child and Family Psychology Review, 2012, Vol.15.
- [16] *Handbook of developmental social neuroscience.* **De Haan, Michelle, and Megan R. Gunnar, eds.** s. 1.: Guilford Press, 2009.
- [17] *Diagnostic and Statistical Manual of Mental Disorders.* **Association., American Psychiatric.** Washington, DC.: American Psychiatric Association., 2013, Vol.5.
- [18] *International Classification of Diseases.* **Organization., World Health.** Geneva: World Health Organization., 2002, Vol.10.
- [19] *Response to joint attention in toddlers at risk for autism spectrum disorder: a prospective study.* **Sullivan M, Finelli J, Marvin A, Garrett - Mayer E, Bauman M, Landa R.** 1, s. 1.: Journal of Autism and Developmental Disorders, 2007, Vol.37.
- [20] *Parental identification of early behavioural abnormalities in children with autistic disorder.* **Young RL, Brewer N, Pattison C.** 2, s. 1.: National Autistic Society, 2003, Vol.7.
- [21] *Testing joint attention, imitation, and play as infancy precursors to language and theory of mind.* **Tony Charman, Simon Baron - Cohen, John Swettenham, Gillian Baird, Antony Cox, Auriol Drew.,** 4, s. 1.: Cognitive Development., 2000, Vol.15.
- [22] *Atypical object exploration at 12 months of age is associated with autism in a prospective sample.* **Ozonoff S, Macari S, Young GS, Goldring S, Thompson M, Rogers SJ.** 5, s. 1.: Autism, 2008, Vol.12.
- [23] *Attentional skills during the first 6 months of age in autism spectrum disorder.* **Maestro S, Muratori F, Cavallaro MC, Pei F, Stern D, Golse B, Palacio - Espasa F.** 10, s. 1.: The American Academy of Child and Adolescent Psychiatry., 2002, Vol.41.
- [24] *Stereotyped motor behaviors associated with autism in high - risk infants: a pilot videotape analysis of a sibling sample.* **Loh A, Soman T, Brian J, Bryson SE, Roberts W, Szatmari P, Smith IM, Zwaigenbaum L.** 1, s. 1.: Journal of Autism and Developmental disorders, 2007, Vol.37.
- [25] *Early social attention impairments in autism: social orienting, joint attention, and attention to distress.* **Dawson G, Toth K, Abbott R, Osterling J, Munson J, Estes A, Liaw J.** 2, s. 1.: Developmental Psychology, 2004, Vol.40.
- [26] *Early language and communication development of infants later diagnosed with autism spectrum disorder.* **Mitchell S, Brian J, Zwaigenbaum L, Roberts W, Szatmari P, Smith I, Bryson S.** 2, s. 1.: Journal of Developmental & Behavioral Pediatrics, 2006, Vol.27.
- [27] *Course of autism signs in the first year of life.* **Maestro S, Muratori F, Cesari A, Cavallaro MC, Paziente A, Pecini C, Grassi C, Manfredi A, Sommarino C.** 1, s. 1.: Psychopathology, 2005, Vol.38.
- [28] *Early behavioral development in autistic children: the first 2 years of life through home movies.* **Maestro S, Muratori F, Barbieri F, Casella C, Cattaneo V, Cavallaro MC, Cesari A, Milone A, Rizzo L, Viglione V, Stern DD, Palacio - Espasa F.** 3, s. 1.: Psychopathology, 2001, Vol.34.

- [29] *Autism and family home movies: preliminary findings.* **Adrien JL, Faure M, Perrot A, Hameury L, Garreau B, Barthelemy C, Sauvage D.1**, s. 1.: Journal of Autism and Developmental disorders, 1991, Vol.21.
- [30] *Early recognition of children with autism: a study of first birthday home videotapes.* **Osterling J, Dawson G.3**, s. 1.: Journal of Autism and Developmental disorders, 1994, Vol.24.
- [31] *Autism during infancy: a retrospective video analysis of sensory - motor and social behaviors at 9 - 12 months of age.* **GT., Baranek.3**, s. 1.: Journal of Autism and Developmental disorders, 1999, Vol.29.
- [32] *Social and communication development in toddlers with early and later diagnosis of autism spectrum disorders.* **Landa RJ, Holman KC, Garrett - Mayer E.7**, s. 1.: JAMA Psychiatry, 2007, Vol.64.
- [33] *Autism risk factors: genes, environment, and gene - environment interactions.* **Chaste P, Leboyer M.3**, s. 1.: Dialogues in Clinical Neuroscience, 2012, Vol.14.
- [34] *Autism genetics - an overview.* **Yin J, Schaaf CP.1**, s. 1.: Prenatal Diagnosis, 2017, Vol.37.
- [35] *A genome - wide association study of autism incorporating autism diagnostic interview - revised, autism diagnostic observation schedule, and social responsiveness scale.* **Connolly JJ, Glessner JT, Hakonarson H.1**, s. 1.: Child Development, 2013, Vol.84.
- [36] *Identification of risk loci with shared effects on five major psychiatric disorders: a genome - wide analysis.* **Consortium., Cross - Disorder Group of the Psychiatric Genomics.9875**, s. 1.: Lancet, 2013, Vol.381.
- [37] *Genome - Wide Association Study for Autism Spectrum Disorder in Taiwanese Han Population.* **Kuo PH, Chuang LC, Su MH, Chen CH, Chen CH, Wu JY, Yen CJ, Wu YY, Liu SK, Chou MC, Chou WJ, Chiu YN, Tsai WC, Gau SS.9**, s. 1.: PLoS One, 2015, Vol.10.
- [38] *Synaptic, transcriptional and chromatin genes disrupted in autism.* **De Rubeis S, He X, Goldberg AP, Poultney CS, Samocha K, Cicek AE, Kou Y, Liu L, Fromer M, Walker S, Singh T, Klei L, Kosmicki J, Shih - Chen F, Aleksic B, Biscaldi M, Bolton PF, Brownfeld JM, Cai J, Campbell NG, Carracedo A, Chahrour MH, Chiacchetti AG, Co.7526**, s. 1.: Nature, 2014, Vol.515.
- [39] *Autism risk factors: genes, environment, and gene - environment interactions.* **Chaste P, Leboyer M.3**, s. 1.: Dialogues Clin Neurosci., 2012, Vol.14.
- [40] *Environmental factors influencing the risk of autism.* **Karimi P, Kamali E, Mousavi SM, Karahmadi M.27**, s. 1.: Journal of Research in Medical Sciences, 2017, Vol.22.
- [41] *Prenatal risk factors for autism: comprehensive meta - analysis.* **Gardener H, Spiegelman D, Buka SL.1**, s. 1.: The British Journal of Psychiatry, 2009, Vol.195.
- [42] *Advanced parental age and the risk of autism spectrum disorder.* **Durkin MS, Maenner MJ, Newschaffer CJ, Lee LC, Cunniff CM, Daniels JL, Kirby RS, Leavitt L, Miller L, Zahorodny W, Schieve LA.11**, s. 1.: American Journal of Epidemiology., 2008, Vol.168.
- [43] *Advancing parental age and autism: multifactorial pathways.* **Lee BK, McGrath JJ.2**, s. 1.: Trends in Molecular Medicine., 2015, Vol.21.
- [44] *Parental age and autism spectrum disorders.* **Parner ET, Baron - Cohen S, Lauritsen MB, Jørgensen M, Schieve LA, Yeargin - Allsopp M, Obel C.3**, s. 1.: Annals of Epidemiology, 2012, Vol.22.
- [45] *Independent and dependent contributions of advanced maternal and paternal ages to autism risk.* **Shelton JF, Tancredi DJ, Hertz - Picciotto I.1**, s. 1.: Autism Research., 2010, Vol.3.
- [46] *Prenatal factors associated with autism spectrum disorder (ASD).* **Ornoy A, Weinstein - Fudim L, Ergaz Z.56**, s. 1.: Reproductive Toxicology., 2015, Vol.15.
- [47] *Environmental factors influencing the risk of autism.* **Karimi P, Kamali E, Mousavi SM, Karahmadi M.27**, s. 1.: Journal of Research in Medical Sciences, 2017, Vol.22.
- [48] *Identification of a primary target of thalidomide teratogenicity.* **Ito T, Ando H, Suzuki T, Ogura T, Hotta K, Imamura Y, Yamaguchi Y, Handa H.5971**, s. 1.: Science., 2010, Vol.327.
- [49] *Autism and Möbius sequence: an exploratory study of children in northeastern Brazil.* **Bandim JM, Ventura LO, Miller MT, Almeida HC, Costa AE.2A**, s. 1.: Arq. Neuro - Psiquiatr., 2003, Vol.61.
- [50] *In utero beta 2 adrenergic agonist exposure and adverse neurophysiologic and behavioral outcomes.* **Witter FR, Zimmerman AW, Reichmann JP, Connors SL.6**, s. 1.: American Journal of Obstetrics and Gynecology., 2009, Vol.201.
- [51] *Neuroinflammation and behavioral abnormalities after neonatal terbutaline treatment in rats: implications for autism.* **Zerrate MC, Pletnikov M, Connors SL, Vargas DL, Seidler FJ, Zimmerman AW, Slotkin TA, Pardo CA.1**, s. 1.: Journal of Pharmacology and Experimental Therapeutics, 2007, Vol.322.
- [52] *Children with autism: quality of life and parental concerns.* **Lee LC, Harrington RA, Louie BB, Newschaffer CJ.6**, s. 1.: Journal of Autism and Developmental disorders., 2008, Vol.38.
- [53] *Perinatal risk factors for infantile autism.* **Hultman CM, Sparén P, Cnattingius S.4**, s. 1.: Epidemiology., 2002, Vol.13.
- [54] *Risk factors for autism: perinatal factors, parental psychiatric history, and socioeconomic status.* **Larsson HJ, Eaton WW, Madsen KM, Vestergaard M, Olesen AV, Agerbo E, Schendel D, Thorsen P, Mortensen PB.10**, s. 1.: American journal of Epidemiology, 2005, Vol.161.
- [55] *Prenatal and perinatal risk factors for autism: a review and integration of findings.* **Kolevzon A, Gross R, Reichenberg A.4**, s. 1.: JAMA Pediatrics, 2007, Vol.161.
- [56] *Perinatal and neonatal risk factors for autism: a comprehensive meta - analysis.* **Gardener H, Spiegelman D, Buka SL.2**, s. 1.: American Academy of Pediatrics, 2011, Vol.128.
- [57] *Socioeconomic Status and the Increased Prevalence of Autism in California.* **King MD, Bearman PS.2**, 2011, Vol.76.

- [58] *Obstetric complications and risk for severe psychopathology in childhood.* **Eaton WW, Mortensen PB, Thomsen PH, Frydenberg M.**3, s. 1.: Journal of Autism and Developmental disorders, 2001, Vol.31.
- [59] *Birth weight and gestational age characteristics of children with autism, including a comparison with other developmental disabilities.* . **Schendel D, Bhasin TK.**6, s. 1.: American Academy of Pediatrics, 2008, Vol.121.
- [60] *Identification and evaluation of children with autism spectrum disorders.* **Johnson CP, Myers SM and Disabilities., American Academy of Pediatrics Council on Children With.**5, s. 1.: American Academy of Pediatrics., 2007, Vol.120.
- [61] *The pediatricians role in the diagnosis and management of autistic spectrum disorder in children.* **American Academy of Pediatrics, Committee on Children With Disabilities.**5, s. 1.: American Academy of Pediatrics, 2001, Vol.107.
- [62] *Autism spectrum disorder.* **Lord C, Elsabbagh M, Baird G, Veenstra - Vanderweele J.**10146, s. 1.: Lancet, 2018, Vol.392.
- [63] *Brain imaging research in autism spectrum disorders: in search of neuropathology and health across the lifespan.* **JE., Lainhart.**2, s. 1.: Psychiatry., 2015, Vol.28.
- [64] *Neuroimaging endophenotypes in autism spectrum disorder.* **Mahajan R, Mostofsky SH.**4, s. 1.: CNS Spectrums, 2015, Vol.20.
- [65] *scMRI reveals large - scale brain network abnormalities in autism.* **Zielinski BA, Anderson JS, Froehlich AL, Prigge MB, Nielsen JA, Cooperrider JR, Cariello AN, Fletcher PT, Alexander AL, Lange N, Bigler ED, Lainhart JE.**11, s. 1.: PLoS One., 2012, Vol.7.
- [66] *Brain and behavior development in autism from birth through infancy.* **Shen MD, Piven J.**4, s. 1.: Dialogues Clin Neurosci., 2017, Vol.19.
- [67] *The developmental neurobiology of autism spectrum disorder.* **DiCicco - Bloom E, Lord C, Zwaigenbaum L, Courchesne E, Dager SR, Schmitz C, Schultz RT, Crawley J, Young LJ.**26, s. 1.: J Neurosci., 2006, Vol.26.
- [68] *The Neurobiology of Autism.* **Pardo, Carlos & Eberhart, Charles.** Zurich, Switzerland: Brain pathology, 2007, Vol.17.
- [69] *Macrocephaly and the control of brain growth in autistic disorders.* **McCaffery P, Deutsch CK.**1 - 2, s. 1.: Prog Neurobiol., 2005, Vol.77.
- [70] *Neuroanatomic observations of the brain in autism: a review and future directions.* . **Bauman ML, Kemper TL.**2 - 3, s. 1.: Int J Dev Neurosci., 2005, Vol.23.
- [71] *The neurobiology of autism.* **Pardo CA, Eberhart CG.**4, s. 1.: Brain Pathol., 2007, Vol.17.
- [72] *Unusual brain growth patterns in early life in patients with autistic disorder: an MRI study.* **Courchesne E, Karns CM, Davis HR, Ziccardi R, Carper RA, Tigue ZD, Chisum HJ, Moses P, Pierce K, Lord C, Lincoln AJ, Pizzo S, Schreibman L, Haas RH, Akshoomoff NA, Courchesne RY.**2, s. 1.: Neurology, 2001, Vol.57.
- [73] *Brain structural abnormalities in young children with autism spectrum disorder.* **Sparks BF, Friedman SD, Shaw DW, Aylward EH, Echelard D, Artru AA, Maravilla KR, Giedd JN, Munson J, Dawson G, Dager SR.**2, s. 1.: Neurology., 2002, Vol.59.
- [74] *Evidence of brain overgrowth in the first year of life in autism.* **Courchesne E, Carper R, Akshoomoff N.**3, s. 1.: JAMA., 2003, Vol.290.
- [75] *Accelerated head growth in early development of individuals with autism.* **Dementieva YA, Vance DD, Donnelly SL, Elston LA, Wolpert CM, Ravan SA, DeLong GR, Abramson RK, Wright HH, Cuccaro ML.**2, s. 1.: Pediatr Neurol., 2005, Vol.32.
- [76] *When is the brain enlarged in autism? A meta - analysis of all brain size reports.* **Redcay E, Courchesne E.**1, s. 1.: Biol Psychiatry., 2005, Vol.58.
- [77] *Minicolumnar pathology in autism.* **Casanova MF, Buxhoeveden DP, Switala AE, Roy E.**3, s. 1.: Neurology., 2002, Vol.58.
- [78] *The neuropathology of autism: a review.* **Pickett J, London E.**11, s. 1.: J Neuropathol Exp Neurol., 2005, Vol.64.
- [79] *Can autism speak to neuroscience?.* **Moldin SO, Rubenstein JL, Hyman SE.**26, s. 1.: J Neurosci., 2006, Vol.26.
- [80] *Early Identification of Autism Spectrum Disorder: Recommendations for Practice and Research.* **Zwaigenbaum L, Bauman ML, Stone WL, Yirmiya N, Estes A, Hansen RL, McPartland JC, Natowicz MR, Choueiri R, Fein D, Kasari C, Pierce K, Buie T, Carter A, Davis PA, Granpeesheh D, Mailloux Z, Newschaffer C, Robins D, Roley SS, Wagner S, Wetherby A.**1, s. 1.: Pediatrics., 2015, Vol.136.
- [81] *Diagnostic evaluation of autism spectrum disorders.* **Huerta M, Lord C.**1, s. 1.: Pediatr Clin North Am., 2012, Vol.59.
- [82] *Autism Diagnostic Observation Schedule, Second Edition.*2012. **Lord, C., Rutter, M., DiLavore, P. C., Risi, S., Gotham, K., & Bishop, S.**1, s. 1.: Journal of Psychoeducational Assessment., 2014, Vol.32.
- [83] *Effects of age on brain volume and head circumference in autism.* . **Aylward EH, Minshew NJ, Field K, Sparks BF, Singh N.**2, s. 1.: Neurology., 2002, Vol.59.