Journal of Advances in Medicine and Medical Research

33(9): 53-62, 2021; Article no.JAMMR.67319
ISSN: 2456-8899
(Past name: British Journal of Medicine and Medical Research, Past ISSN: 2231-0614, NLM ID: 101570965)

Psychiatric Co-Morbidities in Children with Autistic Spectrum Disorder

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2021/v33i930898
Editor(s):
(1) Dr. Nicolas Padilla-Raygoza, University of Celaya. Mexico.
Reviewers:
(1) Nikoletta Mavroeidi, Greece.
(2) Cristina Panisi, Italy.
(3) Maria Malmsten, Kristianstad University, Sweden.
Complete Peer review History: http://www.sdiarticle4.com/review-history/67319

Original Research Article

Received 06 February 2021
Accepted 12 April 2021
Published 20 April 2021

ABSTRACT

Background: Autistic Spectrum Disorder (ASD) is considered a neurodevelopmental disorder, characterized by causing marked decrease in social interaction and communication, conversation skills. The aim of this work was to explore the psychiatric co-morbidities among children with ASD.
Methods: This cross-sectional, descriptive study was carried out 55 children less than 18 years old fulfilled criteria for ASD. All patients were subjected to: Psychiatric interviewing and Psychometric tests that included Stanford-Binet test 5th edition, Arabic version of Kiddie Schedule for Affective Disorders and Schizophrenia "K-SADS, Arabic version of Childhood Autism Rating Scale (CARS), Arabic version of Conner's Scale for ADHD and Arabic version of Screen for Child Anxiety Related Disorders (SCARED) (Child and parent versions).
Results: The majority of the studied ASD children were males younger than 13 years old, from rural areas, with mild and moderate intellectual disability, and with severe ASD symptoms. There is statistically significant difference between severity of ASD in studied children measured by CARS, and number of co-morbidities. The most prevalent psychiatric co-morbidities among studied ASD children were anxiety disorders (41.82%), followed by ADHD (36.36%).

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There is statistically significant difference between severe form of ASD and psychiatric co-morbidities regarding ADHD, Tic disorder, ODD and elimination disorder, While Social anxiety and GAD were more common among children with milder forms. Among the studied children, the specific phobias, ODD and elimination disorders, were more in younger age groups. While social anxiety and psychotic disorders occurred more frequently with older age groups. GAD, somatization and depression were more frequent with females, while ADHD occurred more with males.

Conclusion: Presence of comorbid disorders among children with ASD is the rule rather than exception. Male children had more combined subtype and more severe form of the disorder. The most common comorbid psychiatric disorders with ASD are anxiety disorders and ADHD. The early identification and treatment of ASD and comorbid conditions may reduce the likelihood of impairment and persistence into adulthood.

Keywords: Psychiatric co-morbidities; children; autistic spectrum disorder.

1. INTRODUCTION

Autistic Spectrum Disorder (ASD) is considered a neurodevelopmental disorder. It is a life-long disorder characterized by causing a marked decrease in social interaction and communication, whether verbal or non-verbal, interpersonal interaction, conversation skills. These deficits are mostly significant and persistent, leading to failure of developing relationships at the appropriate developmental level. It is also characterized by stereotypy in motor or verbal behavior, or unusual sensory behavior, whether increased sensitivity (over responsiveness) or decreased sensitivity (under responsiveness) to different stimuli. In addition to, restricted, and fixed interests, excessive adherence to routine, repetitive and ritualized pattern of behavior [1].

Psychiatric symptoms and behavioral disorders are frequently documented in people with ASD: about two-thirds of them are indeed reported to have at least one associated mental health condition. Although in the past, psychiatric symptoms in children and adults with ASD have been attributed to ASD itself, a phenomenon referred to as diagnostic overshadowing, an increasing number of reports suggest that additional behavior disorders in people with ASD potentially indicate the presence of psychiatric and behavioral co-morbidities and demand an additional diagnosis [2].

In the field of ASD, acceptance and help-seeking behavior led to a more positive outcome. Indeed, diagnosis and early intervention before emotional, behavioral, and social problems are firmly ingrained have significant benefits for parental mental health, such as maximizing family acceptance and adjustment to their child's disability, and an impact on child functioning [3].

Autism is a lifelong disability that needs continuous treatment and education in residential settings. Thus, studying comorbid conditions of ASD is very essential in helping to reach perfect diagnosis and management [4].

The aim of this work was to explore the psychiatric co-morbidities among children with ASD and identify risk factors to improve the outcome, to adapt the treatment.

2. SUBJECTS AND METHODS

Patients were recruited prospectively from those attending the outpatient clinic of the child and adolescent psychiatry unit at Tanta Psychiatry, Neurology and Neurosurgery Center. The attending children with ASD aging under 18 years, from both genders, fulfilling inclusion criteria and not having exclusion criteria were included in the study and they were 55 ASD children out of total 668 psychiatric children after a written consent was obtained from the care giver of the children who attempted the study after explanation of the study and its aim.

Inclusion Criteria:

1. Age was under 18 years old.
2. Children fulfilled criteria for ASD according to DSM-5.

Exclusion Criteria:

Patients with any medical disease that affect cognitive function: renal, hepatic, thyroid, neurological disease, diabetes mellitus, etc.

All patients were subjected to:

A) Psychiatric history and examination using DSM-V Criteria
B) Psychometric tests:

- Stanford-Binet test 5th edition: To assess Intelligence.
- Arabic version of Kiddie Schedule for Affective Disorders and Schizophrenia "K-SADS. Based on DSM-Ⅳ criteria.
- Arabic version of Childhood Autism Rating Scale (CARS).
- Arabic version of Conner's Scale for ADHD (Parent and teacher edition):to assess severity of ADHD.
- Arabic Version of Screen for Child Anxiety Related Disorders (SCARED) (Child version), Arabic Version of Screen for Child Anxiety Related Disorders (SCARED) (Parent about child version).

Statistical analysis: The collected data were statistically analyzed by SPSS version 20 (IBM, Chicago, Illinois, USA). For numerical variables the mean and standard deviation were calculated and were compared by student "t test". For categorical variables, the number and percentage were calculated, and chi square or Fisher's exact test was used for data analysis. All tests of statistical significance were adopted at $p<0.05$.

3. RESULTS

This study included 55 children diagnosed with ASD. The age of the studied children ranged from 6 – 17 years, out of them (38.18%) were ≥13 years and (61.82%) were younger than 13 years. The majority of children were males (87.27%) and were from rural areas (52.73%). Regarding IQ assessment, 20% of the children presented by Average IQ, 9.09% had Borderline intellectual disability, 36.36% and 34.55% with Mild and Moderate ID respectively. Most of the studied children in this study were severe ASD according to CARS scale, representing 41.82% (Table 1).

Regarding age groups and residence, there was no statistically significant difference between the two age groups regarding the severity of ASD assessed by CARS. (P value > 0.05). While regarding gender, most of females were noticed to have mild severity of ASD, but no statistically significant difference between both regarding severity.

There was a statistically significant difference between severity of ASD in studied children measured by CARS, and number of co-morbidities was positively and significantly correlated to the severity of ASD (p value = 0.001), as the sever type showed more numbers of psychiatric co-morbidities (Table 2).

There was statistically significant difference between severity of ASD measured by CARS and psychiatric co-morbidities (p value less than 0.05) regarding ADHD, Tic disorder, ODD and elimination disorder are positively and significantly correlated with the severity of ASD, as they were more common among children with higher severity of ASD. While Social anxiety and

Table 1. Sociodemographic characteristics, intelligence quotient (IQ) assessment, severity of ASD of ASD sample (n = 55)

		N	%
Age group	**<13 Years**	34	61.82
	>13 Years	21	38.18
Gender	**Male**	48	87.27
	Female	7	12.73
Residence	**Urban**	26	47.27
	Rural	29	52.73
Intelligence quotient (IQ) assessment according to Stanford–Binet Intelligence Scale (5th edition)	**Average (80-110)**	11	20.00
	Borderline (70-79)	5	9.09
	Mild (55-69)	20	36.36
	Moderate (35-54)	19	34.55
Severity of ASD according to CARS Scale	**Average (80-110)**	11	20.00
	Borderline (70-79)	5	9.09
	Mild (55-69)	20	36.36
	Moderate (35-54)	19	34.55

IQ: Intelligence quotient

GAD were more common among children with milder forms of ASD. Other psychiatric co-morbidities show no significant difference (Table 3).

There was statistically significant difference between age groups regarding Specific phobias, ODD and elimination disorders, which occurred more frequently with younger age group (less than 13 years). While social anxiety and psychotic disorders occurred more frequently with older age groups. (older than 13 years old). Other psychiatric co-morbidities show no significant difference (Table 4).

There was statistically significant difference between gender and psychiatric co-morbidities as GAD, somatization and depression which occurred more frequently with female ASD children. While ADHD occurred more with males (P value < 0.05). Other psychiatric co-morbidities show no statistically significant difference (Table 5).

There was no statistically significant difference between severity of ASD in ASD children with comorbid ADHD and the severity of their ADHD (P value > 0.05). While there was statically significant difference between occurrence of certain co-morbidities as ADHD, ODD and severity of ASD as measured by CARS, they tend to occur more frequently with severe cases of ASD (P value < 0.05).

Table 2. Relationship between severity of ASD measured by CARS and number of psychiatric co-morbidities

No of co-morbidity	CARS								Chi-Square	
	Mild		Moderate		Severe		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
No	6	42.86	0	0.00	0	0.00	6	10.91	39.822	<0.001*
One	3	21.43	2	11.11	0	0.00	5	9.09		
Two	5	35.71	9	50.00	4	17.39	18	32.73		
Three	0	0.00	5	27.78	9	39.13	14	25.45		
Four	0	0.00	2	11.11	9	39.13	11	20.00		
Five	0	0.00	0	0.00	1	4.35	1	1.82		
Total	14	100.00	18	100.00	23	100.00	55	100.00		

Table 3. Relationship between severity of ASD measured by CARS and psychiatric co-morbidities

KSADS	CARS								Chi-Square	
	Mild		Moderate		Severe		Total			
	N	%	N	%	N	%	N	%	X^2	P-value
Anxiety disorders	8	57.14	7	38.89	8	34.78	23	41.82	1.883	0.390
K-SADS - ADHD	0	0.00	3	16.67	17	73.91	20	36.36	25.032	<0.001*
Tic disorder	0	0.00	9	50.00	10	43.48	19	34.55	10.102	0.006*
OCD	5	35.71	6	33.33	7	30.43	18	32.73	0.115	0.944
Specific phobias	3	21.43	3	16.67	7	30.43	13	23.64	1.111	0.574
Oppositional defiant disorders	0	0.00	3	16.67	7	30.43	10	18.18	7.668	0.022*
Depression	3	21.43	2	11.11	1	4.35	6	10.91	2.614	0.271
Elimination disorder	0	0.00	0	0.00	5	21.74	5	9.09	7.652	0.022*
Social anxiety/phobia	5	35.71	0	0.00	0	0.00	5	9.09	16.107	<0.001*
Somatization/psychosomatic	2	14.29	1	5.56	0	0.00	3	5.45	3.444	0.179
Conduct disorders	0	0.00	1	5.56	1	4.35	2	3.64	0.751	0.687
Psychotic disorders	0	0.00	0	0.00	2	8.70	2	3.64	2.888	0.236
GAD	2	14.29	0	0.00	0	0.00	2	3.64	6.078	0.048*

*CARS: Childhood Autism Rating Scale (Arabic version), GAD: * significant as P value <0.05*

Table 4. Distribution of co-morbidities according to age groups

		Age group						Chi-Square	
		<13 years		>13 years		Total			
		N	%	N	%	N	%	X^2	P-value
KSADS	Anxiety disorders	13	38.24	10	47.62	23	41.82	0.470	0.493
	ADHD	10	29.41	10	47.62	20	36.36	1.860	0.173
	Tic disorder	12	35.29	7	33.33	19	34.55	0.022	0.882
	OCD	8	23.53	10	47.62	18	32.73	3.422	0.064
	Specific phobias	13	38.24	0	0.00	13	23.64	10.515	0.001*
	Oppositional defiant disorders	10	29.41	0	0.00	10	18.18	7.549	0.006*
	Depression	3	8.82	3	14.29	6	10.91	0.399	0.528
	Elimination disorder	5	14.71	0	0.00	5	9.09	5.115	0.024*
	Social anxiety/phobia	0	0.00	5	23.81	5	9.09	8.905	0.003*
	Somatization/psychosomatic	1	2.94	2	9.52	3	5.45	1.091	0.296
	Conduct disorders	2	5.88	0	0.00	2	3.64	1.282	0.258
	Psychotic disorders	0	0.00	2	9.52	2	3.64	3.974	0.046*
	GAD	1	2.94	1	4.76	2	3.64	0.123	0.726
No of comorbidity	No	4	11.76	2	9.52	6	10.91	3.676	0.597
	One	3	8.82	2	9.52	5	9.09		
	Two	10	29.41	8	38.10	18	32.73		
	Three	7	20.59	7	33.33	14	25.45		
	Four	9	26.47	2	9.52	11	20.00		
	Five	1	2.94	0	0.00	1	1.82		

Table 5. Distribution of co-morbidities according to gender

		Gender						Chi-Square Or Fisher's Exact	
		Male		Female		Total			
		N	%	N	%	N	%	X^2	P-value
KSADS	Anxiety disorders	18	37.50	5	71.43	23	41.82	2.890	0.089
	ADHD	20	41.67	0	0.00	20	36.36	FE	<0.001*
	Tic disorder	18	37.50	1	14.29	19	34.55	FE	0.228
	OCD	15	31.25	3	42.86	18	32.73	FE	0.541
	Specific phobias	10	20.83	3	42.86	13	23.64	FE	0.200
	Oppositional defiant disorders	10	20.83	0	0.00	10	18.18	FE	0.182
	Depression	1	2.08	5	71.43	6	10.91	FE	<0.001*
	Elimination disorder	5	10.42	0	0.00	5	9.09	FE	0.370
	Social anxiety/phobia	4	8.33	1	14.29	5	9.09	FE	0.609
	Somatization/ psychosomatic	0	0.00	3	42.86	3	5.45	FE	<0.001*
	Conduct disorders	2	4.17	0	0.00	2	3.64	FE	0.582
	Psychotic disorders	2	4.17	0	0.00	2	3.64	FE	0.582
	GAD	0	0.00	2	28.57	2	3.64	FE	<0.001*
No of comorbidity	No	4	8.33	2	28.57	6	10.91	3.673	0.597
	One	4	8.33	1	14.29	5	9.09		
	Two	17	35.42	1	14.29	18	32.73		
	Three	12	25.00	2	28.57	14	25.45		
	Four	10	20.83	1	14.29	11	20.00		
	Five	1	2.08	0	0.00	1	1.82		

FE: Fisher's Exact

4. DISCUSSION

In the current study, about two third of the studied sample were younger than 13 years old, which can be explained that ASD is neurodevelopmental disorder occurring in very early ages.

Regarding the residence, there was no significant difference in prevalence between rural and urban areas, with more slight increase in rural area more than urban, that goes with Amr et al. [5] whose study in Saudi Arabia revealed increased prevalence of ASD among rural areas owing to low socioeconomic state but does not go with his study in Egypt and Jordan where prevalence was higher in urban areas owing to increased awareness and health care facilitates more in urban. Our study results can also be explained as the majority of attendants to Tanta university hospitals are from surrounding rural area, also reflects increased awareness about ASD among rural areas, so that there was no significant difference in prevalence between rural and urban.

According to gender of our sample, the majority of them were males, with male to female ratio about 7:1. That goes with Icasiano et al. [6] who documented male to female ratio 8:1. But differ from Fombonne, et al. [7] who documented a much lower ratio 2:1. It is confirmed in all studies that males are more vulnerable to ASD than females, but the heterogenicity in the studies' results can be explained that large proportion of female patients go under-diagnosed as they have milder form, and greater capacity to camouflage their difficulties.

In the current study, CARS was used to determine the severity of ASD in children presented, it revealed that most of them had severe ASD. That goes with the previous studies of Elbahaaey et al. [8] and Khaled et al. [9].

The possible explanation behind the predominance of high level of severity of autistic symptoms may be attributed to only severe symptoms of ASD attract attention of parents and surrounding due to lack of awareness about mild symptoms of ASD and the normal development of children. Children with more severe presentation tend to be more frequently diagnosed whereas milder cases may escape diagnosis.

In the current study, about ninety percent of ASD children had at least one psychiatric co-morbidity, that goes with Elbahaaey et al. [8] whose study revealed (90%) co-morbidity, but on contradict, Van Steensel et al. [10] who reported a lower percentage of cooccurring co-morbidities (57.5%), which can be explained by variations in the studied sample regarding ASD severity, demographic data and screening tools. Almost one third of our studied children had 2 psychiatric co-morbidities, less children with 4 or 5 co-morbidities.

The severity of ASD was positively and significantly correlated with the number of commodities: severe cases presented with more comorbidities as compared with the milder ones. These findings also go with Elbahaaey et al. [8].

Collectively, males with ASD are more likely to experience externalizing disorders, while females with ASD are more prone to internalizing psychopathology, that goes well with Solomon et al. [11]. The low prevalence percentages of psychosomatic symptoms among male sample can be explained that they suffer difficulties in communicating their feelings, in contrast to females, as they have milder degree of ASD, thus better at expressing their feelings.

In our study, few children had average IQ, while most of them suffered variable degrees of intellectual disability, the most common was Mild and Moderate ID followed by borderline ID. That goes with the results of Meguid et al. [12], whose study results in Egypt also revealed that ID was comorbid with ASD in most of cases, while our results exceeded those of Rao and Landa [13], whose studies in their country revealed less co-morbidity. This can be explained by cultural/genetic variations, presence or lack of facilities. More severe cases are more frequently diagnosed early intervention and better management. Better case management does not account for high percentage of ID. Also, it can be explained that most of the children in our study suffered severe degree of ASD.

In this study, nearly half of ASD children suffered at least one comorbid anxiety disorder, that goes well with the results of studies by Simonoff et al. [2] and Leyfer et al. [14]. Between the studied children with comorbid anxiety disorders, Specific phobia was the most common anxiety disorder. Similar results were reported by de Bruin et al. [15], Leyfer et al. [14]. While lower percentage was reported by Simonoff et al. [2]. Differences in results between studies can be explained by variations in study sample, differences in history taking, evaluation tools and study settings.

Social phobia and GAD were diagnosed in little portion of our sample. That goes well with the results of the study by Leyfer et al. [14]. While some other studies reported higher percentage as Simonoff et al. [2] and Muris et al. [16]. Proportions differences could be explained by sample dissimilarities as well as different ways of interpreting and defining symptoms of anxiety.

While Panic disorder was reported in about 6% of our studied children, which goes with Simonoff et al. [2], while differ from other studies as Leyfer et al. [14], Where no cases were reported. That can be easily explained by sample variations, different tools of screening and diagnosis.

In the current study, a considerable portion of ASD children were diagnosed with OCD, Severe autism was the most type associated with OCD in the current study. The results go well with that of Leyfer et al. [14] and Elbahaaey et al. [8]. While other studies reported less percentage of co-morbidity as van Steensel et al. [10] and Lugnegård et al. [17], The rate of OCD in individuals with autism reported by other investigators has varied greatly from 1.5 to 81% [17-20].

OCD was reported to co-occur with anxiety disorders in about thirty percent of our sample. This can be explained that some brain regions such as the amygdala play a crucial role in ASDs, in relation to abnormal fears, compulsive behaviors, and increased anxiety [21].

In our study, about third of ASD cases suffered comorbid ADHD. This goes with results of the studies by Leyfer et al. [14], Simonoff et al. [2], making it the 2nd most common psychiatric disorder, which is congruent with the findings of Amr et al, [5]. On the other hand, a higher propotion has been reported in clinically referred samples Sinzig et al. [22]; Lee and Ousley [23], and it was the most common psychiatric co-morbidity with ASD in some studies as Joshi et al. [24] and El-abdeen et al. [25].

The predominance of co-occurrence of ASD and ADHD can be explained by many theories, due to the possible overlap between symptoms of ASD and ADHD, other theories may be that the two are independent disorders occurring together by association with a third independent factor, or alternatively they share a common underlying etiology. Leiter and his colleagues believe that both disorders share a common genetic basis.

In our study, ADHD was more common among males and severe degree of ASD. These results go with those by Elbahaaey et al. [8]. Prevalence of ADHD among males is also supported by Whiteley et al. [26]. In the present study, no predominant subtype of ADHD was reported, that doesn't go with Leyfer et al. [14] who reported that the inattentive type was the predominant type and that can be explained by difference in study sample.

About one third of ASD children in this study suffered comorbid tic disorder. that goes with the results of the study by Mattila et al. [27]. While a much larger percentage was reported by Elbahaaey et al. [8]. That can be easily explained by sample variations and the presence of mild cases in our study, difficulties in distinguishing tic disorder from other movement abnormalities could underlie inconsistency in reported rates.

We found that ODD were reported in males in younger age groups. These findings go consistent with that reported by Elbahaaey et al. [8], Van Steensel et al. [10], Gadow et al. [28] and Leyfer et al. [14]. The relatively low percentage of ODD can be explained by the fact that children with autism frequently have difficulty with following directions and being cooperative.

In the current study, only six ASD children (10.9%) were diagnosed with comorbid depression. It occurred more in females and older age groups. While higher percentage were reported by other studies as Wigham et al. [29], van Steensel et al. [10]. This can be owed to variations in sample and methodology, it also reflects that assessment was based on parent information as well as the fact that children with ASD often have difficulties expressing their thoughts and feelings.

Only five (9.09%) ASD children of our study suffered nocturnal enuresis, the condition is more common in male and younger age groups < 13 years. It was also noticed that it occurred with more severe degree of ASD, lower IQ and with anxiety disorder. the results are consistent with El-Baz et al. [30] and Fortuna et al. [31].

We must keep in our mind that there is more work to do to be able to understand and address how co-occurring mental health symptoms impact the diverse population of those diagnosed with ASD. Research must continue to meet the unique needs of those affected children, to reach the best outcome.

Limitations were small sample size, and not evaluating other variables including socioeconomic status and parental care, Number of females was limited in the present study, leading to limitation in exploring certain co-morbidities that occur commonly in females. Also The study did not have a measure to address language and learning disorders although these conditions are common co-morbidities and may play a role in school performance.

Identifying and managing the psychiatric comorbidities should be considered in the overall management of ASD cases.

5. CONCLUSION

ASD was frequently comorbid with a variety of psychiatric disorders. Presence of comorbid disorders among children with ASD is the rule rather than exception. Male children had more combined subtype and more severe form of the disorder. The most common comorbid psychiatric disorders with ASD are anxiety disorders, ADHD and OCD. The early identification and treatment of ASD and comorbid conditions may reduce the likelihood of impairment and persistence into adulthood.

CONSENT

A written consent was obtained from the care giver of the children who attempted the study after explanation of the study and its aim.

ETHICAL APPROVAL

This cross-sectional, descriptive study was carried out at Tanta University Hospitals, Neuropsychiatry Department starting from March 2019 to March 2020 after approval from the Ethical Committee of Faculty of Medicine, Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Faras H, Al Ateeqi N, Tidmarsh L. Autism spectrum disorders. Ann Saudi Med. 2010;30:295-300. DOI:https://doi.org/10.4103/0256-4947.65261
2. Simonoff E, Pickles A, Charman T, et al. 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;47:921-9. DOI:https://doi.org/10.1097/CHI.0b013e318179964f
3. Guerrera S, Menghini D, Napoli E, et al. Assessment of psychopathological comorbidities in children and adolescents with autism spectrum disorder using the child behavior checklist. Front Psychiatry. 2019;10:535-53. DOI:https://doi.org/10.3389/fpsyt.2019.00535
4. Muratori F, Apicella F, Muratori P, et al. Intersubjective disruptions and caregiver–infant interaction in early autistic disorder. Res Autism Spectr Disord. 2011;5:408-17.
5. Amr M, Bu Ali W, Hablas H, et al. Sociodemographic factors in Arab children with autism spectrum disorders. Pan Afr Med J. 2012;13:65.
6. Icasiano F, Hewson P, Machet P, et al. Childhood autism spectrum disorder in the Barwon region: A community based study. J Paediatr Child Health. 2004;40:696-701. DOI:https://doi.org/10.1111/j.1440-1754.2004.00513.x
7. Fombonne E. Epidemiology of pervasive developmental disorders. Pediatr Res. 2009;65:591-8. DOI:https://doi.org/10.1203/PDR.0b013e31819e7203
8. Elbahaaey WA, Elkholy MH, Tobar SS, et al. Egyptian children with autism spectrum disorders: Risk factors and comorbidity in relation to disease severity. Egypt J Psychiatr. 2016;37:59.
9. Khaled EM, Meguid NA, Bjørklund G, et al. Altered urinary porphyrins and mercury exposure as biomarkers for autism severity in Egyptian children with autism spectrum disorder. Metab Brain Dis. 2016;31:1419-26. DOI:https://doi.org/10.1007/s11011-016-9870-6
10. van Steensel FJ, Bögels SM, de Bruin EI. Psychiatric comorbidity in children with autism spectrum disorders: A comparison with children with ADHD. J Child Fam Stud. 2013;22:368-76. DOI:https://doi.org/10.1007/s10826-012-9587-z
11. Solomon M, Miller M, Taylor SL, et al. Autism symptoms and internalizing

psychopathology in girls and boys with autism spectrum disorders. J Autism Dev Disord. 2012;42:48-59.
DOI:https://doi.org/10.1007/s10803-011-1215-z

12. Meguid NA, Nashaat NH, Hashem HS, et al. Frequency of risk factors and coexisting abnormalities in a population of Egyptian children with autism spectrum disorder. Asian J Psychiatr. 2018;32:54-8.
DOI:https://doi.org/10.1016/j.ajp.2017.11.037
13. 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;18:272-80.
DOI:https://doi.org/10.1177/1362361312470494
14. 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;36:849-61.
15. de Bruin EI, Ferdinand RF, Meester S, et al. High rates of psychiatric co-morbidity in PDD-NOS. J Autism Dev Disord. 2007;37:877-86.
DOI:https://doi.org/10.1007/s10803-006-0215-x
16. Muris P, Steerneman P, Merckelbach H, et al. Comorbid anxiety symptoms in children with pervasive developmental disorders. J Anxiety Disord. 1998;12:387-93.
DOI:https://doi.org/10.1016/s0887-6185(98)00022-x
17. Lugnegård T, Hallerbäck MU, Gillberg C. Psychiatric comorbidity in young adults with a clinical diagnosis of Asperger syndrome. Res Dev Disabil. 2011;32:1910-7.
DOI:https://doi.org/10.1016/j.ridd.2011.03.025
18. Ghaziuddin M, Greden J. Depression in children with autism/pervasive developmental disorders: A case-control family history study. Journal of Autism and Developmental Disorders. 1998;28:111-5.
19. Lord C, Rutter M, Le Couteur A. Autism diagnostic interview-revised: A revised version of a diagnostic interview for caregivers of individuals with possible pervasive developmental disorders. J Autism Dev Disord. 1994;24:659-85.
DOI:https://doi.org/10.1007/bf02172145
20. Rumsey JM, Rapoport JL, Sceery WR. Autistic children as adults: psychiatric, social and behavioral outcomes. J Am Acad Child Psychiatry. 1985;24:465-73.
DOI:https://doi.org/10.1016/s0002-7138(09)60566-5
21. Mazzone L, Ruta L, Reale L. Psychiatric comorbidities in asperger syndrome and high functioning autism: Diagnostic challenges. Ann Gen Psychiatry. 2012;11:16.
DOI:https://doi.org/10.1186/1744-859x-11-16
22. Sinzig J, Walter D, Doepfner M. Attention deficit/hyperactivity disorder in children and adolescents with autism spectrum disorder: Symptom or syndrome? J Atten Disord. 2009;13:117-26.
DOI:https://doi.org/10.1177/1087054708326261
23. Lee DO, Ousley OY. Attention-deficit hyperactivity disorder symptoms in a clinic sample of children and adolescents with pervasive developmental disorders. J Child Adolesc Psychopharmacol. 2006;16:737-46.
DOI:https://doi.org/10.1089/cap.2006.16.737
24. Joshi G, Faraone SV, Wozniak J, et al. Symptom profile of ADHD in youth with high-functioning autism spectrum disorder: A comparative study in psychiatrically referred populations. J Atten Disord. 2017;21:846-55.
DOI:https://doi.org/10.1177/1087054714543368
25. El-abdeen AMZ, Haikel AY, Ibrahim N. Comorbid psychiatric problems among children with autism spectrum disorder in an Egyptian Sample; 2018.
26. Whiteley P, Todd L, Carr K, et al. Gender ratios in autism, Asperger syndrome and autism spectrum disorder. Autism Insights; 2010.
27. Mattila ML, Kielinen M, Linna SL, et al. Autism spectrum disorders according to DSM-IV-TR and comparison with DSM-5 draft criteria: An epidemiological study. J Am Acad Child Adolesc Psychiatry. 2011;50:583-92.e11.
DOI:https://doi.org/10.1016/j.jaac.2011.04.001
28. Gadow KD, DeVincent CJ. Comparison of children with autism spectrum disorder with and without schizophrenia spectrum traits: Gender, season of birth and mental health

risk factors. J Autism Dev Disord. 2012;42:2285-96. DOI:https://doi.org/10.1007/s10803-012-1473-4

29. Wigham S, Barton S, Parr JR, et al. A systematic review of the rates of depression in children and adults with high-functioning autism spectrum disorder. J Ment Health Res Intellect Disabil. 2017;10:267-87.

30. El-Baz F, Ismael NA, El-Din SMN. Risk factors for autism: An Egyptian study. Egypt J Med Hum Genet. 2011;12.

31. Fortuna RJ, Robinson L, Smith TH, et al. Health conditions and functional status in adults with autism: A cross-sectional evaluation. J Gen Intern Med. 2016;31:77-84. DOI:https://doi.org/10.1007/s11606-015-3509-x

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/67319