" Autism Spectrum Disorder: A Literature Review "

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Abstract

Autism Spectrum Disorder (ASD) is defined as a multifaceted developmental condition characterized by social communication deficits and repetitive behaviors. With a global prevalence of 1 in 100 children, ASD diagnosis reveals disparities across demographics, necessitating targeted awareness. Genetic complexities, underscored by de novo mutations and specific gene involvement, contribute to ASD's etiology. Clinical manifestations encompass communication challenges, social interaction deficits, and repetitive behaviors, warranting early identification. Management strategies encompass pharmacological and non-pharmacological interventions, emphasizing the need for a multidisciplinary approach. This concise exploration calls for heightened research and awareness to enhance the understanding and management of ASD.

Keywords: Autism Spectrum Disorder; ASD; developmental

1. Introduction

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition impacting social interactions, communication, learning, and behavior, with symptoms typically emerging within the initial two years of life. Defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), individuals with ASD commonly exhibit challenges in communication and interaction, engage in restricted interests, and display repetitive behaviors, affecting their overall functioning in various life domains. Recognized as a "spectrum" disorder, ASD encompasses diverse symptom types and severities. Diagnosis cuts across gender, race, ethnicity, and economic backgrounds, and although it can persist throughout life, interventions and services exist to ameliorate symptoms and enhance daily functioning. The American Academy of Pediatrics advocates for universal autism screening in children, emphasizing the importance of discussions between caregivers and healthcare providers regarding ASD screening and evaluation (National Institute of Mental Health, 2023).

2. Autism Spectrum Disorder

2.1 Definition

As per the guidelines established by the American Psychiatric Association (2021), Autism Spectrum Disorder (ASD) is an intricate developmental anomaly marked by deficiencies in social communication, circumscribed interests, and repetitive behaviors. Simultaneously, autism, as a standalone condition, is acknowledged as a persistent disorder, yet the severity of this disorder exhibits variations among individuals with autism spectrum disorder. Another investigation expounds on ASD as a neurodevelopmental condition grounded in brain-related factors, manifesting in disruptions to social communication, interaction, and the presence of restricted or repetitive behaviors or interests (Lyall et al., 2017). The genetic underpinnings of ASD

are characterized by a robust and intricate component, involving multiple familial inheritance patterns, with estimates suggesting the potential involvement of up to 1000 genes (Ramaswami & Geschwind, 2018).

2.2 Epidemiology

Autism Spectrum Disorder (ASD) poses a significant challenge to contemporary medicine, characterized by an unexplained surge in prevalence (Yenkoyan et al., 2017). Globally, approximately 1 in 100 children are diagnosed with ASD, with anticipated escalating prevalence and notable variations across sociodemographic groups (Zeidan et al., 2022). In 2010, the Global Burden of Disease research estimated 52 million individuals diagnosed with ASD worldwide, equivalent to a prevalence of 1 in 132 people (Lord et al., 2020). Recent estimates suggest that over 70 million individuals globally suffer from ASD, with an overall prevalence ranging between 1.5% and 2% (Jiang et al., 2022).

ASD transcends racial, ethnic, and socioeconomic boundaries, yet its diagnosis lacks uniformity among these groups. Caucasian children are consistently identified with ASD more frequently than their black or Hispanic counterparts, potentially influenced by factors such as stigma, limited healthcare access, and primary language differences. Although ASD is more prevalent in males, a recent meta-analysis indicates a true male-to-female ratio closer to 3:1 than the previously reported 4:1, raising concerns about potential underdiagnosis in girls meeting ASD criteria. The female autism phenotype, characterized by masking social deficits through "camouflaging," may contribute to misdiagnosis, delayed diagnosis, or oversight in girls. Gender biases and stereotypes of ASD as a male-oriented disorder could further impede accurate diagnoses in girls (Hodges, Fealko and Soares, 2020).

While several genetic diagnoses exhibit an elevated co-occurrence with ASD compared to the general population, including fragile X, tuberous sclerosis, Down syndrome, and Rett syndrome, these known genetic disorders represent a small fraction of overall ASD cases. Studies on children with sex chromosome aneuploidy reveal a distinctive social functioning profile in males, suggesting increased vulnerability to autism. The expanded use of chromosomal microarray identifies specific sites, particularly chromosome X, 2, 3, 7, 15, 16, 17, and 22, associated with heightened ASD risk. Additional risk factors for ASD encompass advanced parental age and prematurity, with a theoretical link to increased mutation probabilities in older gametes, potentially leading to obstetrical complications, including prematurity (Hodges, Fealko and Soares, 2020).

2.3 Etiology

Certain instances of autism result from de novo mutations, involving newly occurring genes responsible for neuronal motility, axon guidance, and synaptic development. Research indicates that de novo copy number variations, which are structural changes, manifest more frequently in autistic children than in their non-autistic counterparts. Recent genetic studies associate mutations in the CHD8 (chromodomain helicase DNA binding protein 8) gene with autism, leading to manifestations such as macrocephaly and widened eyes. Beyond genetic influences on autism, environmental factors, including mercury exposure, radiation, and diesel exhaust, have been implicated. Moreover, maternal viral infections, the use of valproic acid and thalidomide during pregnancy, and exposure to pesticides have been reported to impact the central nervous system of the fetal brain, potentially causing autism. Autism's impact extends to the size of the corpus callosum, a bundle of nerve fibers connecting the brain's hemispheres and playing a crucial role in sensory, motor, and cognitive information transmission. Agenesis of the corpus callosum contributes to the development of autism. Studies reveal increased cortical thinning in the frontal lobe, parietal lobe, occipital lobe, and the entire cortex of individuals with ASD. Neuroimaging techniques highlight abnormal brain connectivity in children with ASD, indicating intrinsic differences in brain connectivity compared to their neurotypical counterparts (Bhat et al., 2014).

2.4 Manifestations

Individuals diagnosed with Autism Spectrum Disorder (ASD) commonly encounter challenges in communication, social interactions, and engage in restricted or repetitive behaviors and interests. Observable indicators of communication and social interaction difficulties include limited eye contact, absence of gestures like waving "goodbye" by 12 months, failure to point to interesting objects at 18 months, lack of awareness when others are hurt or disappointed by 24 months, and a deficiency in pretending play activities like imitating a teacher or a chef by 48 months. People with ASD may also have different ways of learning, moving, or paying attention. It is important to note that some people without ASD may also have some of these symptoms. But for people with ASD, these characteristics can make life very challenging (CDC, 2022).

These characteristics may pose significant challenges in the lives of individuals with ASD, although it's noteworthy that some of these symptoms may be present in people without ASD. Moreover, aggressive behavior, including hitting, kicking, biting, and throwing objects during anger episodes, can be particularly distressing for families with children affected by ASD, contributing to heightened parental stress and exacerbating challenging behaviors (SPARK, 2019).

Autism also manifests in widespread impairments in sensory and motor abilities. Unusual movement patterns, such as atypical reaching and aiming at targets, characterize individuals with autism. Notably, individuals with autism often modify their movements retrospectively after initial attempts, relying on a try-and-fail strategy composed of independent motor adaptations rather than cohesive patterns. Research underscores significant distinctions in both local and global sensory and motor processing in individuals with autism compared to their neurotypical counterparts. Trevarthen and Delafield-Butt's work highlights a specific level of motor control where children with autism exhibit less efficient motor skills than typically developing children (Grohmann, 2018).

2.5 Diagnosis

Diagnosing Autism Spectrum Disorder (ASD) poses challenges as there is no specific medical test, such as a blood test, for definitive identification. Instead, clinicians rely on the observation of a child's behavior and development for diagnosis. However, the final diagnosis is often delayed, with many individuals not receiving confirmation until adolescence or adulthood. This delayed diagnosis underscores the potential lack of early intervention, which is crucial for individuals with ASD to receive timely support (CDC, 2022)

The assessment of Autism Spectrum Disorder (ASD) commences with the screening of the general pediatric population to identify children at risk or those displaying potential signs of ASD. The American Academy of Pediatrics (AAP) advocates for developmental surveillance at 9, 15, and 30 months, incorporating specific autism screening at 18 months, and again at 24 or 30 months. Early indicators include deficiencies such as poor eye contact, inadequate response to name, absence of showing and sharing, lack of gesturing by 12 months, and loss of language or social skills. Screening tools like the Modified Checklist for Autism in Toddlers, Revised, with Follow-up (M-CHAT-R/F) and Survey of Wellbeing of Young Children (SWYC) are utilized. Preschoolers and school-age children may present additional red flags, including limited pretend play, intense interests, and behavioral rigidity. In cases of suspicion, referral to specialists and comprehensive assessments are recommended, involving physical exams, parent interviews, and observations of cognitive, language, and adaptive functioning (Hodges, Fealko and Soares, 2020).

For concerns identified during screening, primary care clinicians are advised to direct children to early intervention or the public school system for psychoeducational evaluation, contingent on the child's age. Furthermore, referral to specialists, such as pediatric neurologists or developmental-behavioral pediatricians, is suggested for a definitive diagnosis and comprehensive assessment, encompassing physical examinations, parental interviews, and clinician observations. Co-occurring conditions in children with ASD are prevalent, encompassing developmental, psychiatric, and neurologic diagnoses. Clinical genetic testing is endorsed, and

metabolic evaluations are contemplated based on symptoms. While specific cases may warrant neuroimaging and EEGs, routine testing for various conditions without specific symptoms is generally discouraged (Hodges, Fealko and Soares, 2020).

The lack of clearly defined ASD biomarkers requires a diagnosis founded on descriptive criteria. Clinical genetic testing is advised, encompassing chromosomal microarray and fragile X testing. Routine laboratory assessments are generally not standard practice, but consideration of metabolic evaluations may be warranted based on symptoms. While neuroimaging is not part of routine recommendations, it may be deemed appropriate in certain instances. The rapidly advancing field of genetics indicates that whole exome sequencing could emerge as the preferred method for clinical genetic testing in individuals with ASD. However, other laboratory evaluations, such as those for celiac disease, immunologic or neurochemical markers, mitochondrial disorders, and vitamin deficiencies, are not routinely endorsed unless specific symptoms or relevant clinical history are present (Hodges, Fealko and Soares, 2020).

2.6 Management

Individuals with Autism Spectrum Disorder (ASD) frequently encounter challenges in communication and social interactions. The therapeutic landscape for ASD involves pharmacologic interventions encompassing psychostimulants, atypical antipsychotic drugs, antidepressants, alpha-2 adrenergic receptor agonists, cholinesterase inhibitors, NMDA receptor antagonists, and antiepileptic mood stabilizers, addressing primary and commonly prescribed drug classes for pediatric and adult ASD patients. In addition to pharmacological approaches, non-pharmacological therapies play a pivotal role. Cognitive behavioral therapy (CBT), characterized by its structured nature, emerges as a suitable intervention targeting primary symptoms and comorbid conditions like anxiety and depression (Sharma et al., 2018). Case studies, including the work by Rotheram-Fuller & MacMullen (2011) involving ASD children aged 7–14 years, highlight CBT's efficacy in enhancing social communication, motivation, and awareness. Behavioral therapy also proves effective in reducing aggressive behavior among children with ASD, promoting behavioral control and improving communication skills (Utami, 2020). The gluten-free/casein-free (GFCF) diet, a non-pharmacological intervention, is employed in treating ASD in children, despite limited evidence supporting its efficacy (Piwowarczyk et al., 2017). This dietary approach has shown positive effects on behavior, performance, social interactions, and brain function, emphasizing the potential for improving overall brain function by addressing nutritional needs and eliminating potential disturbances (Essa & Qoronfleh, 2020). Recognizing the limitations of existing treatments and challenges in accessing evidence-based interventions, some families opt for a diet and nutrition approach as a component of ASD treatment (Sathe et al., 2017).

3. Conclusion

Autism Spectrum Disorder (ASD) presents a complex landscape with genetic, environmental, and neurological influences. Diagnosing ASD remains challenging, relying on behavioral observations, leading to delayed identification underscore the need for heightened awareness and research efforts. Disparities in prevalence and gender-based diagnostic difficulties necessitate a comprehensive and multidisciplinary approach to management. Despite advancements, the absence of clear biomarkers underscores the need for ongoing research. Early intervention is crucial, highlighting the importance of increased awareness and research efforts to enhance understanding and management. Timely interventions, both pharmacological and non-pharmacological, are vital for improving outcomes. To address the multifaceted nature of ASD, continued efforts in research, awareness, and holistic care are imperative for enhancing the lives of individuals and families affected by this condition.

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References

American Psychiatric Association. (2021) What Is Autism Spectrum Disorder?. Available at: https://www.psychiatry.org/patients-families/autism/what-is-autism-spectrum- disorder (Accessed: 27 August 2022).

Bhat, S. et al. (2014) "Autism: Cause factors, early diagnosis and therapies," Reviews in the Neurosciences, 25(6). Available at: https://doi.org/10.1515/revneuro-2014- 0056.

CDC. (2022) Signs and Symptoms of Autism Spectrum Disorders. Available at: https://www.cdc.gov/ncbddd/autism/signs.html (Accessed: 14 September 2022).

CDC (2022). What is autism spectrum disorder? [online] Centers for Disease Control and Prevention. Available at: https://www.cdc.gov/ncbddd/autism/facts.html.

Essa, M.M. and Qoronfleh, M. W. (2020) Personalized Food Intervention and Therapy for Autism Spectrum Disorder Management. New York: Springer.

Grohmann, T.D.A. (2018) "A phenomenological account of sensorimotor difficulties in autism: Intentionality, Movement, and proprioception," Psychopathology, 50(6), pp. 408–415. Available at: https://doi.org/10.1159/000481949.

Hodges, H., Fealko, C. and Soares, N. (2020). Autism spectrum disorder: Definition, epidemiology, causes, and clinical evaluation. Translational Pediatrics, [online] 9(1), pp.S55–S65. doi:https://doi.org/10.21037/tp.2019.09.09.

Jiang, C.-C. et al. (2022) "Signalling pathways in Autism Spectrum Disorder: Mechanisms and therapeutic implications," Signal Transduction and Targeted Therapy, 7(1). Available at: https://doi.org/10.1038/s41392-022-01081-0.

Lord, C. et al. (2020) "Autism Spectrum Disorder," Nature Reviews Disease Primers, 6(1). Available at: https://doi.org/10.1038/s41572-019-0138-4.

Lyall, K. et al. (2017) "The changing epidemiology of Autism Spectrum Disorders," Annual Review of Public Health, 38(1), pp. 81–102. Available at: https://doi.org/10.1146/annurev-publhealth-031816-044318.

National Institute of Mental Health (2023). Autism Spectrum Disorder. [online] National Institute of Mental Health (NIMH). Available at: https://www.nimh.nih.gov/health/topics/autism-spectrum-disorders-asd#:~:text=Autism%20Spectrum%20Disorder-.

Piwowarczyk, A. et al. (2017) "Gluten- and casein-free diet and Autism Spectrum Disorders in children: A systematic review," European Journal of Nutrition, 57(2), pp. 433–440. Available at: https://doi.org/10.1007/s00394-017-1483-2.

Ramaswami, G. and Geschwind, D.H. (2018) "Genetics of Autism Spectrum Disorder," Neurogenetics, Part I, pp. 321–329. Available at: https://doi.org/10.1016/b978-0- 444-63233-3.00021-x.

Rotheram-Fuller, E. and MacMullen, L. (2011) "Cognitive-behavioral therapy for children with Autism Spectrum Disorders," Psychology in the Schools, 48(3), pp. 263–271. Available at: https://doi.org/10.1002/pits.20552.

Sathe, N. et al. (2017) "Nutritional and dietary interventions for Autism Spectrum Disorder: A systematic review," Pediatrics, 139(6). Available at: https://doi.org/10.1542/peds.2017-0346.

Sharma, S.R., Gonda, X., and Tarazi, F.I. (2018) "Autism Spectrum Disorder: Classification, diagnosis and therapy," Pharmacology & Therapeutics, 190, pp. 91–104. Available at: https://doi.org/10.1016/j.pharmthera.2018.05.007.

SPARK. (2019) Children With Autism and Aggression. Available at: https://sparkforautism.org/discover_article/children-with-autism-and-aggression/ (Accessed: 14

September 2022).
Utami, R.R. (2020) 'Behavioral therapy Untuk Mengurangi Perilaku Agresi Fisik Pada Anak', Procedia : Studi Kasus dan Intervensi Psikologi, 8(2), p. 72. doi:10.22219/procedia.v8i2.13424.
Yenkoyan, K. et al. (2017) "Advances in understanding the pathophysiology of Autism Spectrum Disorders," Behavioural Brain Research, 331, pp. 92–101. Available at: https://doi.org/10.1016/j.bbr.2017.04.038.
Zeidan, J. et al. (2022) "Global prevalence of autism: A systematic review update," Autism Research, 15(5), pp. 778–790. Available at: https://doi.org/10.1002/aur.2696.