

# The Prevalence of Psychiatric and Behavioral Comorbid Among Autistic Adults

S. Vinola Shrim Mishma and Arun Shanmugam\*

Department of Pharmacy Practice, JKKN College of Pharmacy, Kumarapalayam, Tamil Nadu, India.

<http://dx.doi.org/10.13005/bbra/3242>

(Received: 16 November 2023; accepted: 09 May 2024)

This article aims to shed light on the co-occurrence of behavioural and mental comorbidities in people with Autism. In 1943, psychiatrist Leo Kanner coined the term "Autism." Autism is a neurodevelopmental disease known as autism spectrum disorder (ASD). The three following categories are more likely to cause difficulties for adults with Autism: Social interaction, communication, and flexibility in thought and action. Autism has long-lasting effects on a person's life. People living with ASD are more likely to have one or more co-occurring mental disorders. For people with Autism, adulthood presents more difficulties. Psychiatric symptoms are more common in young people who have autism spectrum disorder (ASD) than in general people. The common mental conditions that can co-occur with ASD are ADHD, schizophrenia, depression, bipolar disorder, suicidal thoughts, and down syndrome, which are all covered in this article. This review provides a piece of in-depth knowledge about the prevalence and the co-occurrence of psychiatric and behavioural comorbidities among autistic adults.

**Keywords:** ADHD; Autism; Bipolar disorder; Prevalence; Psychiatric; Schizophrenia.

Leo Kanner, a psychiatrist, used the word "Autism" in 1943 to describe boys who were verbally deficient or non-existent, socially isolated, and fixated on routine but did not exhibit mental disability. However, Bleuler (1911) coined the word "autism" to describe schizophrenic individuals who were isolated from others and withdrew from social involvement. Additionally, Asperger's was the first to identify specific diseases that "run in families." In the periods that followed, the prevalent psychoanalytic theory of the time strongly influenced the belief that Autism was psychogenic and the product of inadequate parenting.<sup>1</sup>

Autism spectrum disorder, also known as "autism," is a neurodevelopmental disorder<sup>2</sup> or condition that is typically diagnosed in infancy.

Communication and social interaction deficits, repetitive and stereotypical patterns of behaviour, interests, and hobbies are all hallmarks of Autism.<sup>3</sup> Autism affects more males than females, and those who have it also have learning disabilities at a ratio of 4:1.<sup>4</sup> According to WHO, it is estimated that worldwide, about 1 in 100 children has Autism.

A pervasive developmental disorder is an autism (PDD). In contrast to other developmental disorders like Rett's condition (also a PDD) and attention deficit hyperactivity disorder (ADHD), Autism has distinct symptoms. The signs of Autism typically present before the age of three. Frequent tip-toeing, repetitive head banging and hand flapping are some of the defining characteristics of Autism. Autism has long-lasting effects on a person's life. For those who are autistic, adulthood presents extra difficulties.<sup>5,6</sup>

\*Corresponding author E-mail: msarunkutti@gmail.com



Compared to the general population, youth with autism spectrum disorder (ASD) experience psychiatric symptoms more frequently, as is now widely known.<sup>7,8</sup> It is significant because co-occurring psychiatric disorders are linked to increased psychotropic medication use, higher healthcare spending, and stopping ASD-related treatments.<sup>9-11</sup> Age, general intelligence, and gender may all have an impact on how co-occurring ASD symptoms express themselves.

#### **Prevalence**

70-72% of children and adolescents with ASD also have one or more co-occurring mental disorders,<sup>12,13</sup> although prevalence numbers vary depending on the diagnostic technique<sup>14,15</sup> and referral source.<sup>16,17</sup>

#### **Keys to understanding Autism**

- Autism in adults can be treated with a single channel (Instead of doing both at once, individuals can choose to either gaze or listen)
- Autism sufferers struggle to foresee outcomes.
- Because they have trouble predicting results, people with Autism dislike change.<sup>18</sup>

#### **Techniques for Autism Spectrum Individuals**

- Examine how the autistic individual understands what is being expressed or shown.
- Educate that certain physiological and facial expressions might correspond to certain behaviours, feelings, and desires.
- Teach by rote the rules for particular circumstances (We welcome our loved ones, not strangers.)
- Give the autistic individual time to adjust to change whenever possible rather than “springing things” on them.
- Use music, silence, reassurance, breathing exercises, a soothing voice, and any other known stress relievers to calm the autistic person down while they are feeling worried.<sup>18</sup>

#### **Symptoms of autism**

Adapted from the DSM-IV-TR diagnostic criteria for autism disorder, symptom domains.

#### **Impairment in social interaction**

- Impairment in the ability to control social interaction through a variety of nonverbal actions
- Failure to establish suitable peer relations
- Absence of a natural desire to share experiences, passions, or accomplishments with others
- Lacking emotional or social reciprocity

#### **Impairment in communication**

- Delayed language development

- Markedly reduced ability to start or carry on a discussion with people

- Using words in a stereotypical and repetitious manner or in an odd way

- Inadequate social imitative play or inappropriately diverse, spontaneous make-believe play

#### **Restrictive, stereotyped, repetitive behaviour, interest, and activity patterns**

- Fixation with one or more stereotypical and limited patterns of interest

- Rigorous adherence to prescribed, ineffective traditions or practices

- Repetitive and stereotypical motor behaviors

- Persistent attachment to object parts.

#### **Some suspected RISK FACTORS for ASD include**

Being born to elderly parents, having specific genetic abnormalities, fragile X syndrome, and other genetic problems, as well as low birth weight, abnormalities in metabolism, exposure to environmental pollutants and heavy metals, and a history of viral infections in the mother, are all risk factors for Autism—exposure of the fetus to thalidomide or valproic acid.

#### **PSychiatric And Behavioural Comorbid with ASD Adult are**

##### **1. ADHD**

The hallmark of attention-deficit/hyperactivity disorder (ADHD), a neurodevelopmental condition, is impulsivity, hyperactivity, and disorganization. Three different presentations of ADHD exist: Combined presentation primarily consists of symptoms of combining hyperactivity-impulsivity and inattentiveness. Unfocused presentation, which mainly consists of symptoms of inattention. Hyperactive/impulsive presentation mainly consists of symptoms of hyperactivity and impulsivity<sup>19</sup>. Despite prior DSM revisions explicitly dismissing the potential of comorbidity between the two illnesses, the co-occurrence of ADHD and ASD is one of the co-occurring disorders with the most extensive studies in the ASD community.<sup>20-22</sup>

#### **Prevalence**

The frequency of ADHD in the population of children with ASD ranges from 21 to 30%.<sup>23,24</sup> ADHD is diagnosed in 27% of adult outpatients with ASD.<sup>25</sup> Inattentive type ADHD is the most prevalent diagnosis for ASD, hyperactive type and combined type came next.<sup>26,27</sup> Co-occurring

ADHD in ASD is associated with a range of symptoms, including ASD severity, social impairments, impaired cognitive functioning, delays in adaptive functioning, and general internalising and externalizing symptoms.<sup>28-31</sup>

## 2. SCHIZOPHRENIA

Retrospective research has occasionally been used to imply that adults with Autism are more likely to acquire schizophrenia.<sup>32</sup> While the incidence of schizophrenia in people with Autism is minimal, this finding is supported by both prospective research and studies based on a recent standardised psychiatric examination.

### Prevalence

For instance, Howlin carried out follow-up research on 20 individuals with a receptive language deficit and 19 adults with Autism who had been initially evaluated at the age of 7-8 years. In the group with Autism, there were no similar cases, whereas 2 of the 20 people within the linguistic unit experienced vivid, paranoid insanity in the latter stages of adolescence. Only one of the 16 high-functioning autistic children who had follow-up developed schizophrenia.<sup>33</sup> However, 6 (37.5%) of the participants exhibited symptoms of schizophrenia, like hallucinations, paranoid thoughts, and magical thinking. Fourteen men were recruited, at a mean of 28 years old, by Rumsey et al. in 1985. Both the adult autistic person and their parent underwent psychiatric interviews, but neither of them showed that the adult had a present psychotic condition.<sup>34</sup>

### Assessment

The patient's age, the variation of the condition, when an intellectual disability is present, the degree of spoken ability, and the existence of more concurrent conditions all play a part in the diagnosis of schizophrenia in Autism. Because neither disorder can be scientifically determined in this way, organised interviews and grading scales only help with the clinical evaluation of schizophrenia or Autism. The review should be founded on methods employed with people who have cerebral impairments when an adult with significant intellectual disability and Autism is suspected of having psychosis. However, the evaluation of high-functioning autistic individuals should be based on techniques used by the general public. On the other hand, in a grownup who possesses a proven assessment for psychosis or

schizophrenia, it can be challenging to rule out Autism. Obtaining a trustworthy developmental history is necessary, which might sometimes be challenging. The diagnosis of patients who display adverse signs of schizophrenia is more difficult due to the similarities with the passive and distant social ASDS subtypes.<sup>35</sup>

### Depression

The most frequently seen co-occurring psychiatric illnesses in this cohort are affective disorders. Depression is the most prevalent affective illness, accounting for up to 28% of diagnoses, while a prevalence of up to 64% of diagnoses for affective disorders are thought to have occurred.<sup>36,33</sup> According to clinical research, As people age, their chance of developing depression may increase, peaking in adolescence and early adulthood.<sup>36</sup>

The main characteristics of major depressive disorder, according to the DSM-5, are anhedonia and a dull or angry mood. Additionally, there must be five additional symptoms that affect baseline functioning and induce functional impairment during a 2-week time frame. In contrast to a dull mood or anhedonia, depression in youngsters might present as extreme irritability.<sup>19</sup>

### Prevalence

In children and adolescents, the incidence of any co-occurring depressive disorder is estimated to be greater than the average population's rate of depression, ranging from 0.9 to 29%.<sup>7,8</sup> Similarly, In contrast to 46% of people in outpatient treatment without ASD, 77% of adults in outpatient care with ASD have ever been diagnosed with depression.<sup>25</sup> According to these results, people with ASD may be more prone to depression than people in general. It is significant to note that depression in ASD is linked to low life quality and hospitalization as an inpatient,<sup>37</sup> and medical conditions.<sup>38</sup>

### Bipolar disorder

The most severe mental condition that may coexist with illnesses related to the autism spectrum is bipolar disorder. It is perhaps the most prevalent psychiatric condition associated with Autism, along with depression and anxiety. Before examining its comorbidity with Autism, it is imperative to assess its existing categorization swiftly. The Diagnostic and Statistical Manual of Mental Illnesses, Fifth Revision (DSM-5) classifies it as bipolar I, bipolar II, and cyclothymic illnesses.<sup>39</sup> Bipolar I disorder

is the typical manic-depressive condition that manifests as a manic episode, whether or not it is accompanied by depression or psychosis. A history of at least one major depressive episode and at least one hypomanic episode is required for the diagnosis of bipolar II disorder. Between episodes, patients resume their normal levels of functioning. Depression symptoms, some of which are severe, are a common reason why people with bipolar II seek treatment first. A bipolar illness with a milder variant known as cyclothymic disorder has a minimum two-year history of mood fluctuations. When the requirements for any of the three particular categories are not satisfied, a residual classification of other specified bipolar and related disorders is also provided by the DSM-5. Both in the general population and people with ASDs, bipolar disorder itself can co-occur with and be misdiagnosed as several diseases, such as oppositional defiant disorder, drug abuse, attention-deficit/hyperactivity disorder (ADHD), and anxiety disorders.<sup>40</sup>

#### **Prevalence**

It is unclear how common bipolar disorder is in the general population among kids with Autism. Studies conducted in clinics have revealed high frequencies. For example, a study by Wozniak and colleagues<sup>41</sup> reported that 21% of a sample of ASD-affected children under outpatient care had a bipolar illness. Some clinical investigations on adults with ASD found slightly higher rates.<sup>42</sup> For example, Mune Sue and colleagues<sup>43</sup> reported that 16 (34%) of 44 adult outpatients with ASD in their study had a mental condition. Out of these, 4 had significant depression diagnoses, 2 had bipolar one diagnosis, 6 had bipolar II diagnoses, and four had bipolar disorder not else identified. In total, 12 people (or 75%) had a diagnosis of bipolar disorder.

#### **Cause**

The exact causes that lead to bipolar disorder in people, in general, are probably responsible for the condition's co-occurrence with Autism. According to studies, parents of autistic children are more likely to experience depression and, maybe, bipolar illness. Common genes for conditions like Autism, schizophrenia, and bipolar illness have been discovered through genetic research.<sup>44,45</sup>

#### **Presentation**

Irritability and violence are common signs

of bipolar disorder and Autism that can both be seen by medical professionals. These, however, do not represent either disorder's primary symptoms. The main characteristics of Autism include mutual in terms of social and difficulties in communication along with constrained knowledge and behaviours, mood symptoms, and notable grandiosity, which are typical of bipolar illness. When an autistic person has emotional or behavioural swings during episodes that deviate from their usual behaviour, the bipolar illness must be checked out. However, depending on some variables, age, the bipolar disorder subtype, and the autism subtype, among other factors, when intellectual impairment coexists with concurrent mental and physical health conditions, it might provide unique challenges when it manifests in Autism.<sup>46</sup>

#### **Suicidal thoughts**

Suicidal ideas and attempts are far more common in people with ASD than in people who are typically developing, and there is growing worry over this relationship. This could be a result of fear of losing their job, as well as developing depressive and withdrawn symptoms as you move toward independence.<sup>47</sup> stated that compared to 0.4% of typical youth, 13% of moms said their child with ASD had suicidal thoughts or attempts. Abuse at school, behavioural issues, and depression were all contributing reasons. Similar studies have found that adults with ASD have high rates of suicide thoughts (65%), plans or attempts (34%), and depression (30%). In this demographic, it is essential to routinely screen for suicidal ideation while utilizing developmentally appropriate questioning techniques.<sup>48</sup>

#### **Down syndrome**

At one in a thousand live births, it is the most prevalent genetic cause of mental impairment.<sup>49</sup> from 0% to 16.6% of people with Autism has Down syndrome (DS), and 1% to 11% of those with DS also have Autism. It has been proposed that when the risk factor for Autism, mental illness, is taken into account, the combined risk of DS and Autism is not more than would be predicted by chance.<sup>50</sup>

#### **Prevalence**

In contrast to those who suffer from other developmental diseases, such as Down syndrome, adults with Autism have more significant behavioural issues. Seltzer observed that 153

adults with Autism displayed significantly more significant degrees of asocial, externalising, and internalising behaviours in contrast to 148 people with Down syndrome. Adults with Autism had an average of 4.2 behavioural issues, compared to just 1.3 for people who have Down syndrome, about a fourfold rise.<sup>51</sup>

#### Important Points

- Autistic adults frequently have unfavourable being different feelings.
- Autistic adults have received a mental disorder diagnosis and an antipsychotic prescription to manage their behaviour.
- It is essential to recognize that individuals with Autism have distinct mental processing styles.
- For those looking for constructive justifications for “different,” counselling autistic people can be helpful.
- Counseling can assist people with Autism in thinking back on their experiences and realising that others will have similar ones.

#### CONCLUSION

The primary comorbid conditions associated with autistic adults are ADHD, schizophrenia, depression, bipolar disorder, suicidal thoughts, and Down syndrome. 70-72% of adults with ASD have one or more co-occurring mental disorders. The prevalence of co-occurrence of comorbid conditions is ADHD- 30%, schizophrenia- 37.5%, depression- 29%, bipolar disorder- 75%, suicidal thoughts- 65%, and Down syndrome- 16%. Among these, bipolar and suicidal thoughts have the highest prevalence rate. Knowing these conditions and their prevalence helps in improving the quality of life of autistic adults. This review provides a piece of in-depth knowledge about the prevalence and the co-occurrence of psychiatric and behavioural comorbidities among autistic adults.

#### ACKNOWLEDGEMENT

I sincerely thank Dr. Arun Shanmugam, Assistant Professor in the Department of Pharmacy Practice, who supported and contributed to the creation of this article. This job would not have been possible without his tremendous support, advice, and encouragement. I sincerely thank Dr.

N. Venkateshwaramurthy, M.Pharm., Ph.D., Head of the Department, for his direction and experience preparing this review article. Lastly, my heartfelt gratitude goes to my family and friends for their endless encouragement throughout this project.

#### Authors' contributions

I, Vinola Shrim Mishma S, conducted the extensive literature search and data curation, synthesizing the collected information, and drafting the original manuscript. I also summarized the reviewed studies and led the revisions based on feedback received. My guide, Arun Shanmugam, conceptualized the overall scope and direction of the review. He provided continuous supervision, offered critical insights to shape the analytical framework, and contributed substantially to editing the manuscript to ensure its accuracy and depth. Together, we collaborated closely to refine the review and prepare it for publication.

#### Conflict of interest

We declare that there are no conflicts of interest regarding the publication of this paper. Neither Vinola Shrim Mishma S nor Arun Shanmugam has any financial or personal relationships that could inappropriately influence (bias) the work presented. This includes but is not limited to employment, consultancy, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding.

#### Funding sources

There is no funding for this article.

#### REFERENCES

1. Fotheringham JB. The Biology of the Autistic Syndromes, 2nd Edition. *J Psychiatry Neurosci.* 1994;19(3):227-28.
2. Centers for Disease Control and Prevention. Data & Statistics on Autism Spectrum Disorder. Centres for Disease Control and Prevention. Published December 2, 2021.
3. Lyall K, Croen L, Daniels J, et al. The Changing Epidemiology of Autism Spectrum Disorders. *Annu Rev Public Health.* 2017;38:81-102.
4. Gillberg C. Autism and pervasive developmental disorders [published correction appears in *J Child Psychol Psychiatry* 1991 Jan;32(1):213]. *J Child Psychol Psychiatry.* 1990;31(1):99-119.
5. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders:*

- DSM-IV-TR. 4th ed. American Psychiatric Association; 2000.
6. World Health Organization. *The ICD-10 Classification of Mental and Behavioural Disorders = ICD-10: Diagnostic Criteria for Research*. World Health Organization; 1993.
  7. Leyfer OT, Folstein SE, Bacalman S, et al. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. *J Autism Dev Disord*. 2006;36(7):849-861.
  8. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *J Am Acad Child Adolesc Psychiatry*. 2008;47(8):921-929.
  9. Mandell DS, Morales KH, Marcus SC, Stahmer AC, Doshi J, Polsky DE. Psychotropic medication use among Medicaid-enrolled children with autism spectrum disorders. *Pediatrics*. 2008;121(3):e441-e448.
  10. Gurney JG, McPheeters ML, Davis MM. Parental report of health conditions and health care use among children with and without autism: National Survey of Children's Health. *Arch Pediatr Adolesc Med*. 2006;160(8):825-830.
  11. Croen LA, Shankute N, Davignon M, Massolo ML, Yoshida C. Demographic and Clinical Characteristics Associated with Engagement in Behavioral Health Treatment Among Children with Autism Spectrum Disorders. *J Autism Dev Disord*. 2017;47(11):3347-3357.
  12. Levy SE, Giarelli E, Lee LC, et al. Autism spectrum disorder and co-occurring developmental, psychiatric, and medical conditions among children in multiple populations of the United States. *J Dev Behav Pediatr*. 2010;31(4):267-275.
  13. van Steensel FJ, Bögels SM, Perrin S. Anxiety disorders in children and adolescents with autistic spectrum disorders: a meta-analysis. *Clin Child Fam Psychol Rev*. 2011;14(3):302-317.
  14. Joshi G, Faraone SV, Wozniak J, et al. Examining the clinical correlates of autism spectrum disorder in youth by ascertainment source. *J Autism Dev Disord*. 2014;44(9):2117-2126.
  15. Lerner MD, Mazefsky CA, Weber RJ, et al. Verbal Ability and Psychiatric Symptoms in Clinically Referred Inpatient and Outpatient Youth with ASD. *J Autism Dev Disord*. 2018;48(11):3689-3701.
  16. Leyfer OT, Folstein SE, Bacalman S, et al. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. *J Autism Dev Disord*. 2006;36(7):849-861.
  17. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *J Am Acad Child Adolesc Psychiatry*. 2008;47(8):921-929.
  18. Creak M. Reflections on communication and autistic children. *J Autism Child Schizophr*. 1972;2(1):1-8.
  19. Widiger TA, Costa PT. *Personality Disorders and the Five-Factor Model of Personality*. American Psychological Association; 2013.
  20. Antshel KM, Zhang-James Y, Wagner KE, Ledesma A, Faraone SV. An update on the comorbidity of ADHD and ASD: a focus on clinical management. *Expert Rev Neurother*. 2016;16(3):279-293.
  21. Gadow KD, DeVincent CJ. Clinical significance of tics and attention-deficit hyperactivity disorder (ADHD) in children with pervasive developmental disorder. *J Child Neurol*. 2005;20(6):481-488.
  22. Gadow KD, DeVincent CJ, Siegal VI, et al. Allele-specific associations of 5-HTTLPR/rs25531 with ADHD and autism spectrum disorder. *Prog Neuropsychopharmacol Biol Psychiatry*. 2013;40:292-297.
  23. Levy SE, Giarelli E, Lee LC, et al. Autism spectrum disorder and co-occurring developmental, psychiatric, and medical conditions among children in multiple populations of the United States. *J Dev Behav Pediatr*. 2010;31(4):267-275.
  24. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. *J Am Acad Child Adolesc Psychiatry*. 2008;47(8):921-929.
  25. Joshi G, Wozniak J, Petty C, et al. Psychiatric comorbidity and functioning in a clinically referred population of adults with autism spectrum disorders: a comparative study. *J Autism Dev Disord*. 2013;43(6):1314-1325.
  26. Leyfer OT, Folstein SE, Bacalman S, et al. Comorbid psychiatric disorders in children with autism: interview development and rates of disorders. *J Autism Dev Disord*. 2006;36(7):849-861.
  27. Reiersen AM, Constantino JN, Todd RD. Co-occurrence of motor problems and autistic symptoms in attention-deficit/hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry*. 2008;47(6):662-672.
  28. Holtmann M, Bolte S, Poustka F. Attention

- deficit hyperactivity disorder symptoms in pervasive developmental disorders: association with autistic behavior domains and coexisting psychopathology. *Psychopathology*. 2007;40(3):172-177.
29. Rao PA, Landa RJ. Association between severity of behavioral phenotype and comorbid attention deficit hyperactivity disorder symptoms in children with autism spectrum disorders. *Autism*. 2014;18(3):272-280.
  30. Rosen TE, Lerner MD. Externalizing and Internalizing Symptoms Moderate Longitudinal Patterns of Facial Emotion Recognition in Autism Spectrum Disorder [published correction appears in *J Autism Dev Disord*. 2018 May 23;:]. *J Autism Dev Disord*. 2016;46(8):2621-2634.
  31. Storch EA, Sulkowski ML, Nadeau J, et al. The phenomenology and clinical correlates of suicidal thoughts and behaviors in youth with autism spectrum disorders. *J Autism Dev Disord*. 2013;43(10):2450-2459.
  32. Petty LK, Ornitz EM, Michelman JD, Zimmerman EG. Autistic children who become schizophrenic. *Arch Gen Psychiatry*. 1984;41(2):129-135.
  33. Howlin P, Moss P. Adults with Autism Spectrum Disorders. *The Canadian Journal of Psychiatry*. 2012;57(5):275-283.
  34. Rumsey JM, Rapoport JL, Sceery WR. Autistic children as adults: psychiatric, social, and behavioral outcomes. *J Am Acad Child Psychiatry*. 1985;24(4):465-473.
  35. Ghaziuddin M, Ghaziuddin N. Bipolar Disorder and Psychosis in Autism. *Child Adolesc Psychiatr Clin N Am*. 2020;29(3):433-441.
  36. Ghaziuddin M, Ghaziuddin N, Greden J. Depression in persons with autism: implications for research and clinical care. *J Autism Dev Disord*. 2002;32(4):299-306.
  37. Righi G, Benevides J, Mazefsky C, et al. Predictors of Inpatient Psychiatric Hospitalization for Children and Adolescents with Autism Spectrum Disorder. *J Autism Dev Disord*. 2018;48(11):3647-3657.
  38. Greenlee JL, Mosley AS, Shui AM, Veenstra-VanderWeele J, Gotham KO. Medical and Behavioral Correlates of Depression History in Children and Adolescents With Autism Spectrum Disorder. *Pediatrics*. 2016;137 Suppl 2(Suppl 2):S105-S114.
  39. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. American Psychiatric Association; 2013.
  40. Ghaziuddin M. *Mental Health Aspects of Autism and Asperger Syndrome*. Jessica Kingsley Publishers; 2005.
  41. Wozniak J, Biederman J, Faraone SV, et al. Mania in children with pervasive developmental disorder revisited. *J Am Acad Child Adolesc Psychiatry*. 1997;36(11):1552-1560.
  42. Vannucchi G, Masi G, Toni C, Dell'Osso L, Erfurth A, Perugi G. Bipolar disorder in adults with Asperger's Syndrome: a systematic review. *J Affect Disord*. 2014;168:151-160.
  43. Munesue T, Ono Y, Mutoh K, Shimoda K, Nakatani H, Kikuchi M. High prevalence of bipolar disorder comorbidity in adolescents and young adults with high-functioning autism spectrum disorder: a preliminary study of 44 outpatients. *J Affect Disord*. 2008;111(2-3):170-175.
  44. Morgan VA, Croft ML, Valuri GM, et al. Intellectual disability and other neuropsychiatric outcomes in high-risk children of mothers with schizophrenia, bipolar disorder and unipolar major depression. *Br J Psychiatry*. 2012;200(4):282-289.
  45. O'Connell KS, McGregor NW, Lochner C, Emsley R, Warnich L. The genetic architecture of schizophrenia, bipolar disorder, obsessive-compulsive disorder and autism spectrum disorder. *Mol Cell Neurosci*. 2018;88:300-307.
  46. Gutkovich ZA, Carlson GA, Carlson HE, Coffey B, Wieland N. Asperger's disorder and co-morbid bipolar disorder: diagnostic and treatment challenges. *J Child Adolesc Psychopharmacol*. 2007;17(2):247-255.
  47. Cassidy S, Bradley P, Robinson J, Allison C, McHugh M, Baron-Cohen S. Suicidal ideation and suicide plans or attempts in adults with Asperger's syndrome attending a specialist diagnostic clinic: a clinical cohort study. *Lancet Psychiatry*. 2014;1(2):142-147.
  48. Mayes SD, Gorman AA, Hillwig-Garcia J, Syed E. Suicide ideation and attempts in children with autism. *Research in Autism Spectrum Disorders*. 2013;7(1):109-119.
  49. Olsen CL, Cross PK, Gensburg LJ. Down syndrome: interaction between culture, demography, and biology in determining the prevalence of a genetic trait. *Hum Biol*. 2003;75(4):503-520.
  50. Volkmar FR, Lord C, Bailey A, Schultz RT, Klin A. Autism and pervasive developmental disorders. *J Child Psychol Psychiatry*. 2004;45(1):135-170.
  51. Seltzer MM, Krauss MW, Shattuck PT, Orsmond G, Swe A, Lord C. The symptoms of autism spectrum disorders in adolescence and adulthood. *J Autism Dev Disord*. 2003;33(6):565-581.