

## Autism spectrum disorder (ASD) in girls. Co-occurring psychopathology. Sex differences in clinical manifestation.

Agnieszka Rynkiewicz<sup>1,2</sup>, Izabela Łucka<sup>3</sup>

<sup>1</sup> Department of Psychiatry, Medical University of Gdansk

<sup>2</sup> Centre of Diagnosis, Therapy and Education SPECTRUM ASC-MED in Gdansk

<sup>3</sup> Department of Developmental, Psychotic and Geriatric Psychiatry, Medical University of Gdansk

### Summary

**Aim.** The study aims to define the differences in clinical manifestation among adolescent girls and boys with autism spectrum disorder (ASD).

**Methods.** The study group consisted of 15 adolescent girls and 16 adolescent boys with diagnosis of autism or Asperger syndrome and their parents. Adolescents were assessed with ADOS (Autism Diagnostic Observation Schedule, Polish adaptation of the assessment), algorithms of ADOS and ADOS-2 (revised version) were compared. Structured interview was conducted with parents, they fulfilled AQ (Autism Quotient), ASAS (Australian Scale for Asperger Syndrome), GQ-ASC (Girls' Questionnaire for Autism Spectrum Conditions). Medical records were analyzed. Results were analyzed using statistical methods.

**Results.** Patients were assessed with ADOS Module 4. Results indicated statistically significant differences between ASD girls and ASD boys in communication section, both verbal and gestures. The mean scores of AQ for ASD girls and ASD boys were  $M = 33.0$  and  $M = 30.9$ , and of ASAS  $M = 57\%$  and  $M = 61\%$  respectively. ASD girls had more psychiatric hospitalisations than ASD boys (60% vs. 31%), and they were more often treated with antidepressants (67% vs. 31%), anxiolytics (20% vs. 6%), mood stabilizers (40% vs. 19%). ASD boys were more often treated with psychotropic medications (50% vs. 47%) and stimulants (44% vs. 20%) than ASD girls.

**Conclusions.** ASD girls are at risk of receiving non-spectrum classification in ADOS or ADOS-2 while their developmental history and clinical manifestation confirm ASD. Clinical data suggests that ASD girls present more abnormalities in sensory profile. ASD girls are at greater risk for developing anxiety, depression, suicidal ideation, and for psychiatric hospitalization. ASD boys appear to be at greater risk for co-occurring ADHD, OCD and tics.

**Keywords:** autism spectrum disorder, ASD, diagnosis

## Introduction

Autism spectrum disorders (ASD) frequently referred to as autism spectrum conditions (ASC) affect 1% of the world population [1–3]. It is diagnosed more frequently in boys than in girls, with the 4:1 ratio mentioned in published literature [4–7]. However, recent studies show that this proportion may be lower: 2.0–2.6:1 [8–10] which can be attributed to e.g. improved diagnostic skills of mental health professionals as well as revised diagnostic tools and criteria. The girls are diagnosed with autism spectrum disorder less frequently than their male counterparts, which results in less research conducted in this patient group to address the issue of sex-related differences in clinical manifestation, patient functioning or coexistent psychopathology [11–13]. The papers published so far described internally variable study groups of girls and boys with the small number of girl participants [11].

Autism spectrum disorder is a complex neurobiological disorder, which aetiology has not been determined yet. The research so far has pointed out to the numerous genetic, neuroanatomical and immune abnormalities as well as the neurotransmitter dysfunction [14–17]. One of current, interesting theories assumes that the increased level of oxytocin, being a neuromodulator involved in social bonding, exerts a protective effect on manifestation of autistic traits in girls [18]. To certain degree it can explain why the autistic traits are less severe in many high functioning ASD girls as compared to ASD boys [19, 20]. As a result, these girls may not be appropriately diagnosed or be diagnosed with ASD in later age.

The deficits typical of autism spectrum disorder are manifested in the following areas: communication, social competence and rigid, stereotypic behaviours [21]. The symptoms may be noticed and diagnosed even in early childhood [22]. However, they may also become manifested in later age, when the social demand and requirements exceed the limited functional capabilities of an ASD individual. Including the sensory profile abnormalities in the new DSM-5 diagnostic criteria can have positive implications on ASD diagnosis in female population [23] especially as it has been reported that ASD females have greater self-awareness and make greater effort to camouflage their deficits [5, 11, 19, 24]. Diagnostic tests in ASD are developed based on the phenotype typical of ASD boys, which does not include many characteristics of ASD girls [13, 19, 24].

## Material

The study group consisted of 31 participants: 15 adolescent girls and 16 adolescent boys with autism spectrum disorder, and their parents. The inclusion criteria included the age of adolescence (range between 10 and 20 years), average or above average IQ; verbally fluent native speakers of Polish, and the formal diagnosis of autistic disorder or Asperger's syndrome, based on of ICD-10 [25] or DSM-IV [26]

criteria, made by a psychiatrist. The enrolled participants were adolescents treated at Child and Adolescent Mental Health Services and Autism Clinics. The mean age of girls was 16 years and of boys 14.2 years. The control group consisted of 20 normotypic (NT) girls and boys (10 girls and 10 boys), whose age matched their study counterparts and who did not have the diagnosis of ASD, history of another mental health or general health condition. As a part of the study, the structured interview developed by the international research team was conducted with the parents of the enrolled adolescents.

### Ethics and informed consent

The study was approved by Independent Bioethical Committee on Scientific Research at the Medical University of Gdansk (NKEBN/65/2012). The authors of all diagnostic tools used in the studies gave their permission to such use and appropriate licenses were issued by the WPS publisher (Western Psychological Services, USA). Written informed consent was obtained from all participants in accordance with procedures approved by the above mentioned Bioethical Committee.

### Method

Adolescents were assessed with ADOS, Autism Diagnostic Observation Schedule, Polish version [27, 28] and the results of both algorithms ADOS and ADOS-2, Autism Diagnostic Observation Schedule Second Edition [29] were compared and analysed. Both tests have been referred to as the gold standard observational assessment for diagnosing ASD. This is a semi-structured, standardized assessment of communication, social interaction, play, imaginative use of materials, as well as restricted and repetitive behaviours. The authors of ADOS are Catherine Lord, Michael Rutter, Pamela DiLavore, Susan Risi. The above mentioned authors and Katherine Gotham, Somer Bishop, Rhiannon Luyster and Whitney Guthrie are the authors of ADOS-2. The copyright belongs to American publisher Western Psychological Services. The copyright to Polish version belongs to Czech publisher Hogrefe Testcentrum. The full availability of Polish version of this assessment to all interested and appropriately trained clinicians is being planned for 2016. ADOS-2 has 5 Modules according to an individual's age and language abilities. ADOS Module 4 in Polish version was used in this research. Module 4 is designed for use with older adolescents and adults with fluent language skills. Coding of both ADOS and ADOS-2 are according to the algorithm. It is advised to have two specialists who reach 80% and above consensus on the coded items. It is also advised to have ADOS or ADOS-2 sessions video recorded which had been also done in this study. All described procedures increase the reliability and accuracy of the diagnosis. Module 4 ADOS or ADOS-2 sessions last from 40 to 60 minutes. The full description of both ADOS and ADOS-2 assessments

have already been published in Polish peer-reviewed journals [11, 27]. The ADOS [28] provided scores based on the old algorithm while ADOS-2 [29] provided scores based on the new algorithm which has been in force since 2012 after the diagnostic tool's revision.

All parents provided information regarding their child by completing the Polish adaptations of the following tests: Autism Quotient – Adolescent (AQ for adolescents aged 12–15) [30], ASAS (Australian Scale for Asperger's Syndrome) [31] and GQ-ASC (Girls' Questionnaire for Autism Spectrum Conditions) [19, 32, 33]. 16 years old and older adolescents completed AQ [34, 35] by themselves. Patients' IQ were assessed with the Wechsler Intelligence Scale in Polish adaptation by Brzeziński et al. & Matczak et al. [36].

Both questionnaires AQ and AQ – Adolescent (for the age group 12–15) consist of 50 statements which are used to assess the intensity of autistic traits presented by an individual. ASAS questionnaire consists of 24 questions and 10 additional characteristics. It identifies the behaviours and skill level which is suggestive of Asperger's syndrome, still a separate clinical entity of ASD in ICD-10 [25]. GQ-ASC is a screening diagnostic tool designed to identify behaviours and abilities in girls that could be associated with the characteristic of autism spectrum conditions (ASC), also defined as autism spectrum disorders (ASD). Questionnaire have two forms depending on the age of a respondent: aged 5 to 12 and 13 and older. Both forms contain four sections of different aspects of functioning: A – “Play”, B – “Friendships and Social Situations”, C – “Abilities and Interests”, D – “Sensory Profile”, and E – “Medical History”. Each section comprises a list of questions and statements for parents regarding their child to rate how strongly they agree or disagree. GQ-ASC for younger girls (aged 5–12) contains 54 questions and statements whereas GQ-ASC for older girls (13 and older) contains 58. As a part of the study, the structured interview developed by the international research team was conducted with the parents of the enrolled participants. Additionally, the medical records of adolescents were analysed thoroughly, mainly for concomitant disorders based on ICD-10 and used pharmacotherapy.

## Results

Statistical analysis included mean values or mean frequencies of analysed parameters in order to determine differences which can be directly attributed to sex. The results were plotted on graphs (mean + standard error) created using MS Excel. The GQ-ASC results were analysed using the Chi-square test. All statistical analyses were carried out using SPSS software (IBM SPSS Statistics v. 21). All adolescents were assessed with ADOS Module 4. Results indicated statistically significant differences between ASD girls and ASD boys in communication section, both verbal and gestures (Figure 1–2). The results from other research with ADOS-2 and younger

population of ASD indicate similar results in regard to gestures [37]. The mean score of AQ and AQ – Adolescent aged 12–15 for ASD girls and ASD boys was  $M = 33$  and  $M = 30.9$  respectively. In the control group, the score of the NT girls ( $n = 10$ ) and NT boys ( $n = 10$ ) was  $M = 15.4$  and  $M = 16.0$ . The mean Australian Scale for Asperger’s Syndrome score (ASAS) for the same ASD girls and ASD boys was  $M = 57\%$  and  $M = 61\%$ . The score in the control group was  $M = 12\%$  and  $M = 25\%$ . As shown in medical records, the IQ (Wechsler Intelligence Scale) for ASD girls vs. ASD boys was: full scale  $M = 105.7$  vs.  $M = 101.2$ ; performance scale:  $M = 100.3$  vs.  $M = 95.3$ ; verbal scale  $M = 108.3$  vs.  $M = 105.8$ . The records also showed that the ASD girls were hospitalised in mental health facilities more frequently than ASD boys (60% vs. 31%). The mean age of ASD girls at first hospitalisation was 14.3 years and 12.2 years for ASD boys. ASD girls were treated with antidepressants (67% vs. 31%), anxiolytics (20% vs. 6%) and mood stabilizers (40% vs. 19%) more often than ASD boys. ASD boys were treated with psychotropic medications (50% vs. 47%) and stimulants (44% vs. 20%) more often than ASD girls. Significant data from medical records and the structured interview is presented in Table 1.

Table 1. **Data from medical records (ASD adolescent girls and ASD adolescent boys)**

	FEMALES	MALES
Complications in pregnancy	+ (40%)	+ (50%)
Labour in-term	73%	69%
pre-term	+ (13%)	+ (19%)
First autistic signs noticed (age)		
First ASD signs noticed by...	$9.4 \pm 1.4$	$5.9 \pm 0.9$
– parent	57%	75%
– professional	43%	25%
Official ASD diagnosis (age)	$14.9 \pm 0.6$	$9.5 \pm 1.2$
Co-occurring psychopathology	depression and anxiety (40%) ADHD (20%) Sensory Processing Disorder (27%)	ADHD (47%) oppositional defiant disorder (33%) OCD and tics (13%)
Sleep problems in early childhood	80%	44%

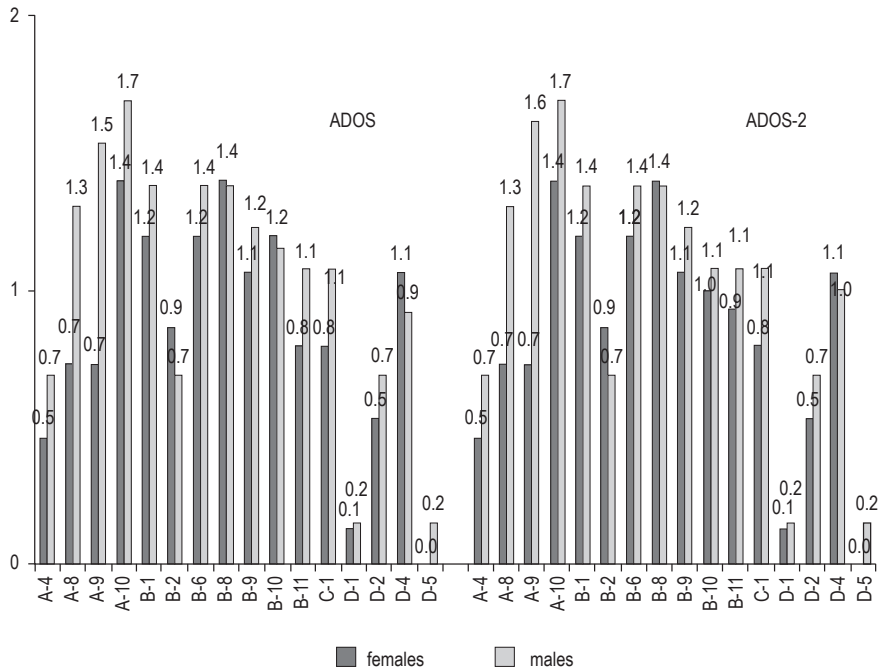


Figure 1. Comparison among the codes – ADOS and ADOS-2 Module 4 algorithms (ASD adolescent girls and ASD adolescent boys)

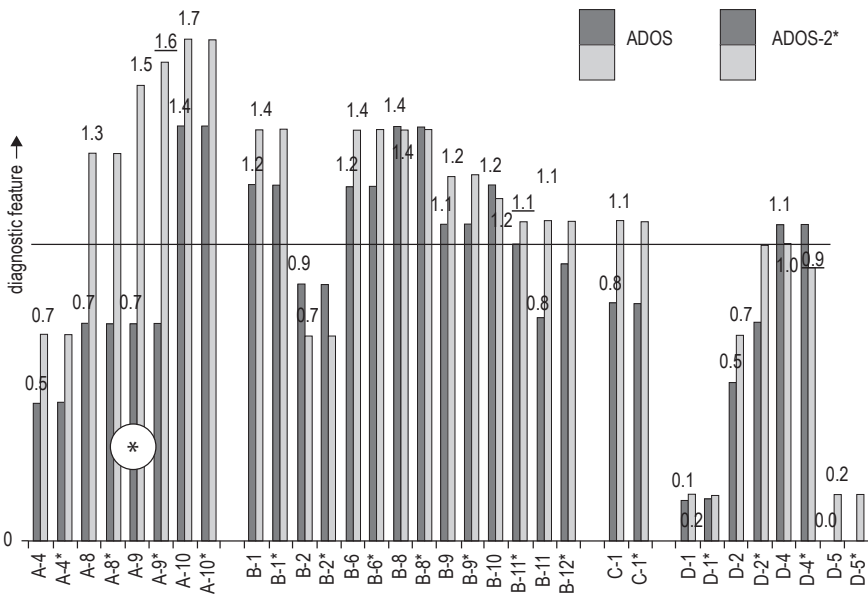


Figure 2. Comparison among the codes – ADOS and ADOS-2\* Module 4 algorithms (ASD adolescent girls and ASD adolescent boys)

For the purpose of the study the results of GQ-ASC from the sections D–E: Sensory Profile and Medical History are presented. The sections comprise a list of questions and statements, where the girl's parents have to rate how strongly they agree or disagree. The obtained results are as follow: most ASD girls have intense emotions (5–12:  $\chi^2 = 10.8^{**}$ ; 13:  $\geq \chi^2 = 30.2^{***}$ ) and express distress during grooming or touching (5–12:  $\chi^2 = 11.2^{**}$ ; 13:  $\geq \chi^2 = 6.1^*$ ), they also feel bothered by bright lights (13:  $\geq \chi^2 = 9.6^{**}$ ). Only adolescent ASD girls have poor endurance (13:  $\geq \chi^2 = 24.1^{***}$ ). Some of adolescent ASD girl seeks specific sensations (13:  $\geq \chi^2 = 7.2^*$ ) or avoid certain sensations e.g. head upside down, heights etc. (13:  $\geq \chi^2 = 13.9^{**}$ ). Most of ASD girls are distracted during any task or conversation when there is noise around (5–12:  $\chi^2 = 11.2^{**}$ ; 13:  $\geq \chi^2 = 56.7^{***}$ ). More than half ASD girls are attached to certain toys or objects which make them calm (5–12:  $\chi^2 = 11.2^{**}$ ; 13:  $\geq \chi^2 = 7.0^*$ ). Adolescent ASD girls very often present symptoms typical for anxiety (13:  $\geq \chi^2 = 4.7^*$ ) and majority of them have never been diagnosed with eating disorder (13–19:  $\chi^2 = 30.9^{***}$ )<sup>1</sup>.

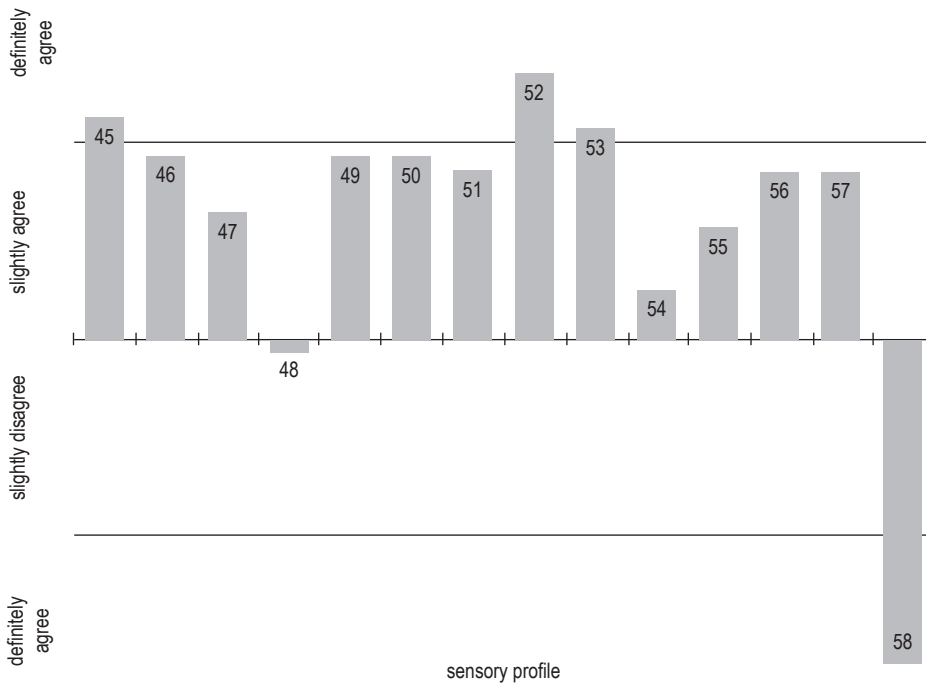


Figure 3. GQ-ASC, section D–E: Sensory profile and medical history

<sup>1</sup> \*  $\alpha < 0.05$ ; \*\* $\alpha < 0.01$ ; \*\*\* $\alpha < 0.001$

## Conclusions

The study results have indicated statistically significant differences between ASD adolescent girls and ASD adolescent boys in communication section of ADOS and ADOS-2 algorithms. On the standard administration and scoring of ADOS and ADOS-2, ASD adolescent girls present less or no autistic in comparison to ASD adolescent boys on items in gestures and verbal communication in both algorithms. Since ASD adolescent girls present less or no autistic in comparison to ASD adolescent boys on gestures and verbal communication items in ADOS and ADOS-2 algorithms, ASD girls might be at risk of receiving non-spectrum classification in ADOS or ADOS-2 while their developmental history and clinical manifestation confirm ASD. ASD adolescent girls show fewer behavioural autistic features than ASD adolescent boys under communication section in both ADOS and ADOS-2 algorithms, but they have higher scores representing autistic features in self-reported questionnaires and in the clinical interview. This might confirm ASD girls' greater self-awareness, greater effort to camouflage the deficits and greater determination to learn social norms and nuances than ASD boys. ASD adolescent girls and ASD adolescent boys appear to be similar on stereotyped behaviours. Clinical data suggests that ASD girls present more abnormalities in sensory profile than ASD boys.

Additionally the results indicate that ASD adolescent girls appear to be at greater risk for developing anxiety, depression, suicidal ideation and psychiatric hospitalization than ASD boys. ASD boys appear to be at greater risk for co-occurring ADHD, obsessive-compulsive disorder (OCD) and tics. ASD girls present clinically much later (three and a half years) and are diagnosed with autism spectrum disorder five and a half years later than ASD boys. Depression and anxiety are most frequent prior diagnosis for girls before they receive ASD diagnosis while for boys it is ADHD and oppositional defiant disorder. In regards to depression both ASD boys and girls present with the increased internalizing psychopathology as compared to the normotypic (NT) individuals [7]. The studies show that the prevalence of early childhood depression does not differ between the NT boys and NT girls. However, NT girls present with mood disorders more frequently than NT boys during adolescence. It has particular clinical importance for ASD adolescent girls, who are therefore susceptible to the so-called "double hit" of affective disorder during adolescence. The word "double" indicates the two factors predisposing ASD girls to develop affective disorder during puberty: that is, female sex and autism spectrum disorder. Perhaps these findings also apply to other disorders co-occurring with ASD

Presented results are part of bigger research of the authors' on ASD females. The authors hope this information may contribute to increased diagnosis of autism spectrum disorder (ASD) in girls, which can ultimately improve the efficacy of treatments and therapies in this patient group.



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Address: Agnieszka Rynkiewicz  
Department of Psychiatry  
Medical University of Gdansk  
University Clinical Centre in Gdansk  
80-211 Gdańsk, Dębinki Street 7