Research Article / Araştırma Makalesi

The Prevalence of Comorbid Psychiatric Disorders in Children and Adolescents with Asperger Syndrome

Asperger Sendromu Olan Çocuk ve Ergenlerde Komorbid Psikiyatrik Bozuklukların Yaygınlığı

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Abstract

Background: Most studies in the literature on comorbid psychiatric conditions in children and adolescents with Asperger syndrome (AS) either consist of individual case reports or have evaluated cases only in terms of a specific comorbid psychiatric diagnosis. Therefore, especially in recent years, there are few studies in the literature examining the comorbidity of all psychiatric disorders in patients with AS in a holistic manner. The present study aimed to determine the prevalence and types of comorbid psychiatric disorders in a clinic-based sample of 34 children and adolescents with AS.
Materials and Methods: Thirty-four children and adolescents with AS [31 males (91.2%), 3 females (8.8%) mean age 12.62±3.75 years] were gathered from clinical referrals between 2017 and 2024. Participants' sociodemographic characteristics, age at first diagnosis of AS, clinical features, comorbid psychiatric disorders, and treatment regimens were retrospectively reviewed from each hospital's records. AS diagnosis was made according to the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) criteria. Psychiatric comorbidity was assessed using DSM-5 criteria.
Results: Comorbid psychiatric disorders were present in 31 (91.2%) of the cases, with 5 (14.7%) having a single comorbid disorder and 26 (76.5%) having at least two. The most common comorbid diagnoses were anxiety disorders (67.6%, n=23), attention deficit hyperactive disorder (64.7%, n=22), obsessive-compulsive disorder (29.4%, n=10), and depression (29.4%, n=10). No cases were identified with post-traumatic stress disorder, panic disorder, eating disorders, alcohol or substance use, bipolar disorder, and psychotic disorders. In age-related comparisons, conduct disorder, specific phobia, separation anxiety disorder, and enuresis were more frequently observed in childhood, whereas social phobia, obsessive-compulsive disorder, and depression were more prevalent in adolescence.
Conclusions: Our findings highlight the high prevalence of psychiatric comorbidity in children and adolescents with AS, often involving multiple conditions. Routine assessment of psychiatric comorbidity should be an integral part of clinical evaluations for this population.

Keywords: Asperger syndrome, Autism spectrum disorder, Psychiatric comorbidity, Psychopathology, Child-adolescent

Öz

Amaç: Literatürdeki Asperger sendromu (AS) olan çocuk ve ergenlerde komorbid psikiyatrik durumlar üzerine yapılan çalışmaların çoğu ya bireysel vaka raporlarından oluşmaktadır ya da vakaları yalnızca belirli bir eşlik eden psikiyatrik tanı açısından değerlendirmiştir. Bu nedenle, özellikle son yıllarda literatürde AS hastalarında tüm psikiyatrik bozuklukların komorbiditesini bütüncül bir şekilde inceleyen az sayıda çalışma bulunmaktadır. Bu çalışmada, AS'li 34 çocuk ve ergenden oluşan klinik bir örneklemde komorbid psikiyatrik bozuklukların yaygınlığının ve türlerinin belirlenmesi amaçlanmıştır.
Materyal ve Metod: AS'li otuz dört çocuk ve ergen [31 erkek (%91,2), 3 kız (%8,8) ortalama yaş 12,62±3,75 yıl] 2017-2024 yılları arasındaki klinik başvurulardan toplandı. Katılımcıların sosyodemografik özellikleri, ilk AS tanı yaşı, klinik özellikler, komorbid psikiyatrik bozukluklar ve tedavi rejimleri her bir hastanenin kayıtlarından retrospektif olarak incelendi. AS tanısı, Ruhsal Bozuklukların Tanısal ve İstatistiksel El Kitabı 4. Baskı (DSM-IV) kriterlerine göre konuldu. Psikiyatrik komorbidite DSM-5 kriterlerine göre değerlendirildi.
Bulgular: Olguların 31'inde (%91,2) komorbid psikiyatrik bozukluk, 5'inde (%14,7) tek bir komorbid psikiyatrik bozukluk, 26'sında (%76,5) ise en az iki komorbid psikiyatrik bozukluk vardı. En sık komorbid tanılar anksiyete bozuklukları (%67,6, n=23), dikkat eksikliği hiperaktivite bozukluğu (%64,7, n=22), obsesif kompulsif bozukluk (%29,4, n=10) ve depresyondu (%29,4, n=10). Hiçbir olguda travma sonrası stres bozukluğu (TSSB), panik bozukluğu, yeme bozuklukları, alkol veya madde kullanımı, bipolar bozukluk ve psikotik bozukluklar saptanmadı. Yaşa göre karşılaştırmalarda çocukluk çağında davranım bozukluğu, özgül fobi, ayrılma kaygısı bozukluğu ve enürezis daha sık görülürken, ergenlikte sosyal fobi, obsesif kompulsif bozukluk ve depresyon daha sık görüldü.
Sonuç: Bulgularımız AS'li çocuk ve ergenlerde psikiyatrik komorbiditenin yüksek yaygınlığını vurgulamaktadır ve bu sıklıkla birden fazla durumu içermektedir. Psikiyatrik komorbiditenin rutin değerlendirmesi bu popülasyon için klinik değerlendirmelerin ayrılmaz bir parçası olmalıdır.

Anahtar Kelimeler: Asperger sendromu, Otizm spektrum bozukluğu, Psikiyatrik komorbidite, Psikopatoloji, Çocuk-ergen

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Introduction

Asperger syndrome (AS) is a disorder that falls under the large umbrella of autism spectrum disorders (ASDs) and is distinguished by social-communication impairment, overfocused, repetitive interests and behavior patterns, and lack of any substantial learning disability or language delay (1-3). AS was included in the psychiatric diagnostic system with the name Asperger Disorder in the Diagnostic and Statistical Manual of Mental Disorders, 4th ed. (DSM-IV) in 1994 and began to be included as a separate diagnosis, but it was removed from the diagnostic system in DSM-5 and included in the scope of ASD (3, 4). Even though classic autism and AS are both classified as ASDs, people with AS typically have a unique pattern of social impairment that appears to be less severe than that of people with classic autism (1,2), but, as with other types of autistic disorders, the main difficulty in AS is the deficit in social learning and social awareness (5).

Despite intact language and cognitive development, individuals with AS experience social difficulties due to significant deficiencies in nonverbal communication and pragmatic language skills, impairment in reciprocal social interaction, unusual, isolated special interests and preoccupations, low empathy, a lack of understanding of social norms, misinterpreting figurative and intended meanings, and difficulty in coping with their own emotions (1-7). These children have difficulty socializing with their peers, usually do not have close friends, avoid others, and are often lonely and solitary. Some researchers have identified three different types of AS: "withdrawn-aloof", "active-odd", and "passive-friendly" (7). Even though children with AS sometimes make an effort and are willing to engage in communication, others frequently reject or exclude them due to their inappropriate and clumsy social interaction approaches and their inability to accurately read the emotions, intentions, and subliminal cues of others (1, 2, 6, 7). They cannot look at events from the other person's perspective and empathize with the others, so they cannot give appropriate emotional responses, mutual emotional sharing, and long-term interpersonal relationships (5). Over time, most realize that they are different, strange, and unusual (1, 2, 5-7). Furthermore, they frequently lack passion for other facets of life due to their intensely focused unique hobbies, which hinders communication and connection with others (1, 2, 5-7). Previous studies have reported higher rates of psychiatric disorders in children and adolescents with AS compared to their healthy peers and that comorbid psychiatric disorders may contribute to functional impairments in these children (8-14). Although all types of psychiatric disorders can be seen in children and adolescents with AS, the most common comorbid conditions are attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder (ODD), conduct disorder (CD), anxiety disorders, mood disorders, obsessive-compulsive disorder (OCD), eating behavior disorders, post-traumatic stress disorder (PTSD), tic disorders, learning disorders, and psychosis (8-16).

However, the rates of psychiatric comorbidity reported in studies vary widely (from 44% to 100%) (8-16). In conclusion, it is emphasized that the occurrence of psychiatric comorbidities in children and adolescents with AS is almost the rule rather than the exception. These conditions can cause significant distress for both the child and the family, contribute to functional impairments, and further impair quality of life (7, 9, 10, 12, 14-18).

Given this, it is essential to thoroughly assess psychiatric comorbidities in individuals with AS, and clinicians must be particularly vigilant in identifying them (6, 12). However, most existing studies on psychiatric comorbidities in AS are either limited to case reports or focus on specific psychiatric diagnoses. Therefore, especially in recent years, there is a notable lack of comprehensive research evaluating the full spectrum of psychiatric comorbidities in children and adolescents with AS (7, 9, 10, 12, 13). Thus, this study aimed to investigate the frequency and types of comorbid psychiatric disorders in a clinic-based sample of children and adolescents with AS.

Materials and Methods

***Participants*:** The study sample consisted of 34 children and adolescents [31 males (91.2%), 3 females (8.8%) mean age 12.62±3.75 years] diagnosed with AS who applied to three different Child and Adolescent Psychiatry outpatient clinics. Participants' sociodemographic characteristics, age at first diagnosis of AS, clinical features, comorbid psychiatric disorders, and treatment regimens were retrospectively reviewed from each hospital's records. AS diagnosis was made according to DSM-IV criteria, because AS is not included as a separate diagnostic category in DSM-5 (3). Psychiatric comorbidity was assessed using DSM-5 criteria (4); the Wechsler Intelligence Scale for Children (WISC) was administered to assess IQ (19, 20). Participants with missing data were not included in the study, and no further exclusion criteria were applied.

The local ethics committee approved the study protocol (Date: 17.05.2023, No: 2023-05/11) and conducted it according to the principles of the Helsinki Declaration and Good Clinical Practice for Biomedical Research.

Statistical Analysis: Statistical data were analyzed using IBM SPSS 22.0 (SPSS Inc., Chicago, IL, USA). Quantitative variables were presented as mean and standard deviation (SD), and qualitative data were presented as number (n) and percentage (%) whenever appropriate. Descriptive statistics were used to summarize variables. The Shapiro-Wilk test was employed to assess the normality of continuous variables. Comparisons of the groups were performed using the chi-square test for categorical variables. The p-value of <0.05 was accepted as an indication of statistical significance.

Results

Descriptive and clinical characteristics of the sample

Thirty-one (91.2%) of the participants were male, three (8.8%) were female, and the mean age was 12.62±3.75 (min-max: 8-17) years. The mean age at AS diagnosis was 9.44±1.96 years. The total intelligence score mean was 108.53±8.40 (min-max: 96-129). When the cases were separated according to age groups, fourteen (41.2%) were children and twenty (58.8%) were adolescents. The mean age of the mothers was 40.71±4.62 years, fourteen (41.2%) were university graduates, and twelve (35.3%) were working in a regular job. The mean age of the fathers was 42.21±4.76 years, 25 (73.5%) were university graduates, and 31 (91.2%) were working in a regular job. 73.5% of the sample (n=25) had a family income above minimum wage. Sociodemographic characteristics of the participants are presented in Table 1.

Table 1. Sociodemographic characteristics of the sample

Variables	Number (%) or mean±SD
Age (mean-years±SD)	12.62±3.75
Age at first Asperger Syndrome diagnosis (mean-years±SD)	9.44±1.96
Age groups	
School-age group (<12 ages)	14 (41.2)
Adolescent group (≥12 ages)	20 (58.8)
Sex	
Male	31 (91.2)
Female	3 (8.8)
Total intelligence score (mean±SD)	108.53±8.40
Academic performance	
Average	13 (38.2)
Below average	11 (32.4)
Above average	10 (29.4)
Age of mother (mean-years±SD)	40.71±4.62
Level of education of the mother	
High school and lower	20 (58.8)
University	14 (41.2)
Regular job of the mother	
Yes	12 (35.3)
No	22 (64.7)
Age of father (mean-years±SD)	42.21±4.76
Level of education of the father	
High school and lower	9 (26.5)
University	25 (73.5)
Regular job of the father	
Yes	31 (91.2)
No	3 (8.8)
Family income level	
The minimum wage/less than minimum wage	9 (26.5)
Above the minimum wage	25 (73.5)

Abbreviations: AS: Asperger Syndrome; SD: Standard Deviation.

Upon analyzing the sample's past psychopathological status, it was found that 88.2% (n=30) of the participants had received a prior diagnosis of any comorbid psychiatric condition. When the number of past psychiatric comorbidities was examined, it was determined that 17.6% (n=6) of the cases had a single comorbid psychiatric disorder and 70.6% (n=24) had at least two comorbid psychiatric disorders. The most frequently diagnosed comorbid psychiatric disorders in the past were ADHD (64.7%, n=22), anxiety disorders (52.9%, n=18), and ODD (32.4%, n=11). Previously diagnosed comorbid psychiatric disorders were, in order of frequency, ADHD (64.7%, n=22), specific phobia (47.1%, n=16), separation anxiety disorder (38.2%, n=13), ODD (32.4%, n=11), OCD (23.5%, n=8), enuresis (23.5%, n=8), social phobia (14.7%, n=5), depression (11.8%, n=4), tic disorders (11.8%, n=4), CD (8.8%, n=3), encopresis (8.8%, n=3), generalized anxiety disorder (GAD) (5.9%, n=2), and PTSD (2.9%, n=1). Psychopharmacological agents used in the past, in decreasing order of frequency, were antipsychotics (61.8%, n=21), antidepressants (47.1%, n=16), methylphenidate (44.1%, n=15), and atomoxetine (29.4%, n=10). Alcohol or substance use, panic disorder, eating disorders, bipolar disorder, and psychotic disorders were not detected as past psychiatric disorders in the sample. The past psychopathological status and psychopharmacological drug use of the sample are shown in Table 2.

Table 2. Past psychopathological status and psychopharmacological drug use of the sample

Variables	Number (%)
Presence of a past diagnosis of a psychiatric disorder	30 (88.2)
Past psychopathology status	
No	4 (11.8)
A single comorbid psychiatric disorder	6 (17.6)
At least two comorbid psychiatric disorders	24 (70.6)
Previous history of ADHD	22 (64.7)
Previous history of CD	3 (8.8)
Previous history of ODD	11 (32.4)
Previous history of any anxiety disorder	18 (52.9)
Previous history of GAD	2 (5.9)
Previous history of specific phobia	16 (47.1)
Previous history of social phobia	5 (14.7)
Previous history of separation anxiety disorder	13 (38.2)
Previous history of OCD	8 (23.5)
Previous history of tic disorder	4 (11.8)
Previous history of PTSD	1 (2.9)
Previous history of depression	4 (11.8)
Previous history of enuresis	8 (23.5)
Previous history of encopresis	3 (8.8)
Previous history of antipsychotic use	21 (61.8)
Previous history of antidepressants use	16 (47.1)
Previous history of methylphenidate use	15 (44.1)
Previous history of atomoxetine use	10 (29.4)

Abbreviations: *ADHD: Attention Deficit Hyperactive Disorder; CD: Conduct disorder; GAD: Generalized Anxiety Disorder; OCD: Obsessive Compulsive Disorder; ODD: Oppositional Defiant Disorder, PTSD: Post-Traumatic Stress Disorder.*

When the reasons for the sample's current applications to psychiatric clinics were examined, it was seen that 8 (23.5%) applied with symptoms specific to AS only, 11

(32.4%) with other psychiatric symptoms not directly related to AS, and 15 (44.1%) with both symptoms specific to AS and other psychiatric symptoms not directly related to AS. Regarding the socialization status of the cases, it was learned that 9 (26.5%) were withdrawn-aloof, 19 (55.9%) were active-odd, and 6 (17.6%) were passive-friendly. It was found that 31 (91.2%) of the cases had comorbid psychiatric disorders, 5 (14.7%) had a single comorbid psychiatric disorder, and 26 (76.5%) had at least two psychiatric disorders. When current comorbid psychiatric disorders were examined, the most common diagnoses were anxiety disorders (67.6%, n=23), ADHD (64.7%, n=22), OCD (29.4%, n=10) and depression (29.4%, n=10). Current comorbid psychiatric disorders, in decreasing order of frequency, were ADHD (64.7%, n=22), social phobia (35.3%, n=12), OCD (29.4%, n=10), depression (29.4%, n=10), ODD (26.5%, n=9), specific phobia (23.5%, n=8), tic disorders (20.6%, n=7), GAD (14.7%, n=5), separation anxiety disorder (11.8%, n=4), CD (8.8%, n=3), enuresis (8.8%, n=3) and encopresis (2.9%, n=1). In the current psychopathology examination of the sample, PTSD, panic disorder, eating disorders, alcohol or substance use, bipolar disorder, and psychotic disorders were not detected in any case. Regarding current psychopharmacological agent use, the most frequently prescribed drugs, in decreasing order of frequency, were antidepressants (76.5%, n=26), antipsychotics (73.5%, n=25), methylphenidate (47.1%, n=16), and atomoxetine (29.4%, n=10). Current psychopathological status and psychopharmacological drug use in the sample are given in Table 3.

Table 3. Current psychopathological status and psychopharmacological drug use of the sample

Variables	Number (%)
Reason for applying to the psychiatric clinic	8 (23.5)
Symptoms specific to AS only	11 (32.4)
Other psychiatric symptoms not directly related to AS	15 (44.1)
Both AS-specific symptoms and psychiatric symptoms not directly related to AS	
Socialization status	
Withdrawn-aloof	9 (26.5)
Active-odd	19 (55.9)
Passive-friendly	6 (17.6)
Current diagnosis of a psychiatric disorder	31 (91.2)
Current psychopathology status	
No	3 (8.8)
A single comorbid psychiatric disorder	5 (14.7)
At least two comorbid psychiatric disorders	26 (76.5)
Presence of current ADHD diagnosis	22 (64.7)
Presence of current CD diagnosis	3 (8.8)
Presence of current ODD diagnosis	9 (26.5)
Presence of current any anxiety disorder diagnosis	23 (67.6)
Presence of current GAD diagnosis	5 (14.7)
Presence of current specific phobia diagnosis	8 (23.5)
Presence of current social phobia diagnosis	12 (35.3)
Presence of current separation anxiety disorder diagnosis	4 (11.8)
Presence of current OCD diagnosis	10 (29.4)
Presence of current tic disorders diagnosis	7 (20.6)
Presence of current PTSD diagnosis	0 (0)
Presence of current depression diagnosis	10 (29.4)
Presence of current enuresis diagnosis	3 (8.8)
Presence of current encopresis diagnosis	1 (2.9)
Current antipsychotic use	25 (73.5)
Current antidepressants use	26 (76.5)
Current methylphenidate use	16 (47.1)
Current atomoxetine use	10 (29.4)

Abbreviations: ADHD: Attention Deficit Hyperactive Disorder; CD: Conduct Disorder; GAD: Generalized Anxiety Disorder; OCD: Obsessive Compulsive Disorder; ODD: Oppositional Defiant Disorder, PTSD: Post-Traumatic Stress Disorder.

When the existing comorbid psychopathologies were compared according to age groups, it was found that the frequency of having at least two comorbid psychiatric disorders was significantly higher in the adolescent group than in the child age group (p=0.036). There was no significant difference in the rates of comorbid ADHD, ODD, any anxiety disorder, GAD, tic disorders, and encopresis between age groups (p=0.275, p=0.435, p=0.793, p=0.379, p=0.410, p=0.412, respectively). However, comorbid CD, specific phobia, separation anxiety disorder, and enuresis were significantly higher in the childhood age group (p=0.030, p=0.004, p=0.022, p=0.030, respectively), while comorbid social phobia, OCD, and depression were significantly higher in the adolescent group (p<0.001, p=0.024, p=0.024,

respectively). Regarding the psychopharmacological agents used, the frequency of prescription of antipsychotics, methylphenidate, and atomoxetine was similar between the two groups (p=0.116, p=0.092, p=0.928, respectively), while the frequency of prescription of antidepressants was significantly higher in the adolescent group than in the childhood age group (p=0.004). The comparison of current comorbid psychopathologies according to age groups is shown in Table 4.

Table 4. Comparison of current comorbid psychopathologies according to age groups

	Children group (N=14)	Adolescent group (N=20)	p-value*
Current psychopathology status			
No	2 (14.3)	1 (5.0)	0.036
A single comorbid psychiatric disorder	4 (28.6)	1 (5.0)	
At least two comorbid psychiatric disorders	8 (57.1)	18 (90.0)	
Presence of current ADHD diagnosis	11 (78.6)	11 (55.0)	0.275
Presence of current CD diagnosis	3 (21.4)	0 (0)	0.030
Presence of current ODD diagnosis	5 (35.7)	4 (20.0)	0.435
Presence of current any anxiety disorder diagnosis	10 (71.4)	13 (65.0)	0.793
Presence of current GAD diagnosis	1 (7.1)	4 (20.0)	0.379
Presence of current specific phobia diagnosis	7 (50.0)	1 (5.0)	0.004
Presence of current social phobia diagnosis	0 (0)	12 (60.0)	<0.001
Presence of current separation anxiety disorder diagnosis	4 (28.6)	0 (0)	0.022
Presence of current OCD diagnosis	1 (7.1)	9 (45.0)	0.024
Presence of current tic disorders diagnosis	4 (28.6)	3 (15.0)	0.410
Presence of current depression diagnosis	1 (7.1)	9 (45.0)	0.024
Presence of current enuresis diagnosis	3 (21.4)	0 (0)	0.030
Presence of current encopresis diagnosis	1 (7.1)	0 (0)	0.412
Current antipsychotic use	8 (57.1)	17 (85.0)	0.116
Current antidepressants use	7 (50.0)	19 (95.0)	0.004
Current methylphenidate use	9 (64.3)	7 (35.0)	0.092
Current atomoxetine use	4 (28.6)	6 (30.0)	0.928

*The chi-square test for categorical variables was used to test group differences.
Abbreviations: ADHD: Attention Deficit Hyperactive Disorder; CD: Conduct disorder; GAD: Generalized Anxiety Disorder; OCD: Obsessive Compulsive Disorder; ODD: Oppositional Defiant Disorder, PTSD: Post-Traumatic Stress Disorder.

Discussion

In this study, the reasons for psychiatric referral and the frequency and distribution of psychiatric comorbidities in children and adolescents with AS were evaluated. It was revealed that 88.2% of the participants had at least one comorbid psychiatric disorder in the past and 91.2% had at least one current comorbid psychiatric disorder. Regarding psychopharmacological agent use, the most frequently prescribed drugs, in decreasing order of frequency, were antidepressants (76.5%), antipsychotics (73.5%), methylphenidate (47.1%), and atomoxetine (29.4%).

No large community studies show definitive incidence and prevalence rates regarding comorbid psychiatric conditions seen in AS, and existing studies vary in terms of diagnostic criteria, age of subjects, and sampling methods, making it difficult to generalize the data. Numerous studies examining comorbid psychopathology in children with AS have shown a wide range of psychiatric comorbidity rates, from 44% to 100%, probably due to methodological variations, such as very few samples, heterogeneity in study settings, data sources, case definitions, and included age ranges, highly variable exclusionary criteria, and possible clinical misinterpretation of symptoms (8-14).

However, it is known that children and adolescents with AS are at higher risk for psychiatric comorbidity when compared with a sample from the general population, and some researchers even report that the occurrence of psychiatric comorbidities in AS is almost the rule rather than the exception (7,9,10,12,14-18). The increased risk of comorbid psychopathology in children with AS has been linked to their greater likelihood of attending mainstream school, their disadvantages such as being bullied and having less social support than typically developing children, low-quality social relationships, and poor socialization skills; and these are often associated with increased psychiatric comorbidities such as conduct problems, anxiety and depression (8,12,21). Children and adolescents with AS may exhibit serious psychiatric breakdowns even in mild-stress situations and experience distress and anxiety as a result of even the slightest changes in their environment. In such cases, the likelihood of secondary psychological problems is high (8,12,21). In our study, we determined that 91.2% of the sample have comorbid psychiatric disorders, 14.7% of them have a single psychiatric disorder, and 76.5% have at least two psychiatric disorders.

The most common comorbid psychiatric diagnoses we found were anxiety disorders (67.6%), ADHD (64.7%), OCD (29.4%) and depression (29.4%). When the literature data on the subject is examined, it is seen that our findings are compatible with the results of previous studies. A study of children with high-functioning autism (HFA) and AS found that 44.2% of the sample had at least one comorbid psychiatric disorder, and the most common comorbid diagnosis was ADHD (12). Other comorbid psychiatric diagnoses are depression, bipolar disorder, generalized anxiety disorder (GAD), positive psychotic symptoms, learning disability, OCD, eating disorders, ODD, tics, and Tourette's syndrome (12). Another study screening for comorbid psychiatric disorders in children with ASD yielded that 70% of the sample had at least one comorbid disorder and 41% had two or more comorbid disorders (11). In the same study, the most common comorbid psychiatric diagnoses were found to be social phobia (29.2%), ADHD (28.2%), and ODD (28.1%), and a second comorbid diagnosis was found in 84% of those with ADHD comorbidity (11). Again, another study showed the rate of psychiatric comorbidity as 74% in children and adolescents with AS and HFA, and the rate of more than one comorbid psychiatric disorder was also high (14). The researchers revealed that 44% of the sample had behavioral disorders, 42% had anxiety disorders, and 26% had tic disorders (14). The same study showed that comorbidity of ODD, major depressive disorder, and anxiety disorders was associated with significantly worse levels of functioning and highlighted the importance of routinely assessing psychiatric comorbidity in these patients to target therapies (14). In a study examining the rate and type of comorbid psychiatric disorders in children and adolescents with HFA and AS, a very high rate of comorbid psychiatric disorders was found, 100% in the AS group and 93.3% in the HFA group, and the most common comorbid diagnosis was reported to be ADHD (13).

None of the participants in this study had PTSD, panic disorder, eating disorders, alcohol or substance use, bipolar disorder, or psychotic disorders. Bipolar disorder has also been reported as a comorbidity in ASD, especially in adolescence, although not as frequently as depression (8,9,12,22,23). However, it has been emphasized that the rates reported for bipolar disorder are very high and that the developmental characteristics of autism can be confused with symptoms of mania. It has been stated that the enthusiastic and long-winded conversations and mental preoccupations of individuals with ASD regarding their own special interests can be confused with symptoms of hypomania (22,23). As for psychotic disorders, although some studies have identified psychotic disorders as a comorbid diagnosis in children and adolescents with AS (24-26), some studies have not identified psychotic disorders as comorbidity, consistent with our results (27,28). Inconsistent results may be due to methodological differences across studies. In addition, considering that both bipolar disorder and psychotic disorders are often diagnosed in late adolescence or young adulthood, symptoms suggestive of bipolar disorder and psychotic disorders may not have started yet in our cases, and this finding may be related to the age group of our sample. There are also studies in the literature showing the association of eating disorders with AS (29,30), and the fact that eating disorders were not detected in our study may be related to the small sample size. None of our participants had panic disorder. This result is consistent with the studies that detected panic disorder in this population at least or not at all (28,31). Similarly, we did not detect alcohol or substance use in our sample, consistent with studies showing that alcohol or substance use is quite rare in individuals with AS (31) and this finding can also be attributed to the age group of our sample.

It is unclear what factors increase a child's chance of developing comorbid mental health disorders if they have Asperger syndrome. Nonetheless, previous studies have emphasized the importance of psychiatrists assessing psychiatric comorbidity in children and adolescents with AS, since in these children, additional psychiatric disorders can create significant distress for both the child and the family and further impair quality of life (7,9,10,12). These comorbid psychiatric conditions may also lead to loss of functionality and increased morbidity and mortality rates, decreased compliance with treatment, increased risk of drug interactions due to multiple drug use, increased likelihood of medical complications, and increased healthcare costs (7,9,10,12,14-16,32). However, the diagnosis of psychiatric comorbidity in AS patients can be very challenging, since these children may have difficulties processing and identifying their own emotions and feelings (6,8,10,32,33). Indeed, although AS children have better verbal expressions than children with ASD, their verbal expressions are still inadequate compared to their typically developing peers, their empathy skills are limited, and their ability to recognize and express their own emotions is weak (1-7). These difficulties make it difficult for children with AS to define and describe their own mental states and the situations they have difficulty with in daily life (1,8,12). Furthermore, comorbid psychiatric symptoms in children with AS may occur atypically compared to the general population and may be masked by the core symptoms of AS (12). Add to these difficulties the confusion regarding diagnostic criteria and the lack of diagnostic tools to assess comorbid psychiatric problems specific to these individuals, it is quite difficult to identify and recognize comorbid psychiatric problems in AS and they may be overlooked in the clinical setting (1,8,12). Despite self-report questionnaires, checklists, and clinical interviews being helpful diagnostic aids in clinical settings, they may not always be suitable for AS because most of these tools are geared toward identifying psychopathological symptoms in the general population (8). Therefore, just as the validity of these tools needs to be tested in individuals with AS, their application may also be problematic in individuals with AS due to their lack of ability

to maintain a reciprocal conversation, talk about themselves, convey events, and understand and empathize with other people's feelings. All these problems make it more difficult to evaluate responses correctly, which misinterprets the genuine nature of comorbidity symptoms (8,12). In addition, there is debate over whether comorbid psychiatric conditions are part of the basic symptoms of AS and overlap or whether they should be considered a separate disorder added to AS. Thus, one of the most common difficulties in assessing psychiatric comorbidity is deciding whether symptoms are a manifestation of AS itself or are symptoms representing a concomitant psychiatric disorder (8,12,21,33). The primary reason for this is that the core symptoms of AS frequently obscure the symptoms of the comorbid disorder(s) (8). Sometimes symptoms of comorbid psychiatric conditions are severe enough to be the main reason for clinical presentation and determine the main goals of treatment. On the other hand, it has also been suggested that the lines separating core AS symptoms from comorbid psychiatric symptoms may become blurred and that AS-specific symptoms may disguise signs of comorbid psychopathologies (8,12,21,33). Therefore, it is underlined that when diagnosing comorbid psychiatric conditions in children and adolescents with AS, it would be healthier to gather clinical information primarily from family members or by closely observing people in their social environment, rather than collecting it directly from children with AS (8,12,21,33).

On the other hand, it is also known that AS, which has milder core symptoms, is far less recognized and diagnosed. Therefore, children with AS may present to the clinic with other psychiatric symptoms that do not clearly suggest the presence of AS (21,34). In this situation, early detection of AS can often be difficult since AS symptoms can be masked or confused with those of other psychiatric disorders (12,21,34).

In this study, when we compared the existing comorbid psychopathologies according to age groups, we determined that the frequency of having at least two comorbid psychiatric disorders was significantly higher in the adolescent group than in the child age group. Consistent with our results, although certain types of comorbidities affect every age group in AS, it has been discovered that adolescence is the age group with the highest prevalence of psychiatric comorbidity, and the prevalence of multiple comorbidities increases in adolescence (7,12,14). Possible reasons for our result include increased social expectations during adolescence, individuals with AS becoming more aware of their own inadequacies, social withdrawal, and poor communication skills (7,35). Because adolescence is a period when peer relationships become increasingly important and social and emotional expectations rise, adolescents with AS may experience extreme distress and withdraw from the social world due to the expectation of complex social skills (35,36). Especially during this period, their awareness of being different from their peer increases (1,2,5-7). In addition, adolescents with AS will most likely have more negative social experiences, which will make the adolescents with AS more vulnerable, have lower self-esteem, and increase the risk of psychopathology (5,33). There was no significant difference in the rates of comorbid ADHD, ODD, any anxiety disorder, GAD, tic disorders, and encopresis between age groups, in our study. However, comorbid CD, specific phobia, separation anxiety disorder, and enuresis were significantly higher in the childhood age group, while comorbid social phobia, OCD, and depression were significantly higher in the adolescent group. Previous studies have also found that ADHD and disruptive behavior disorders are the most common comorbid diagnoses in the pre-pubertal period, while mood disorders are more common in adolescence (7,12). In the present study, among anxiety disorders, specific phobia and separation anxiety disorder were significantly more frequently comorbid diagnoses in the childhood age group, while social phobia was significantly more frequent in the adolescent group. This situation can be explained by the fact that specific phobia and separation anxiety disorder decrease developmentally with age, while social phobia becomes more evident in adolescence. A study of adolescents with AS/HFA revealed that social anxiety increases with age in the HFA/AS group, while behavioral avoidance decreases with age in the control group. Especially, those who were active-odd in childhood may develop social phobia in adolescence (35,37).

There are several limitations of this study. The important limitations of the study are the moderate sample size, the lack of a comparison group, the fact that psychiatric diagnoses were not made through a semi-structured diagnostic interview, and the retrospective nature of the study. These limitations prevent our results from being generalized and revealing a cause-effect relationship. Despite these limitations, the present study makes important contributions to expanding the literature by providing data on the frequency and type of comorbid psychiatric conditions in children and adolescents with AS. To enhance our understanding of psychiatric comorbidities in AS, future research should focus on: (1) Prospective Studies: Longitudinal studies with larger sample sizes are needed to monitor the development and progression of psychiatric comorbidities in individuals with AS over time; (2) Diagnostic Tools: Developing and validating assessment tools specifically designed for individuals with AS will improve the accuracy of diagnosing comorbid psychiatric conditions; (3) Intervention Efficacy: Evaluating the effectiveness of tailored intervention programs in reducing psychiatric comorbidities and enhancing functional outcomes in AS populations is crucial. Addressing these areas will contribute to more effective management strategies and better quality of life for individuals with AS.

Clinical Implications and Early Intervention

The high rate of psychiatric comorbidities in individuals with AS necessitates early identification and tailored interventions. Clinicians should conduct thorough assessments to detect comorbid conditions promptly, facilitating timely and appropriate treatment strategies. Intervention programs

should address basic social and communication skills (with a focus on pragmatic communication), adaptive functioning, and academic or vocational skills, while ensuring that learned skills generalize to naturalistic environments. Early intervention can mitigate the impact of comorbid psychiatric conditions, improving the overall quality of life for individuals with AS. Implementing appropriate interventions based on individual needs, considering social skills training, cognitive-behavioral therapy, and other evidence-based approaches, is essential.

Conclusion

Our findings indicated that comorbid psychiatric disorders are common and often multiple in children and adolescents with AS, and knowing this may provide targets for intervention and that psychiatric comorbidity should be routinely assessed in the clinical evaluation of this group. Routine screening for common psychiatric comorbidities such as anxiety disorders, ADHD, and depression should be included in regular evaluations of children and adolescents with AS. Utilizing standardized tools like the Child Behavior Checklist (CBCL) can aid in the early detection of these conditions. Early identification and intervention for these comorbid conditions are crucial, as they can significantly improve the child's daily functioning and overall quality of life. Research in this area will also be important for preventive mental health services. However, especially considering the relative decrease in interest in this topic in recent years, longitudinal studies are necessary to draw definitive conclusions about whether children with AS have an increased risk of developing psychiatric disorders or whether they have a constitutional predisposition in this regard.

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