PREVALENCE OF ATTENTION-DEFICIT/HYPERACTIVITY DISORDER, OPPOSITIONAL DEFIANT DISORDER AND CONDUCT DISORDER IN CHILDREN WITH AUTISM SPECTRUM DISORDER

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ABSTRACT | Aim: To estimate the prevalence of attention-deficit/hyperactivity disorder (ADHD), oppositional defiant disorder (ODD) and conduct disorder (CD) in children and adolescents previously diagnosed with autism spectrum disorder (ASD). **Methods:** A cross-sectional study involving 71 children and adolescents previously diagnosed by a psychiatrist as having ASD. All were enrolled at a school that accompanies only individuals with ASD. The evaluation instruments consisted of a sociodemographic questionnaire and the Brazilian version of the semi-structured interview Kiddie-SADS-PL for the investigation of psychiatric disorders in children and adolescents. **Results:** Overall, 62% of the children in the sample had some psychiatric comorbidity: 49.3% had some form of ADHD, 11.3% ODD and 1.4% CD. In relation to the children with ADHD, 11.3% fulfilled the criteria for the inattentive subtype, 12.7% for the hyperactive/impulsive subtype, 7.1% for the combined subtype and 18.3% for ADHD not otherwise specified. **Conclusion:** These results ratify the clinical heterogeneity of ASD and highlight the importance of diagnosing comorbidities that could affect the clinical status and functioning level of children and adolescents with ASD.

Keywords: attention deficit; autism; comorbidities; hyperactivity; oppositional behavior

INTRODUCTION

Autism spectrum disorder (ASD) affects 0.6 to 1% of the population worldwide, constituting an important public health issue[1]. ASD has an early onset and its symptoms and associated functional impairment persist throughout the individual's life[1]. According to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), ASD consists of persistent deficits in social communication and social interaction across multiple contexts associated with restricted patterns of behavior, interests or activities, with the severity of symptoms being categorized into three levels: mild, moderate and severe[2]. In addition to the symptoms that characterize autism, there are overlapping signs and symptoms of other psychiatric disorders[3-5], which also account for the clinical heterogeneity of ASD. The coexistence of comorbidities may have important consequences and may result in disadvantages insofar as prognosis is concerned, both in relation to adaptive functioning and with regards to the quality of life of these children and adolescents and their families[3,4,6,7].

Studies conducted with school-aged children and adolescents[1,8,9] and with preschoolers[10] with ASD indicate a high prevalence of other comorbid psychiatric disorders. Of the psychiatric disorders present in children with ASD, attention-deficit/hyperactivity disorder (ADHD) is the most notable, with a prevalence of up to 50%[3,4,7,10-14]. Both the prevalence and severity of the symptoms of ADHD, oppositional defiant disorder (ODD) and anxiety disorder were greater in preschoolers compared to a group of schoolchildren and adolescents[15]. The instruments used by those authors were based on the diagnostic criteria defined in the Diagnostic and Statistical Manual of Mental Disorders, 4th edition, text revision (DSM-IV-TR).

Oppositional defiant disorder (ODD) and conduct disorder (CD) are also commonly associated with children with ASD. Using the criteria outlined in the International Classification of Diseases, revision 10 (ICD-10), Simonoff et al. estimated prevalence rates of 28% for ODD and 3.2% for CD in children with ASD1. Kanne et al. used the Child Behavior Checklist (CBCL) to evaluate the occurrence of psychiatric syndromes in a well-characterized sample of young people with autism spectrum disorder, reporting prevalence rates of 16% for ODD and 15% for CD[16]. In younger children (3-5 years of age), the prevalence of symptoms of ODD, estimated using a questionnaire completed by the parents, was 13%; however, when their teachers completed the same questionnaire this prevalence was 21%. In the case of older children (6-12 years of age), the estimated prevalence of ODD was 27% when the parents completed the instrument and 25% when the teachers completed it[15].

Different studies have reported a high prevalence of comorbid symptoms in children and adolescents with a diagnosis of ASD; however, reports on the prevalence of these comorbidities have differed, indicating substantial variability, not only as a function of the evaluation instrument used but possibly also indicating differences that may depend on the sample studied. Therefore, psychiatric disorders are common and numerous in children with autism spectrum disorders and it is important to identify them to enable appropriate interventions to be implemented[16,17]. The objective of this study was to estimate the prevalence of comorbidities in ASD, specifically with respect to the symptoms of ADHD, ODD and CD in children and adolescents with ASD in a special school located in the city of Salvador, Bahia, Brazil. It is hypothesized that children attending special schools, rather than regular schools, have a disorder with more severe behavioral symptoms. Thus, the objective of this study is to estimate the prevalence of comorbidities in autistic children that possibly has a symptomatic profile with greater impairment in relation to social adaptation.

PATIENTS AND METHODS

Sample selection

A cross-sectional cohort study was conducted using a questionnaire completed by parents to estimate the prevalence of symptoms of ADHD, ODD and CD in children and adolescents with a diagnosis of

ASD. The target population consisted of children enrolled in a school that serves only individuals with ASD. The school works with an individualized pedagogical plan, and each student is accompanied by a teacher, individually. Of 115 children enrolled at the school, 94 were invited to participate in the study; however, in 23 cases the parents declined the invitation. Therefore, the final sample consisted of 71 children. Data were collected between October 1, 2012 and April 31, 2013. The internal review board of the Bahia School of Medicine and Public Health approved the study protocol under reference number 109.380 on September 11, 2012 (CAAE 03886812.8.0000.5544). All the participants of the study were provided with verbal and written information on the study objectives and all signed an informed consent form.

Instruments

Two data collection instruments were used: a questionnaire designed to collect sociodemographic data and the Brazilian version of the Kiddie-SADS-PL semi-structured interview18. This interview consists of semi-structured questions based on the DSM-IV and is used to estimate the prevalence of psychiatric disorders in children, both currently and in the past. The sub-scales of conduct disorder, oppositional defiant disorder and attention-deficit/hyperactivity disorder were investigated. A screening interview, conducted by two previously trained medical students, was held with the mothers of all the children included in the sample. The supplementary questionnaires were applied to the mothers according to the results of the screening interview.

Agreement between the two investigators who collected the data was tested to avoid interview bias. For this, both investigators applied all the instruments to ten participants and the level of agreement between them was verified using Kendall's tau-c test. In the three sub-scales, agreement was poor in only three items, one in the ADHD scale and two in the CD scale. In addition, there was a lack of agreement for one item in the CD scale. To correct the distortion, the items were adjusted to ensure that both interviewers used the same command.

Data Analysis

A database was created and analyzed using the Statistical Package for the Social Sciences (SPSS®, version 17.0). Pearson's chi-square test was used to analyze the association between each variable and the outcome.

RESULTS

The number of individuals included in the study (n=71) corresponded to 61.7% of the total number of children enrolled at the school at the time of data collection. All the children included had been previously diagnosed with autism spectrum disorder according to the ICD-10 and DSM-IV-TR. The mean age of the children was 9.6 years, with 38% being between 3 and 6 years of age and 62% being over 7 years of age. Of the total sample, 88.7% were male and 11.3% female. The majority (73.2%) started walking at the appropriate age (≤ 18 months) and 49.3% first started talking prior to completing 18 months of age. Sphincter control was achieved after 36 months of age in 52.1% of the children. In 90.1% of the sample, ASD was first suspected when the child was already over 25 months of age, with 52.1% having received a definitive diagnosis after 37 months of age. Overall, 71.8% of the children were reported to be in use of medication, with the most commonly used drug being risperidone. In relation to therapeutic interventions, all the children in the study were attending a special school and 60.6% also participated in other activities such as regular school, occupational therapy, speech therapy, etc. (Table 1).

Table 1. Description of the individuals in the sample according to their sociodemographic and developmental characteristics

Variables	n	%
Sex		
Male	62	87.3
Female	9	12.7
Child's age		
3-6 years	27	38
≥ 7 years	44	62
Father's age*		
≤ 39 years	60	84.5
≥ 40 years	11	15.5
Mother's age*		
≤ 34 years	57	80.3
≥ 35 years	14	19.7
Age at first steps		
Appropriate (≤ 18 months)	52	73.2
Late (≥19 months)	19	26.8
Age at first words		
Appropriate (5-18 months)	35	49.3
Late (≥ 19-72 months)	26	36.6
Age at suspicion of autism		
Appropriate (≤ 24 months)	6	8.5
Late (≥ 25 months)	65	91.5
Age at diagnosis		
Early (≤ 36 months)	29	40.8
Late (≥ 37 months)	37	52.1
In use of medication		
No	20	28.2
Yes	51	71.8
Therapeutic interventions		
Only special school	28	39.4
Other activities	43	60.6

n = total number of participants. * Parent's age at the time of the child's birth.

The mean age of the mothers at the time of the child's birth was 28 ± 6.1 years (mean ± standard deviation) (range 17-44 years). The mean age of the fathers at the child's birth was 32 ± 7.2 years (range 21-55 years). Most the fathers (84.5%) were under 39 years of age at the time of their child's birth, while 80.3% of the mothers were aged ≤ 34 years. Mean family income was 3 ± 2.8 minimum salaries (range 2-4 minimum salaries).

Based on the results from the Kiddie-SADS-PL we estimate that 62% of the population evaluated in this study had other coexisting disorders in addition to ASD. The estimated prevalence of ADHD was 49.3%, with 11.3% having the inattentive subtype, 12.7% the hyperactive/impulsive subtype, 7.1% the combined subtype and 18.3% having ADHD not otherwise specified, which includes all individuals with symptoms of ADHD below the cut-off limit for classification as one of the other subtypes (Table 2). Symptoms suggestive of oppositional defiant disorder were identified in 11.3% of the sample, while symptoms suggestive of conduct disorder were found in 1.4% (Table 2).

Table 2. Prevalence of coexisting comorbidities with autism spectrum disorder

Variables	n	%
ADHD	35	49.3
Inattentive	8	11.3
Hyperactive/impulsive	9	12.7
Combined	5	7.1
Not otherwise specified	13	18.3
ODD	8	11.3
CD	1	1.4

n = total number of participants. ADHD: Attention-deficit/hyperactivity disorder; ODD: Oppositional defiant disorder; CD: Conduct disorder.

We sought to analyze whether comorbidities were more frequent according to differences in socio-demographic covariables or child developmental milestones listed in Table 1. For this purpose, the prevalence of comorbidities was stratified according to each covariable, considering that there was a significant difference when the value of p estimated was <0.05. The results show the distribution of the comorbidities to be similar in the children in the 3-6-year age group and in those over 7 years of age. The parents' age at their child's birth had no statistically significant effect on the prevalence of comorbidities nor did the age at which the child started walking or speaking, the age at which ASD was first suspected, the age at which diagnosis was confirmed, the age at which sphincter control was achieved, therapeutic interventions or family income. In addition, there was no statistically significant association with the sex of the child, although the prevalence of all the comorbidities was slightly higher in males. When all the subtypes of ADHD were analyzed together rather than analyzing each subtype separately, the prevalence of the disorder was higher in the boys than in the girls, with this difference being statistically significant (46.8% versus 11.1%; p<0.05). The use of medication was more common in the children with

the hyperactive/impulsive subtype of ADHD compared to those without this comorbidity (23.5% versus 5%). Although this difference was not statistically significant (p<0.09), there would appear to be a trend.

DISCUSSION

These results confirm that other psychiatric disorders frequently coexist with autism, since indication for at least one coexisting psychiatric disorder was found in 62% of the sample. These findings are consistent with the results of other studies: Mattila et al. reported a prevalence rate of 74% for comorbidities of ASD (3); Siminoff et al. 70.8%[1] and Gjevik et al. 72%[4].

The prevalence of cases suggestive of ADHD in this study was 49.3%, a figure that is in agreement with the findings of previous studies conducted using similar evaluation instruments. Ghanizadeh found that 54% of a clinic-based sample of autistic patients fulfilled the DSM-IV criteria for ADHD[14]. In a previous study conducted with the same target population as the present study and using the same evaluation instrument, the prevalence of symptoms of ADHD in children with ASD was found to be 53%[13]. A lower prevalence rate (28.2%) was reported in a study conducted with a population-based sample[1]. The different figures suggest that the prevalence of ADHD in patients with ASD may vary as a function of the recruitment source (clinic-based samples, children enrolled in a special school or population-based samples).

In relation to symptoms for the subtypes of ADHD, 11.3% fulfilled the criteria for the inattentive subtype, 12.7% for the hyperactive subtype, 7.1% for the combined subtype and 18.3% for ADHD not otherwise specified. These figures vary in the different studies published. Pondé et al. reported a rate of 5.8% for the inattentive subtype[13], while Gjevik et al. reported a rate of 21%[4] and Ghanizadeh 19.1%[14]. For the hyperactive subtype, the reported prevalence rates were 31.2% in the study conducted by Pondé et al. 13, 6% by Gjevik et al. 4 and 11.8% by Ghanizadeh[14]. The combined subtype had a prevalence of 18.7% in the study carried out by Pondé et al.13, 4% by Gjevik et al.[4] and 20.6% by Ghanizadeh[14]. In relation to symptoms of ODD, the prevalence of 11.3% found in the present study is lower than the rate of 28% found in a population-based study conducted in England1 and higher than the rate of 4% reported in a study conducted in Norway with a population of children enrolled in a special school4. The large variations in the prevalence rates of the subtypes of ADHD and ODD in the different populations evaluated probably reflect the diversity of clinical phenotypes of ASD as a function of the population evaluated. It could also reflect different methodologies used to establish the diagnosis.

The prevalence of symptoms suggestive of conduct disorder in this study was 1.4%. Previous studies have also reported low prevalence rates for this disorder: Gjevik et al. 2.8%[4] and Simonoff et al. 3.2%[1].

In the present study, a high rate of medicalization was found (71.8%), which is in agreement with reports in the literature indicating that 50% to 75% of the population with ASD had been prescribed some form of medication, with 45-56% having been prescribed at least one psychotropic drug[19,20]. There was a greater tendency to prescribe psychotropic medication for children with the hyperactive/impulsive subtype, with risperidone being the most commonly prescribed drug. This result may reflect the fact that the scientific literature indicates the use of risperidone for the control of behavioral disorders in children with ASD[21,22].

LIMITATIONS

The Kiddie-SADS-PL consists of an interview conducted with parents to identify their child's symptoms; hence, it is not a direct clinical evaluation of the child. In addition, since the sample evaluated consisted of children enrolled in a special school for

ASD children, those with milder symptoms enrolled in regular schools were not included in the present evaluation. Thus, the results of this study cannot be generalized to data from individuals in the community.

CONCLUSION

Children and adolescents with ASD are and should be considered different from each other, with each one presenting with a unique range of symptoms and characteristics3. This study used a standardized questionnaire to estimate the prevalence of current psychiatric comorbidities in a population of children and adolescents with ASD attending a special school. A high prevalence of associated disorders was found, particularly ADHD and ODD. The importance of diagnosing comorbidities that could affect the clinical status of children and adolescents with ASD as well as their functioning should be emphasized. Further studies are required to analyze possible causal relationships between environmental factors and behaviors.

AUTHOR CONTRIBUTIONS

Matos ML was responsible for data collection, dataset construction and lierature review. Pires CCPBO was responsible for data collection, dataset construction and writing. Ponde MP was responsible for data collection, children assessment, equip training and supervision, writing and critical review of the manuscript.

COMPETING INTERESTS

No financial, legal or political competing interests with third parties (government, commercial, private foundation, etc.) were disclosed for any aspect of the submitted work (including but not limited to grants, data monitoring board, study design, manuscript preparation, statistical analysis, etc.).

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